SUVN-M8036, Serotonin/Dopamine Modulator for Psychiatric Disorders

Current Status: GLP Toxicity Study in Planning

SUVEN Life Sciences

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SUVN-M8036: Overview

- Shows potent affinity towards serotonin 5-HT_{1A} & 5-HT_{2A} and dopamine D_2 receptor
- No species difference in affinity between human and rat receptors
- No significant affinity towards other receptors and transporters
- D_2 modulator class of antipsychotic with superior separation between efficacy and safety
- Highly permeable and not a substrate of P-gp
- Moderately stable in human hepatocytes
- Good brain penetration and high unbound concentrations in rats
- Excellent ADME properties with no drug-drug interaction liability
- Robust efficacy in preclinical animal models of psychosis and depression
- Modulates dopamine and norepinephrine levels in cortex; no effects in striatum
- Wide margin of safety in preliminary toxicity studies

Psychiatric Drug Therapy: Limitations

https://www.onwardmentalhealth.com/schizophrenia

SUVN-M8036: Medicinal Chemistry & Intellectual Property

Medicinal Chemistry

- SUVN-M8036 is innovatively designed clinical candidate selected from several diverse chemical scaffolds using focussed SAR
- Synthesis comprises fewer steps, cost effective building blocks and easily scalable process
- SUVN-M8036 is a crystalline compound with desirable physicochemical and pharmaceutical properties

Intellectual Property

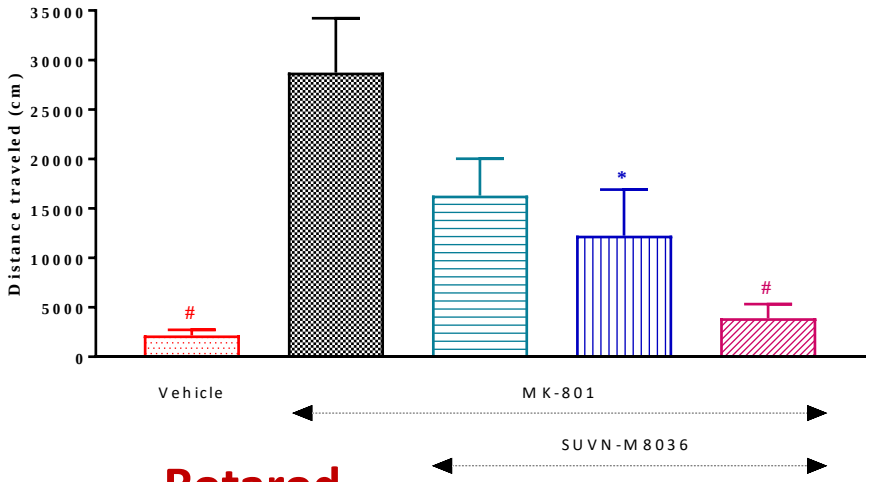
- Series is patentable. Drafting of patent application is in progress

SUVN-M8036: In Vitro Efficacy Profile

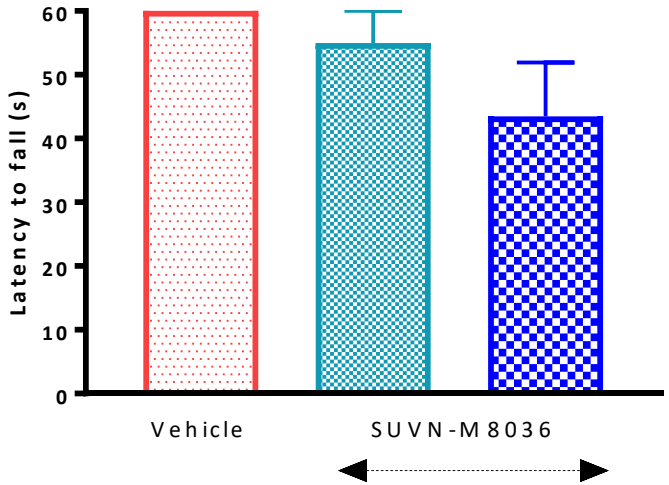
Target Receptor	Dopamine D_2	5-HT_{2A}	5-HT_{1A}	5-HT_7
***In Vitro* Affinity**	Ki 3.3 ± 0.5 nM	Ki 0.8 ± 0.1 nM	Ki 0.2 ± 0.01 nM	Ki 25.7 ± 8.1 nM
Functional Nature	Antagonist	Antagonist	Antagonist	Antagonist
Features	• Fast dissociating D_2 antagonist • Antipsychotic efficacy for positive symptoms	• Improves quality of sleep • Reduces anxiety and hostility • Improves symptoms of schizophrenia • Quicker onset of action	• Improves symptoms of schizophrenia • Aids for quicker onset of action • Procognitive effects	• Role in learning, memory and sleep • Involved in mood regulation

