



Grünenthal's cebranopadol, a novel strong analgesic, meets primary efficacy endpoint in Phase 3 trial in cancer pain

Results to be presented at the 2016 IASP conference

- **Statistically significant data in cancer pain add to the large positive database also in chronic pain due to osteoarthritis, chronic low back pain and diabetic peripheral neuropathy**

Yokohama, Japan, September 30, 2016 - Grünenthal presents data for the first time of its compound cebranopadol in patients with cancer-related pain¹. The cebranopadol data is from a Phase 3 randomized, double-blind, double-dummy, active-controlled multiple dose study with patients randomized to either once-daily cebranopadol or twice-daily morphine sulfate PR (prolonged release). Results reached statistical significance for non-inferiority and even superiority for the primary endpoint (average amount of daily rescue medication intake over the last two weeks of the maintenance phase in the trial, $p < 0.05$). Cebranopadol was well tolerated, with side effects comparable to morphine sulfate PR. Enrollment in this trial, which is one of the largest trials conducted in cancer pain to date, was stopped for strategic reasons. Cebranopadol, a novel first-in-class analgesic, discovered and developed by Grünenthal, has previously demonstrated strong efficacy in moderate to severe, chronic neuropathic pain and musculoskeletal pain. Grünenthal is actively seeking for development and commercialization partners to make cebranopadol available for patients in Asia.

“We are very proud to have discovered and developed this effective, well tolerated drug. Moreover, cebranopadol is clearly differentiated from other strong analgesics by its unique mechanism of action, improved safety profile with potentially limited effects on respiration and low abuse potential. Cebranopadol addresses a high unmet medical need in several chronic pain types, and these new data show its potential in patients with cancer pain as well,” said Klaus-Dieter Langner, Chief Scientific Officer of Grünenthal. “Following the partnership with Depomed for the US territory, we are actively looking for a strong partner who is interested in developing and marketing cebranopadol in the Asian region including Japan to ensure that also in this part of the world, patients will be able to benefit from cebranopadol.”

Further, *in-vivo* data presented at IASP 2016 showed that the therapeutic window between antinociception and respiratory depression is larger for cebranopadol than for fentanyl, because the NOP receptor agonist action of cebranopadol appears to counteract the side effects that result from its MOP receptor agonist action²

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Press Release



Data on cebranopadol presented at recent PAINWeek (6-9 September 2016, Las Vegas, USA) confirm its efficacy and safety

Six abstracts reporting on efficacy and safety data from the cebranopadol clinical development program were presented at the PAINWeek conference which took place in Las Vegas, USA, in September 2016³⁻⁷.

Grünenthal has discovered and developed cebranopadol. While for the US market, development and commercialization is established together with Depomed, opportunities for partnering in Asia including Japan are still available.

About cebranopadol

Cebranopadol is a novel, first-in-class analgesic that acts as a nociceptin/orphanin FQ peptide (NOP) receptor and opioid receptor agonist. These mechanisms, which have been shown to synergize, result in both a comparable efficacy and broader analgesic spectrum versus standard mu-opioid receptor agonists as well as an improved safety profile, particularly as it pertains to respiratory depression. In total, cebranopadol has been studied in approximately 2,000 patients worldwide having completed several Phase II trials in diabetic peripheral neuropathy (DPN), osteoarthritis (OA) and chronic low back pain (cLBP) and is ready for further Phase III development.

About Grünenthal

The Grünenthal Group is an independent, family-owned, international research-based pharmaceutical company headquartered in Aachen, Germany. We are an entrepreneurial specialist delivering true benefits to patients. By sustainably investing in research and development above the industrial average, we are committing to innovation in order to treat unmet medical needs and bring value-adding products to markets. Grünenthal is a fully integrated research & development company with a long track record of bringing innovative pain treatments and state-of-the-art technologies to patients.

Altogether, the Grünenthal Group is present in 32 countries with affiliates in Europe, Latin America and the US. Grünenthal products are sold in more than 155 countries and approx. 5,400 employees are working for the Grünenthal Group worldwide. In 2015, Grünenthal achieved revenues of € 1.2 bn. More information: www.grunenthal.com.

Literature

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- 5 Cebranopadol, a Novel First-in-class Analgesic: Efficacy, Safety, Tolerability in Patients With Pain Due to Diabetic Peripheral Neuropathy. PAINWeek 2016, poster #N36. M Eerdeken, ED Koch, M Kok, M Sohns, T Forst
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- 7 Cebranopadol: a Novel First-in-Class Analgesic in Development for Chronic Pain Conditions – Effects on Respiration in Healthy Human Volunteers. PAINWeek 2016, poster #N96. A Dahan, J Hay, GJ Groeneveld, M Neukirchen, J Bothmer, E Olofsen

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