DBPR116: An Antagonist-to-Agonist Allosteric Modulator- Pain Relief Agent with Limited Side Effects of Opioids

INDICATIONS:

renal colic, acute pancreatitis, angina, post-operative pain, chronic neuropathic pain, regional complex pain syndrome, chronic back pain and cancer pain

PATENTS:

TWI625120B, US9827228B2, CN108883099B, HK1253294, J/005174, EP3344997B, CA2996281, JP7181536

TWI691332B, US10544113B, EP1060005, CN 108369222B, HK1258687, J/005474, KR10-2365673, JP7132849, AU2017229129

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1. Bioorganic chemistry, 128,105905.
2. Eur J Med Chem, 167, 312-323

DEVELOPMENT STATUS:

Pre-clinical

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INVENTION DESCRIPTION

The invention relates to antagonist-to-agonist allosteric modifiers (AAM) of a mu-opioid receptor (MOR) for treating an opioid receptor-associated condition. In the presence of this unique AAM (DBPR116), MOR could be selective activated by general opioid antagonist naloxone or naltrexone, and produces antinociceptive effect without developing severe side effects in vivo. In combination with naltrexone (1 mg/kg), the median effective antinociceptive dose (ED50) of the AAM in mouse model of acute thermal pain is lower than 10 mg/kg (i.v.). DBPR116 is a crystalline solid with acceptable maximum tolerate dose (MTD > 40 mg/kg) in rodents.

COMPETITIVE ADVANTAGES

DBPR116/naltrexone combination showed greater analgesic effects than morphine in an animal model of cancer pain, as well as in an animal model of 2'-3'-dideoxycytidine (ddc)-induced neuropathic pain. Subchronic treatment using the DBPR116/naltrexone combination still exerted good analgesic effects in both animal models of disease-related pain, whereas treatment using morphine either exerted poor analgesic effect in the animal model of cancer pain or caused development of analgesic tolerance in the animal model of ddc-induced neuropathic pain.

MARKET POSITIONING/OPPORTUNITY

There remain many unmet therapeutic needs in the treatment of pain, as well as high demand for analgesic treatments worldwide. In 2014, the global opioids market generated revenues over $20 billion. The invention demonstrates antinociceptive effect through MOR, so it is appropriate to use the DBPR116/naltrexone combination as most opioids for the treatment of acute and chronic pain, including renal colic, acute pancreatitis, angina, post-operative pain, chronic neuropathic pain, regional complex pain syndrome, chronic back pain and cancer pain, with fewer side effects. Due to the novel mechanism of action of DBPR116, there is few competitors relates to the invention. In the future, it should be a potentially First-in-Class drug for treating severe pain

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