

# A New Chapter in The World of Painkillers

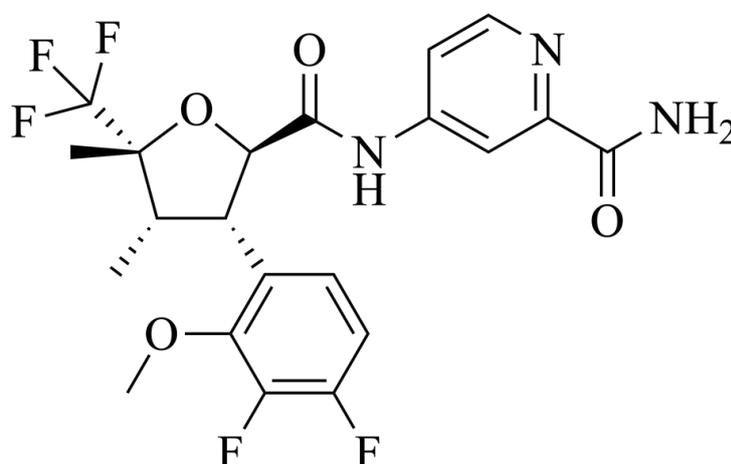
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**P**ain is one of the most critical signals in our body that keeps us alive. Although it is crucial for survival, it is an unpleasant feeling that disturbs people throughout their daily lives. Pain is a familiar feeling to every human being on this planet, and it can be defined as discomforting emotional and sensory experiences [1]. To reduce the pain, most people use different types of painkillers.

Opioids are one of the most commonly used classes of painkillers and are synthetically produced. The most well-known examples of opioids are morphine and heroin. Opioids are used in acute pain treatments, and their working mechanism is based on their interactions with opioid receptors. Opioid receptors are a class of G protein-coupled receptors (GPCRs) that are responsible for the transfer of information coming from nociceptive receptors. In these pathways, opioids act as inhibitory agents. They affect both afferent and efferent pain pathways by decreasing the release of neurotransmitters. Thus, they inhibit the flow of information and reduce pain [2]. Opioids are effective drugs, and they work well in theory; however, in real-life usage, they are highly addictive drugs even in the short term. This is because they activate the brain's strong reward centers and trigger the release of endorphins, which are neurotrans-

mitters that produce a sense of well-being. Today, opioid addiction remains at an epidemic level worldwide [3].

As an alternative to opioid drugs, in January 2025, the U.S. Food and Drug Administration (FDA) approved a novel non-opioid painkiller. This new drug is known as suzentrigine with the market name of "Journavx" [4]. Journavx's action mechanism depends on voltage-gated sodium channels on pain-sensing nerve cells. These Na<sup>+</sup> channels are responsible for generating electrical signals, also known as action potentials, in response to pain. Then, this action potential is transferred to the related regions of the brain, and pain perception is completed. The human nervous system has ten subtypes of voltage-gated sodium channels, and old technology



**Figure 1.** Chemical structure of suzentrigine



drugs such as local anesthetics block all of them. As an alternative, Journavx targets one of the most important subtypes: NaV 1.8 [5]. This receptor is exclusively found in peripheral sensory neurons, also known as nociceptors, and this feature makes it a promising target for pain inhibition with minimal side effects. Journavx binds to the channel's second voltage-sensing domain (VSD2) and inhibits the activation. This is a different approach compared to that of old drugs that directly block the pores of the channels. Journavx's mechanism works regardless of neural activation and thus can be effective in many situations. Additionally, since it works on a specific Na<sup>+</sup> channel, it does not trigger a reward mechanism like opioids, and this reduces the risk of developing an addiction [5].

In summary, Journavx is a new alternative to the commonly used opioid painkillers. Unlike the opioids that act on GPCRs, Journavx directly acts on a specific Na<sup>+</sup> channel in nerve cells responsible for pain sensing. This novel mechanism has the potential to represent a paradigm shift in pain treatments, with the expectation of pioneering many new drugs. Unlike opioids, the risk of addiction is extremely low in the use of Journavx; it offers hope and relief instead of a life full of addiction. Rather than being another painkiller that is destined to be lost in the crowd of countless painkillers, it may be the beginning of a new age in how modern medicine treats pain.

#### Works Cited

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## DID YOU KNOW?

Dr. House, the famous grumpy doctor that we all recognize from his medicine box, actually uses an opioid. It is called hydrocodone, or as you may remember, Vicodin. No wonder he's always cranky- in addition to solving medical riddles, he is also searching for his next dose!

