

Discovery of Novel EP₁ Ligands for the Treatment of Pain

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Prostaglandin E₂ (PGE₂) is a proinflammatory mediator, produced from arachidonic acid by the action of the cyclooxygenase (COX) enzymes and Prostaglandin E₂ synthase (PGES). PGE₂ mediates its physiological actions via the activation of four GPCRs known as EP₁₋₄. In recent years several reports have established the potential of EP₁ antagonists as a novel approach for the treatment inflammatory and visceral pain, as well as for overactive bladder and cerebral ischemia.

During a public-private partnership (PPP) project aimed to find new compounds for the treatment of neuropathic pain, we identified several potent and selective EP₁ leads, which were optimized in terms of efficacy, PK/PD and safety properties to provide a potential clinical candidate.