

Quick Facts

Indication

Major Depressive Disorder

US Market Size

\$2.8 Billion US

Development Stage

Preclinical

Milestones:

1. Assay Development (*completed*)
2. Pilot Screen (*completed*)
3. Hit identification and validation (*completed*)

Principal Investigator

José Nobrega, PhD
Francis Bambico, PhD

Academic Institution

Centre for Addiction and Mental Health (CAMH), owner of all IP
Toronto, Ontario, Canada

Business Opportunity:

CAMH is seeking partners to license, invest in or co-develop this technology

CONTACT

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Unmet Need

Major depressive disorder (MDD) is a complex mood disorder characterized by emotional, physical, behavioral and cognitive symptoms for which there is no cure. While there are numerous antidepressants on the market, these drugs can take up to eight weeks for therapeutic benefits to emerge – a feature that especially exacerbates mortality among suicidal patients. In addition, approximately 90 million patients worldwide fail to respond to any available treatment. There is a need for new antidepressants that are fast-acting and effective for treatment-resistant patients.

Commercial Landscape

Commonly prescribed antidepressants such as selective serotonin reuptake inhibitors (SSRIs) are largely effective but suffer from the limitations of non-response in a significant number of patients (~30%), high relapse rates, and slow therapeutic onset. A new approach comprises rapid-acting antidepressants (RAADs). The approved RAAD, Spravato™ (esketamine; Janssen Pharmaceuticals), shows effects within hours post-administration; however, mechanistic questions remain and its clinical utility is limited by its potential for abuse and induction of psychosis.

Opportunity

Dr. Nobrega and Dr. Bambico have discovered that the therapeutic activity of ketamine (precursor of Spravato™) involves small conductance calcium-activated potassium channels (SKCs) suggesting a novel mechanism for targeted RAAD effects. These channels are key determinants of synaptic plasticity in limbic circuits mediating emotional and stress responses. Brain SKC density is increased and neural activity decreased in brain areas implicated in a rat model of depression. Furthermore, SKC antagonists such as apamin show dose-dependent effects on depressive-type behaviour in animal models. Dr. Nobrega's group, in concert with Evotec and TIAP, developed specialized screening assays to identify novel small molecule inhibitors of SKCs. HTS activities followed by hit profiling and hit expansion have now yielded multiple chemical series with suitable properties for further development, including: desirable potency, selectivity, early DMPK and predictive CNS scores. This program has the potential to yield novel RAADs that are safer and more effective than those currently available.

Principal Investigator

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