

## Novel Small Peptide Antidepressant

### Market Need

Depression is a prevalent mood disorder that results in significant human suffering, loss of productivity, and an increased economic burden. The pervasiveness of major depression is 4.0% in Canada and 3.9-4.2% in the United States. It is estimated that by 2020, depression will be the second leading cause of illness worldwide. Given the prevalence of depression and economic burden of disease, many drugs have been developed to alleviate symptoms. Current common antidepressants have severe undesirable side effects partially attributed to the non-specific actions of these drugs. With the widespread occurrence of side effects associated with antidepressants, there is a need for the development of novel and more specific antidepressant medications.

### Technology Description

Our scientists have identified a coupling between two functionally distinct dopamine D1 and D2 receptors via direct protein-protein interactions, markedly increased in patients with major depressive disorder. We have developed a small peptide that selectively interferes with this coupling, thereby leading to the development of a breakthrough therapy capable of delivering enhanced affinity, efficacy, and a superior side effect profile. The novel cell permeable D1-D2 interfering peptide reduces D1-D2 heterodimer formation, and attenuates depression-like behavior (Figure 1).

### Stage of Development

- Through a collaboration with Impel NeuroPharma, we have successfully administered this interfering peptide through the nasal cavity using their pressurized olfactory delivery device and confirmed the antidepressant effect of our peptide in the animal model of depression.
- Administration of nmol amounts of the interfering peptide shows an antidepressant effect in the forced swim test in mice, and effects are comparable to the effects of the antidepressant imipramine.
- While antidepressant effects were observed, total D1 and D2 protein levels remained constant.
- We are pursuing the identification of small molecules mimicking the functional effect of our peptides.

### Advantages

- Small peptide, CNS targeting, with a *novel and highly specific mechanism of action*.
- The peptide does not block ligand binding; thus it does not interfere with normal physiological functions associated with the D1 and D2 receptors, potentially reducing occurrence of unwanted side effects.
- Safety & Toxicity - Agents that selectively inhibit receptor interaction are likely to be safer than receptor antagonists.

### Notable Publication(s)

Brown V, Liu F (2014) *Neuropsychopharmacology* 17 March 2014; doi: 10.1038/npp.2014.61.

Pei L, Li S, Wang M, Diwan M, Anisman H, et al. (2010) *Nature Medicine* 16(12):1393-1395.

### Intellectual Property

Issued US and CA patents. Issued EP patent validated in FR, DE.

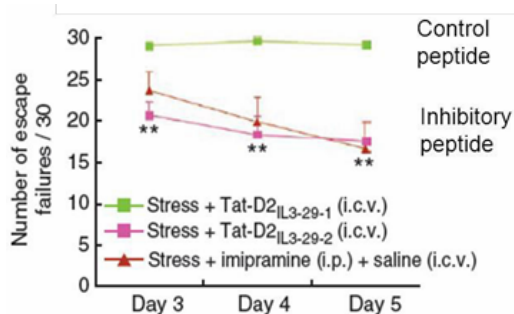


Figure 1: Inhibitory peptide attenuates depression-like behavior similar to imipramine antidepressant treatment in rats compared to control peptide (n=19).