SUVN-M8036: Key Biology Results

MK-801 Antagonism



Rotarod

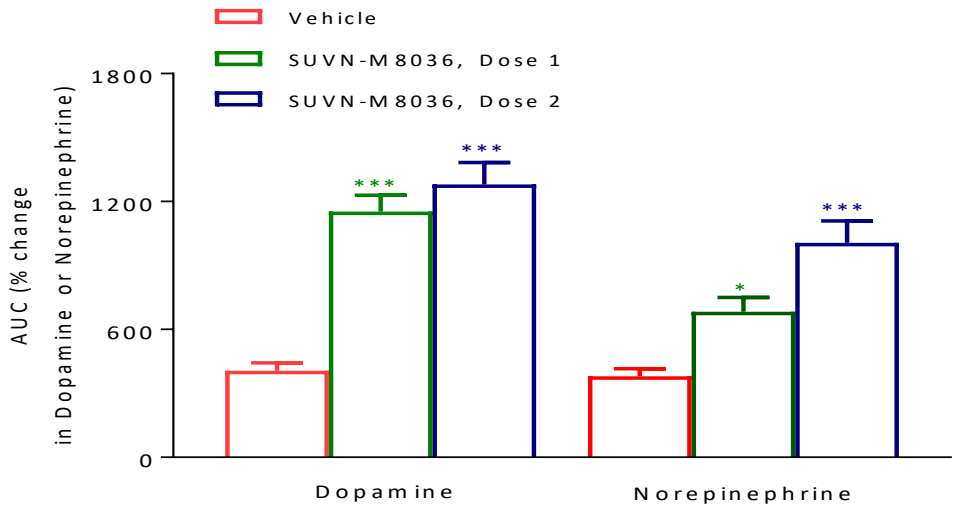


Robust efficacy in animal models of psychosis

Wide separation between the doses which produces efficacy and side effects

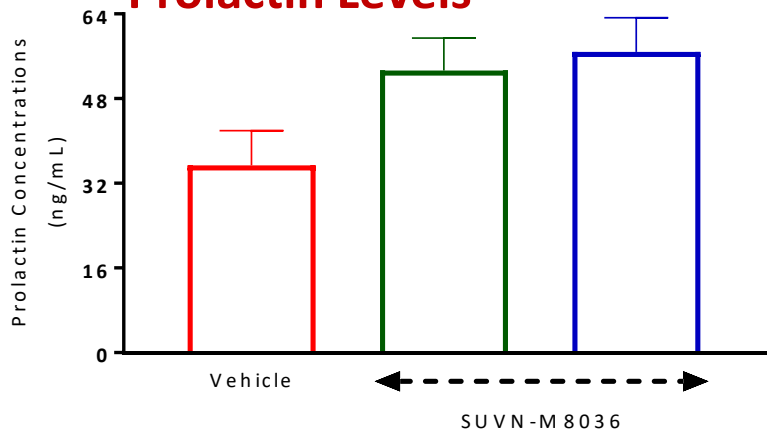
SUVN-M8036: Key Biology Results

Neurochemistry



Dose dependent increase in dopamine and norepinephrine levels in cortex

Prolactin Levels



No significant effects on plasma prolactin levels at therapeutically effective doses

SUVN-M8036: Non-Clinical Safety

Non-Clinical Toxicology

- Safety was evaluated in 28- day repeated dose toxicity study in rats and no safety concerns for further development
- Non mutagenic in bacterial reverse mutation (AMES) test