Docket #: S19-327

Biased positive allosteric modulators of cannabinoid receptor type 1 for the treatment of neuropathic pain

Disease Indication: Pain relief

Drug Format: Small molecule

Drug Class: First in class

Research Stage: In vitro/Lead selection

Target: CB1R

Background
Neuropathic pain is a poorly understood and poorly treated condition that underlies complications in diabetic neuropathy, fibromyalgia, and back and neck pain. Only 30% of patients respond to first-line treatments, while the opioids that make up the second line are even less effective with more severe side effects.

While agonism of the cannabinoid type 1 receptor (CB1R) has been hypothesized as a means of addressing neuropathic pain, available agonists against the receptor also engage the unwanted psychoactive aspects of cannabinoids.

Technology
Researchers at Stanford have synthesized a library of positive allosteric modulators (PAMs) that can bias the signaling of endogenous CB1R ligands away from psychoactive, orthosteric binding. Using novel assays to characterize compounds in their PAM library, researchers evaluated GTP turnover and beta arrestin recruitment as methods that can help identify the best candidate compounds to maximize pain relief. Selected compounds induce active conformations of the receptor that increase the tone of basal endocannabinoid CB1R signaling in a functionally

selective way to minimize adverse effects.

Applications

- Neuropathic pain relief
- CB1R-targeted drug discovery
- Cannabinoid-derived therapeutics

Advantages

- Opioid-sparing pain relief
- Selection of preferred agonist profiles
- Improved side effect profile for CB1R activation

Patents

- Published Application: WO2021162918
- Published Application: 20230047251
- Published Application: 20260115176

Innovators

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