



## Neuropathic pain, severe pain

# Pharmaleads announces the opening of French sites in its international Phase IIa clinical study of PL37

*ANSM (French National Agency for Medicines and Health Products Safety) authorizes the extension of the clinical trial for pain in diabetic neuropathy*

Paris, September 28, 2015 - Pharmaleads, the biotech company developing its proprietary Dual Enkephalinase Inhibitors (DENKIs) for the treatment of severe pain, announces today the opening of the first French investigative sites in the Phase IIa clinical study of oral PL37 for pain in diabetic neuropathy.

### Review of the study:

- **Great Britain:** 11 active sites
- **France:** 6 diabetology sites: Centre Hospitalier Universitaire (CHU) **Lyon-Sud**, coordinating centre, Centre Hospitalier Universitaire (CHU) de **Nantes**, Centre Hospitalier Sud Francilien in **Corbeil Essonnes**, Centre Hospitalier Régional Universitaire de **Nancy**, Centre Hospitalier Universitaire de **Caen** and Centre Hospitalier de **Valenciennes**.
- **Bulgaria:** pending regulatory approvals

According to Michel Wurm, MD, Corporate Development Director at Pharmaleads: *"This clinical study for the PL37 proof of concept is evolving according to the provisional schedule. The enthusiasm and commitment among the investigators confirm their interest in DENKIs, a new class of analgesics for which PL37 is paving the way. In a field where no first-line treatment has obtained*

*marketing authorization since Lyrica® in 2004, this drug candidate offers real prospects for the treatment of neuropathic pain."*

Dr Julien Vouillarmet, diabetologist at the Centre Hospitalier-Universitaire Lyon-Sud, Coordinator of the clinical study in France, says: *"Today, the standard treatments do not provide sufficient relief of neuropathic pain in diabetic patients. This is why I am very proud to be coordinating this clinical study on DENKIs which represent a new path for the treatment of neuropathic pain that will bring, I hope, a real benefit for patients."*

### **European development**

**This Phase IIa study of PL37 follows a major Phase I program which demonstrated the tolerance and safety of PL37 in 136 healthy volunteers. This proof of concept trial started in April 2015 in eleven British hospitals.**

After France, four sites will be opened for recruitment in Bulgaria, for a total of 21 investigative sites in the three countries.

### **The clinical study**

This on-going clinical study recruits patients with diabetic neuropathy and incomplete pain relief provided by Lyrica® or gabapentin, the most commonly prescribed treatments for neuropathic pain and for which considerable synergy with DENKIs has been demonstrated in pharmacology studies.

### **DENKIs**

DENKIs act specifically on nociceptors (sensory neurons that react to painful stimuli) located on peripheral nerve endings. They increase the levels of enkephalins (our internal morphine) specifically in sensory areas where the painful stimulus produces an abundance of them. In the absence of PL37, the enkephalins are very quickly inactivated by two enzymes, the enkephalinases. By inhibiting these enkephalinases, DENKIs induce a lasting analgesic effect without major side effects.

### **Neuropathic pain**

Neuropathic pain (NP) is the consequence of nerve damage or dysfunction. These lesions can be caused by numerous conditions affecting the peripheral nervous system, e.g. diabetes, postherpetic neuralgia, postsurgical neuropathy, or neuropathy induced by certain drugs such as those used for cancer or HIV infections. Neuropathy is associated with pain triggered by a stimulus that normally would not elicit pain (allodynia) or would elicit only low-level pain (hyperalgesia), local numbness, burning sensations, or constant or intermittent spontaneous or provoked pain. NP can have a very significant impact of the patients' quality of life.

NP remains difficult to treat irrespective of its origin. It is refractory to standard analgesics, and recommended drugs, of middling efficacy, were not initially developed for this indication. A recent study (Lancet Neurology 2015) demonstrated that 6 out of 7 patients are not adequately relieved by Lyrica® or gabapentin, whose side effects are dose-limiting.

### **The market for Pharmaleads DENKIs**

The worldwide market for neuropathic pain management is estimated at €6 billion in 2015. This type of pain, mainly associated with diabetes, shingles, antitumor and antiviral drugs, and surgery, affect 6 to 8% of the population in developed countries. This market is growing at a constant rate of 8 to 10% per annum.

Pharmaleads' DENKIs, such as PL37, will constitute a true therapeutic progress in severe pain relief without the side effects of opiates or of current treatments.

### **About Pharmaleads: [www.pharmaleads.com](http://www.pharmaleads.com)**

Founded in 2000 and based, in Paris, France, Pharmaleads has developed a coherent set of first-in-class molecules, thanks to its world-class medicinal chemistry expertise, providing ground-breaking solutions in pain treatment. Pharmaleads designs and manages the early-stage development of small protease inhibiting molecules for diagnostic and therapeutic use.

### **Articles on DENKIs recently published by Pharmaleads in major international journals:**

Roques B.P., Fournié-Zaluski M.C., Wurm M. Inhibiting the breakdown of endogenous opioids and cannabinoids to alleviate pain. *Nature Rev. Drug Discov.*, 2012, 11, 292-310.

Poras H., Bonnard E., Dangé E., Fournie-Zaluski M-C., Roques B.P. New orally active dual enkephalinase inhibitors (DENKIs) for central and peripheral pain treatment. *J. Med. Chem.*, 2014, 57, 5748-5763.

Bonnard E., Poras H., Nadal X., Maldonado R., Fournie-Zaluski M-C., Roques B.P. Long lasting oral analgesic effects of N-Protected aminophosphinic dual enkephalinase inhibitors (DENKIs) in peripherally-controlled pain. *Pharma. Res. Per.*, 2015, 3(2), e00116, doi: 10.1002/prp2.116

### **Pharmaleads Contacts**

Thierry Bourbié

CEO

[thierry.bourbie@pharmaleads.com](mailto:thierry.bourbie@pharmaleads.com)

Michel Wurm, MD

Development Director

[Michel.wurm@pharmaleads.com](mailto:Michel.wurm@pharmaleads.com) +33 (0) 1 44 06 70 00

### **Press Contact: NewCapMedia**

Annie-Florence Loyer

[afloyer@newcap.fr](mailto:afloyer@newcap.fr) / +33 (0) 1 44 72 00 12/ + 33 (0)6 88 20 35 59

Nadège Le Lezec : [nlelezec@newcapfr](mailto:nlelezec@newcapfr) / +33 (1) 44 71

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