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MEDIA RELEASE

Spinifex Pharmaceuticals' Phase 2 Results Published in *The Lancet* Show EMA401 to be Effective in Reducing Pain in Postherpetic Neuralgia

- Phase 2 trial met its primary endpoint, reduced pain in postherpetic neuralgia (PHN) versus placebo
- Significant patient response to EMA401 treatment and drop in pain intensity compared with placebo, meeting a key secondary endpoint
- First published demonstration of the therapeutic potential of angiotensin II type 2 (AT_2) receptor antagonists
- EMA401 identified as a possible new treatment for neuropathic pain with a novel mechanism of action

Spinifex Pharmaceuticals, an Australian pain drug development company, today announces that *The Lancet* has published the results of its Phase 2 clinical trial of its lead candidate, EMA401, in postherpetic neuralgia (PHN)[1]. EMA401 is a novel angiotensin II type 2 (AT_2) receptor antagonist under development as a potential first-in-class oral treatment for chronic pain without CNS side effects. PHN is a painful condition that develops in some patients following herpes zoster (shingles) and where existing therapy does not relieve pain in all individuals.

The Phase 2 trial met its primary endpoint by showing that patients randomised to EMA401 achieved a greater reduction in pain from baseline to the last week of 28 days of treatment than patients randomised to placebo. Analysing all patients randomised (intent to treat population), the mean pain intensity reduction from baseline after 4 weeks treatment was as follows: EMA401: -2.29; Placebo: -1.60; $p = 0.007$.

A significantly greater proportion of patients on active treatment reported a more than 30% reduction in mean pain intensity score compared to baseline (i.e. responder rate) (EMA401: 57.6%; Placebo: 35.2%; $p = 0.0023$), meeting a key secondary endpoint.

A subgroup of patients who had moderate or severe pain at study entry continued to take a single existing medicine for their PHN during the study (45% of patients in the EMA401 group and 40% of patients in the placebo group). In this subgroup, patients randomised to EMA401 achieved significantly greater pain reduction when compared to patients randomised to placebo. In addition, pain relief was also observed in those patients that were not taking a single existing medicine for their PHN. These results indicate that EMA401 may have the potential to provide relief for patients with PHN who don't achieve optimal pain relief with current treatments or who don't wish to continue with these medicines due to their side effects.

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[1] EMA401, an orally administered highly selective angiotensin II type 2 receptor antagonist, as a novel treatment for postherpetic neuralgia: a randomised, double-blind, placebo-controlled phase 2 clinical trial, Rice, A.S.C. *et al*., *The Lancet*, Published Online, February 5, 2014; http://dx.doi.org/10.1016/S0140-6736(13)62337

EMA401 was generally safe and well tolerated with no serious treatment related adverse events reported.

In a commentary also published in the Lancet[2], Dr Nanna Finnerup, of the Danish Pain Research Center, Aarhus University, described this first clinical study to evaluate the efficacy of an AT_2 receptor antagonist in neuropathic pain as encouraging adding: "Most importantly, their work identifies a possible new drug for the treatment of neuropathic pain with a novel mechanism of action, and thus offers hope for patients who have insufficient pain relief with presently available drugs."

Andrew Rice, a Professor of Pain Research at Imperial College, Hon. Consultant in Pain Medicine at Chelsea and Westminster Hospital, and lead author of *The Lancet* paper said: "These results demonstrated EMA401 was able to significantly reduce pain in patients with postherpetic neuralgia and was well tolerated. This paper is the first publication of the clinical effects of any AT_2 receptor antagonist and contributes to our understanding of the potentially important role of this new drug class in relieving chronic pain. These results are an exciting step in the development of a novel approach to the treatment of neuropathic pain and chronic pain more generally."

Spinifex Pharmaceuticals' CEO Tom McCarthy said: "There is a clear need for new treatments that bring patients pain relief with fewer CNS side effects. The publication of the Phase 2 data with EMA401 in such a prestigious publication is an endorsement of the quality of our scientific development capabilities. We are pleased *The Lancet*, in the associated commentary, recognises the significant milestone we have achieved in translating basic science on a new pain pathway into clinical efficacy in patients. As stated in the commentary, in addition to PHN, we see broad potential for EMA401 to treat a range of chronic painful conditions such as pain due to osteoarthritis and diabetes. We look forward to delivering on the further development of EMA401."

The paper is available via the following link:
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)62337/abstract.

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EMA401
EMA401 is an angiotensin II type 2 (AT_2) receptor antagonist. The discovery that AT_2 receptor antagonists offer an innovative approach to the treatment of neuropathic and inflammatory pain was originally made by Professor Maree Smith at The University of Queensland. Having acquired the technology, Spinifex has conducted a comprehensive pre-clinical and early clinical development program on

[2] Angiotensin II: from blood pressure to pain control, Finnerup, N. B. *et al.*, *The Lancet*, Published Online, February 5, 2014; http://dx.doi.org/10.1016/S0140-6736(13)62638-0

EMA401. In addition to positive Phase 2 results, EMA401 has shown efficacy in a number of relevant pre-clinical models and good human safety and pharmacokinetics in Phase 1 studies. Spinifex's clinical program for EMA401 includes an ongoing Phase 2 study in the treatment of pain in patients with cancer chemotherapy. Spinifex continues to conduct research into the role of the AT_2 receptor in nociceptive, inflammatory and neuropathic pain states and these fundamental studies support not only the EMA401 clinical program but also Spinifex's ongoing AT_2 receptor antagonist drug discovery program.

Spinifex Pharmaceuticals

Spinifex Pharmaceuticals is an Australian biotechnology company developing new drug candidates for the treatment and management of pain.

Established in 2005 and based in Melbourne, Spinifex has applied its world-class drug development capabilities to advance product candidates. Its lead product EMA401 is under development as a potential first-in-class oral treatment for chronic pain and related symptoms without CNS side effects. Spinifex's Phase 2 program for EMA401 includes clinical trials in a number of chronic pain conditions. Spinifex investors are GBS Venture Partners, Brandon Capital Partners, Uniseed and UniQuest.

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