Allosteric Modulators for the Treatment of Opioid Use Disorder

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OVERVIEW

A novel mechanism of action and approach for treating opioid use disorder was identified and promises to provide an effective, well-tolerated medication assisted treatment option. Novel, drug-like, orally bioavailable negative allosteric modulators of the mu-opioid receptor (MOR) were identified, optimized and demonstrate promising efficacy in models of opioid use disorder and represent a potential treatment paradigm shift.



DESCRIPTION

These are orally bioavailable, brain-penetrant molecules that prevent opioid drugs from activating the MOR, the main gateway that opioids use to produce their effects in the body and brain. Unlike current treatments, which compete with opioids at the same site (and can be overridden by high opioid doses), these molecules bind to a different (allosteric) binding site on MOR and significantly inhibit MOR activation, while still allowing for minimal function of the muopioid signaling pathway. This provides a treatment option with a much improved side effect profile and patient compliance, yet without the addiction and respiratory depression liabilities exhibited by current standard of care options. This rationale for superiority of the approach is supported by animal studies.

VALUE PROPOSITION

- **Non-addictive**: Functional antagonists with no abuse liability, a critical advantage versus current opioid use disorder therapies like methadone or buprenorphine.
- **Superior efficacy**: Non-competitive, non-surmountable inhibition of opioid activation ensures consistent effectiveness, even at high opioid concentrations.
- **Flexible administration**: Excellent brain penetration and high oral bioavailability allow for easy dosing and increased patient compliance.

TECHNOLOGY READINESS LEVEL

Therapeutics Technology Readiness Levels



MARKET OPPORTUNITY

There is a large and growing unmet medical need for non-addictive therapies for treating opioid addiction, especially as current options have severe side effects, maintain addiction, can be misused, and have generally low compliance. With over 3 million Americans affected by opioid use disorder and tens of thousands of annual overdose deaths, health systems and regulators are urgently seeking safer, more reliable alternatives.

Recent market data shows strong demand and investment in safer pharmacotherapies for opioid use disorder, driven by the escalating opioid epidemic and tightening regulation of conventional therapies.