

## **REVIVE THERAPEUTICS LTD. ANNOUNCES ENCOURAGING INTERIM RESULTS FROM ONGOING PHASE 2A PROOF-OF-CONCEPT STUDY OF REV-001 FOR THE PREVENTION OF OPIOID-INDUCED RESPIRATORY DEPRESSION**

**Toronto, Ontario** (February 12, 2014) Revive Therapeutics Ltd. (TSXV:RVV) (“**Revive**”) announced today encouraging interim results of the first eight patients from its ongoing Phase 2a proof-of-concept study (the “**Study**”) of REV-001 for the prevention of opioid-induced respiratory depression.

The preliminary data from the Study yielded the following key findings:

- Treatments with REV-001 was safe and well tolerated at the 37.5 mg dose, was not associated with serious adverse events, and there was no treatment-related discontinuations
- Encouraging clinical activity in resting ventilation, breathing frequency and tidal volume following administration of REV-001 and exposure to alfentanil (a potent opioid analgesic)
- Treatments with REV-001 did not affect analgesia

Based on the interim results of the Study, Revive is continuing with the Study protocol on a blinded basis and investigating the dose response at 50 mg per dose in the remaining eight healthy subjects. Upon completion of the Study, including the analysis of, but not limited to, resting ventilation, resting breathing frequency, tidal volume, end-tidal Partial Pressure of Carbon Dioxide (PCO<sub>2</sub>) and blood oxygen saturation (SpO<sub>2</sub>), carbon-dioxide responses, and antinociception, Revive will determine the appropriate next phase of clinical development. Revive plans to present the comprehensive data from the Study, once it has been completed, at a future scientific meeting.

“I am pleased to see that REV-001 has shown initial clinical response signals as we continue to advance the clinical development of this compound for the prevention of opioid-induced respiratory depression in an acute setting,” said Fabio Chianelli, Revive’s Chief Executive Officer. “I look forward to sharing additional information from the next cohort of the Study and outlining future clinical and business development plans.”

“To my knowledge, this is the only drug being repurposed for opioid-induced respiratory depression and the compelling proof-of-concept data will provide critical information on the potential therapy for this unmet medical need,” said Prof. Dr. Albert Dahan M.D., Ph.D., Principal Study Investigator and Professor of Anesthesiology at the Leiden University Medical Center, The Netherlands.

The goal of the Study, which is being conducted at the Leiden University Medical Center in The Netherlands under the supervision of Prof. Dr. Albert Dahan, M.D., Ph.D., is to determine the effect of an oral dose of tianeptine on alfentanil-induced respiratory depression and antinociception. Revive is developing REV-001 for the prevention of opioid-induced respiratory depression aimed for patients with sleep apnea.

### **About REV-001 (Tianeptine)**

REV-001 is the repurposing of the drug tianeptine, an old but unique anti-depressant drug, which is marketed in Asia, parts of Europe (e.g. France) and South America. Despite its narrow geographic scope, the decades-long clinical experience of tianeptine suggests much about its safety. In fact, tianeptine has been shown to have substantial cardiovascular and other safety at both normal doses and in overdose. (Source: Wilde, M. I. & Benfield, P. *Drugs* 49, 411–439 (1995)). More recently, in animal studies conducted by Revive, tianeptine was shown for the first time to prevent opioid(morphine)-induced respiratory depression in an animal model. The novel findings in Revive’s animal studies enabled Revive to apply for intellectual property protection covering the use of tianeptine to treat respiratory depression.

### **About Sleep Apnea and Opioid-induced respiratory depression**

According to the Centers for Disease Control and Prevention, approximately 70 million people in the United States are affected by sleep disorders, such as obstructive sleep apnea (“**OSA**”). According to an article titled “A Rude Awakening - The Perioperative Sleep Apnea Epidemic” published in the *New England Journal of Medicine* in June 2013, the risk of perioperative complications increase substantially with those who have OSA. With 51.4 million inpatient surgical procedures performed annually (2010) in the United States (Source:

<http://www.cdc.gov/nchs/fastats/insurg.htm>), hospitals must take into consideration the financial implications that may become prevalent for patients who have OSA in order to reduce the risk of adverse events, such as opioid-induced respiratory depression. It has been estimated that between 29% and 41% are at high risk of opioid-induced respiratory depression. (Source: Hanna MH et al. *Anesthesiology*. 2005;102(4): 815-821 and Overdyk FK et al. *Anesth Analg*. 2007;105(2): 412-418). Currently, there are no approved drugs for OSA and the only drug treatments to counter opioid-induced respiratory depression is to administer opiate receptor antagonists such as naloxone (Narcan®). However, those antagonists eliminate the analgesic activity of the opioid drug and thus are rarely used by hospitals and healthcare facilities to prevent or treat opioid-induced respiratory depression. According to the article “A Rude Awakening - The Perioperative Sleep Apnea Epidemic”, perioperative sleep apnea in the United States has been considered as an ‘Epidemic’.

### **About Revive Therapeutics Ltd.**

Revive Therapeutics Ltd. is a Canadian public company (TSXV:RVV) focused on acquiring, developing and commercializing treatments for major market opportunities such as sleep apnea, gout and rare diseases. Revive aims to bring drugs to market by finding new uses for old drugs, also known as drug repurposing, and improving the therapeutic performance of existing drugs for underserved medical needs. Additional information on Revive is available at [www.revivetherapeutics.com](http://www.revivetherapeutics.com).

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