Press Release
GRÜNENTHAL

Peripheral NOP agonist addressing chronic peripheral neuropathic pain enters clinical development

Aachen, Germany, 16 December 2020 – Grünenthal announced today that the first participants have been enrolled in a Phase I trial of a peripherally restricted Nociceptin/orphanin peptide receptor (NOP) agonist, an oral investigational medicine with a unique mechanism of action for the treatment of chronic peripheral neuropathic pain.

The Phase I trial will include 76 healthy participants. The trial aims to demonstrate a favourable safety and tolerability profile and to confirm the pharmacokinetic characteristics of the compound following single and multiple-ascending doses. The results of the study are expected to be available in 2021.

“Pain remains a high unmet medical need that we strive to address with innovative medicines. Progressing our peripheral NOP agonist into clinical development is a major success in our efforts to build an industry-leading pipeline of investigational medicines,” says Jan Adams, M.D., Chief Scientific Officer, Grünenthal. “By driving the development of innovative medicines, we strive to change the life of patients for the better and make progress towards our vision of a world free of pain.”

The investigational medicine is a Grünenthal proprietary development based on extensive research in the field of the NOP receptor and currently the most advanced compound of the company’s peripheral, selective Nociceptin/orphanin FQ (N/OFQ) peptide receptor agonist programme. Pre-clinical data has shown an analgesic effect in a wide range of models[1]. In addition, the investigational medicine’s selectivity for the NOP receptor, combined with its peripherally restricted mode of action, may lead to an improved safety profile compared to the currently available standards of care.

About chronic neuropathic pain

Neuropathic pain is defined as pain that arises as a direct consequence of a lesion or diseases affecting the somatosensory system, i.e. a complex system of sensory neurons and pathways that responds to changes at the surface or inside the body. Neuropathic pain can result from nerve injury or disease affecting the peripheral or central nervous system. It is characterised by symptoms such as shooting or burning pain, numbness, altered sensation, and sensations that are very difficult to describe. General population studies, using validated screening instruments, have found that 7-10% of adults currently have chronic pain with neuropathic characteristics.[2] According to the International Association for the Study of Pain (IASP), this pain is generally more severe, and is associated with worse health, in every

[1] Grünenthal Data on file
[2] Colloca L et al. Nat Rev Dis Primers. 2017 Feb 16

measured dimension compared to non-neuropathic pain.[3] 17% percent of those who had pain with neuropathic characteristics had health-related quality of life scores equivalent to “worse than death” in a U.K study, compared to only 3% of those without neuropathic characteristics.[4] Patients with neuropathic pain generally do not respond to analgesics such as acetaminophen, NSAIDs or weak opioids such as codeine.[5] Despite the availability of various treatment options as well as guidelines, treatment remains a challenge.[6]

About NOP Receptor

The nociceptin opioid peptide receptor (NOP), also known as the nociceptin/orphanin FQ (N/OFQ) is a G protein-coupled receptor whose natural ligand is the 17 amino acid neuropeptide known as nociceptin (N/OFQ).[7] NOP agonists have been shown to act as powerful, non-addictive painkillers in pre-clinical models.

Although NOP shares high sequence identity (~60%) with classical opioid receptors μ-OP (MOP), κ-OP (KOP), and δ-OP (DOP), it possesses little or no affinity for opioid peptides or morphine-like compounds. Likewise, classical opioid receptors possess little affinity towards NOP's endogenous ligand nociceptin.[8]

About Grünenthal

Grünenthal is a global leader in pain management and related diseases. As a science-based, privately-owned pharmaceutical company, we have a long track record of bringing innovative treatments and state-of-the-art technologies to patients worldwide. Our purpose is to change lives for the better – and innovation is our passion. We are focussing all of our activities and efforts on working towards our vision of a world free of pain.

Grünenthal is headquartered in Aachen, Germany, and has affiliates in 29 countries across Europe, Latin America and the US. Our products are available in more than 100 countries. In 2019, Grünenthal employed around 4,700 people and achieved sales of € 1.4 bn.

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[3] IASP, Factsheet “Epidemiology of Neuropathic Pain”, 2014, https://s3.amazonaws.com/rdcms-iasp/files/production/public/AM/Images/GYAP/Epidemiology%20of%20Neuropathic%20Pain.pdf
[4] Torrance N et al 2014 Oct; 155 (10): 1996
[5] Torrance N et al 2014 Oct; 155 (10): 1996
[6] Colloca L et al. Nat Rev Dis Primers. 2017 Feb 16
[7] Henderson G, McKnight AT (August 1997). "The orphan opioid receptor and its endogenous ligand--nociceptin/orphanin FQ". Trends in Pharmacological Sciences. 18 (8): 293–300. doi:10.1016/S0165-6147(97)90645-3. PMID 9277133.
[8] Butour JL, Moisand C, Mazarguil H, Mollereau C, Meunier JC (February 1997). "Recognition and activation of the opioid receptor-like ORL 1 receptor by nociceptin, nociceptin analogs and opioids". European Journal of Pharmacology. 321 (1): 97–103. doi:10.1016/S0014-2999(96)00919-3. PMID 9083791.

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