

## Pharmaleads Reports Positive Phase I SAD data with its Dual ENKephalinase Inhibitor (DENKI) PL265 for the Treatment of Neuropathic Pain

**Paris, France, 29 June 2017** – Pharmaleads, an emerging pharmaceutical company developing innovative products for the management of acute and chronic severe pain, today announced it has successfully completed a Phase I single ascending dose (SAD) trial in France with its oral DENKI candidate PL265 that is being developed for the treatment of neuropathic pain. The Company is now preparing to start a Phase I multiple ascending dose (MAD) study with oral PL265 in the UK. Data from the MAD study is expected in 2018.

The Phase I SAD results have shown that single doses of PL265, administered orally were safe and well-tolerated. Pharmacokinetic and pharmacodynamic studies showed that PL265, which is a pro-drug, was slowly transformed in plasma into its active metabolite (PL254). PL254 inhibited both of its target enzymes, aminopeptidase N (APN) and neprilysin (NEP), which are responsible for the physiological degradation of enkephalins. This inhibition was effective for more than 24 hours after single doses of 400 and 800mg of PL265, making it an ideal oral candidate for the treatment of neuropathic chronic pain.

Pharmaleads' DENKIs, are the only drugs in clinical development that can inhibit both enkephalin-degrading enzymes APN and NEP, thereby increasing the local concentration of enkephalins resulting in local and sustained pain relief without the side-effects observed with opioids. PL265 is the second DENKI to start human clinical development at Pharmaleads.

**Michel Wurm, MD, Director of Corporate Development**, said: *“We are pleased with the encouraging data from this first-in-human study with PL265, a DENKI which we believe is an ideal oral candidate for the treatment of neuropathic pain. Results from this study show that PL265, via its active metabolite PL254, is able to inhibit its two key targets and provide strong evidence supporting our hypothesis that DENKIs are the only drug candidates in development that harbor the analgesic properties of opiates without their side-effects.”*

The Phase I study was a randomised, double-blind, placebo-controlled single oral dose escalation study aimed to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of PL265. The study was conducted at Eurofins-Optimed Phase 1 unit in France in 32 healthy male volunteers. Four cohorts of eight subjects each were randomised 6:2 (active:placebo) to receive single doses of PL265 ranging from 100 to 800mg or matching placebo. The maximum tolerated dose was not reached, but as optimal target engagement was achieved, higher doses were not tested.

PL265 is also a promising candidate for local administration such as eye-drops for ophthalmic pain for which Pharmaleads is currently completing its evaluation for the treatment of ocular pain and dry eye syndrome in animal models.

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**About Pharmaleads**

Pharmaleads is an emerging pharmaceutical company developing innovative products for the management of acute and chronic severe pain, a growing market with significant unmet medical need. Pharmaleads' drugs are based on its deep knowledge and understanding of enkephalins, a key element of the body's natural pain management system.

Pharmaleads' compounds, (Dual ENKephalinase inhibitors) DENKIs, aim to protect enkephalins, hence increasing their local concentrations and thereby inducing a physiological analgesia which improves pain management.

Pharmaleads has two compounds in clinical development which are targeting four multi-billion markets:

PL265 is being developed for the treatment of neuropathic pain (oral) and ocular pain/dry eye syndrome (eye drops). PL37 is being developed for the treatment of post-surgical / traumatic / breakthrough cancer pain as a substitute for injectable opiates (IV) and acute migraine pain (oral route)

Pharmaleads was founded in 2000. It is headquartered in Paris, France, and is funded by private investors.

For more information about Pharmaleads please visit [www.pharmaleads.com](http://www.pharmaleads.com)