ESTEVE announces the publication of comprehensive Phase I data for a novel oral, first-in-class new chemical entity (NCE), E-52862, a sigma-1 receptor antagonist (S1RA) being developed for pain

- **E-52862 is a potent, highly selective NCE with a novel mechanism of action (MOA; Sigma 1 Receptor (S1R) antagonism) currently being evaluated for the treatment of pain**
- **Key data are outlined from three Phase I studies involving 175 male and female human subjects**
- **These studies demonstrate a favourable safety, tolerability, pharmacokinetic and pharmacodynamic profile for E-52862**
- **Phase II clinical trials evaluating E-52862 are ongoing**

September 4th, 2012, Barcelona, Spain. ESTEVE announces the recent publication of data from the Phase I clinical trial programme of a novel, highly potent and selective, once-daily, S1RA E-52862, developed by the ESTEVE R&D team, in the British Journal of Clinical Pharmacology[1].

Mariano Sust, M.D., corresponding author, stated that "E-52862 represents a NCE with a novel, unprecedented mechanism of action for pain of different aetiologies. We are very encouraged by these results and look forward to future findings from the E-52862 clinical trial programme in due course."

To fully validate the safety and tolerability of E-52862, ESTEVE performed a rigorous phase I programme. This publication reports results from three, Phase I studies involving 175 human subjects. E-52862 demonstrated a favourable safety and tolerability profile across a robust panel of assessments including adverse event recording following questioning and spontaneous reporting; physical examinations; vital signs measurements; laboratory safety tests (haematology, blood coagulation, biochemistry, urinalysis); multiple psychometric tests; computerized cognitive evaluations (including assessment of executive function, working memory and learning, reaction time and psychomotor functions); and thorough cardiac monitoring (telemetry, triplicate 12-lead ECGs, 24-hour Holter ECGs). Pharmacokinetic assessments were performed in each study and results demonstrate a favourable pharmacokinetic and pharmacodynamic profile, supporting oral, once-daily administration of E-52862.

The E-52862 Phase I programme is now complete and included over 300 human subjects (more than 250 received E-52862). Results from the overall programme show favourable safety, tolerability, pharmacodynamic and pharmacokinetic profiles at all doses of E-52862 tested.

Today, the E-52862 clinical programme focuses on pain management – highlighting both neuropathic pain and the potentiation of opioid analgesia. The Phase II clinical trial programme for E-52862 began early in 2012. The clinical project leader for E-52862, Roser Vives, M.D. commented that "Because of the MOA and data available to date, we are evaluating E-52862 in four different types of neuropathic pain and for treatment of pain in patients receiving opioids (for the enhancement of the analgesic effect and better tolerability). E-52862 also has potential applications for other neurological and psychiatric indications".

E-52862, whose MOA is both novel and complementary to that of other analgesic compounds, could provide a much-needed addition to future pain management choices with, perhaps, the option to be used as monotherapy, as well as in combination with other pain relief compounds, depending on the type of patient and clinical indication.

All these projects have been supported by the Spanish Ministry of Economy and Competitiveness

About ESTEVE

ESTEVE is a leading pharmaceutical chemical group based on Barcelona (Spain) with significant international presence. Since it was founded in 1929, ESTEVE has been firmly committed to excellence in healthcare, dedicating efforts to innovative R&D of new medicines for unmet medical needs and focusing on high science and evidence-based research. ESTEVE has a strong partnership approach to drug discovery, development and commercialisation. The company works both independently and in collaboration to bring new, differentiated best-in-class treatments to patients who need them. The company currently has a team of about 2800 professionals, and has subsidiaries and production facilities in several European countries, USA, China and Mexico.

About E-52862 and Pain R&D at ESTEVE

ESTEVE's dedicated in-house R&D team is focused on the development of novel pain medications, an area of high unmet medical need. Considerable progress in the knowledge of the biology and pharmacology of the S1R (a unique protein) during recent years has re-energised research into the potential benefits of S1R ligands in a range of neurological and psychiatric conditions.

New data has addressed key questions on modulation, MOA and pathophysiology of the S1R. The proprietary knockout mouse demonstrated a direct role of the S1R in sensitisation phenomena associated with neuropathic pain mechanisms and behaviours. E-52862 exerts robust, dose-dependent analgesic activity in multiple preclinical neuropathic pain models and enhances opioid analgesia. E-52862 could have potential applications for other neurological and psychiatric indications. Besides information reported here, an extensive preclinical regulatory safety package is available for E-52862 (including 13-week repeat dose toxicity studies in various animal species). E-52862 also has robust intellectual property protection.

ESTEVE's portfolio in pain also includes a technology platform-derived new co-crystal entity (E-58425) developed by the in-house R&D team. E-58425 has completed Phase I, with Phase II currently ongoing. E-58425 is being developed for moderate to severe acute and chronic pain.

Reference

[1] Abadias, M. et al. Safety, Tolerability and Pharmacokinetics of Single and Multiple Doses of a Novel Sigma-1 Receptor Antagonist in Three Randomized Phase I Studies. Br J Clin Pharmacol 2012 [Epub ahead of print]. DOI: 10.1111/j.1365-2125.2012.04333.x

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