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Dr Ronald Aung-Din
Scientific Advisor,
Psycheceutical Bioscience

Dr Aric Logdson
Scientific Director,
Psycheceutical Bioscience

BEYOND MANUFACTURING: BROADENING HORIZONS OF CDMOS

As strategic partners for pharma and biotech companies, CDMOs are ramping up their expertise to span the entire life sciences value chain and become enablers of success

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INTERVIEW

Creating non-habit forming formulations and treatment protocols for psychedelic substances is crucial

Despite challenges, there's increasing interest in the therapeutic potential of psychedelic substances, more so after the US FDA released its first draft guidance on psychedelic drug trials in June this year. In an email interaction with **Viveka Roychowdhury**, **Dr Ronald Aung-Din**, scientific advisor and **Dr Aric Logdson**, Scientific Director, Psycheceutical Bioscience detail the regulatory challenges and why Psycheceutical's NeuroDirect topical cream to be applied to the back of the neck at the hairline, currently undergoing a Phase I trial in Australia, offers an innovative way to reduce the complexity of delivering drugs across the blood-brain barrier

What are the challenges of developing safe and non-habit forming therapeutic use psychedelic compounds?
Dr Aung-Din: One significant hurdle is navigating the regulatory landscape, as all psychedelic substances aside from ketamine are classified as Schedule I drugs, indicating a high potential for abuse and no recognised medical use. This classification often complicates the process of obtaining permissions for research and clinical trials. The legal status of these substances also contributes to a scarcity of comprehensive, quality research–making it difficult to fully grasp their effects, ideal dosages, and potential risks.

Safety is another major concern. Psychedelic substances can sometimes trigger adverse reactions like severe anxiety or paranoia, necessitating the development of protocols to manage these risks, which could include careful screening procedures, supervised administration, and follow-up care. Standardisation and quality control of psychedelic substances is critical in order to establish safety, efficacy, and appropriate dosages.


Dr Ronald Aung-Din


Dr Aric Logdson

Public perception is also a significant obstacle. The association of psychedelic substances with recreational use and abuse rather than medical treatment creates a stigma that can be hard to overcome.

Finally, while many psychedelic substances aren't considered physically addictive, they have the potential for abuse through habit formation or psychological dependence. Therefore, creating non-habit forming formulations and treatment protocols is crucial.

Despite these challenges, there's a surge of interest in the therapeutic potential of psychedelic substances. As our understanding of these substances expands, we inch closer to developing safe, effective, and non-habit forming treatments for various mental health conditions.

What is the mode of action of Psycheceutical's NeuroDirect delivery platform?
Dr Aung-Din: Psycheceutical's NeuroDirect topical cream is applied to the back of the neck at the hairline to deliver neuroaffective compounds directly to the nervous system. Topical ketamine activates receptors on free nerve endings under the skin's surface at this critical location adjacent to the brainstem. Here, neurochemical reactions communicate with the brain to promote therapeutic benefits without the restrictions of the blood-brain barrier (BBB). This drug delivery method produces therapeutic benefits within minutes, while reducing or eliminating the side effects commonly associated with other forms of ketamine delivery such as hallucinations, nausea, and dizziness.

Psycheceutical's NeuroDirect ketamine is reportedly the first-ever programme to test the topical application of ketamine for treating mental health disorders. What have been the pre-clinical results and the way forward?
Dr Aung-Din: NeuroDirect ketamine topical cream for the treatment of Post-traumatic Stress Disorder (PTSD) has already shown positive results in an observational preclinical setting. As the inventor of the NeuroDirect delivery system, I've been treating PTSD patients with this novel topical ketamine formulation for a number of years through my General Neurology and Neuropsychiatry practice, and currently have several hundred patients using it on a regular basis.

I recently published a peer-reviewed study in Drug Development & Delivery which describes the potential of NeuroDirect ketamine topical cream as an improved treatment for PTSD. In 100 patients experiencing intractable depression, anxiety, and other symptoms commonly associated with PTSD, who had failed numerous other treatments–more than 80 per cent experienced symptom relief from the NeuroDirect ketamine cream.

As quoted in the study: "Discernible improvement[s] in anxiety, depression, paranoia and unrealistic fear, focusing issues, cloudy thinking, neuro-pathic pain, and other such symptoms were noted within 8-10 minutes of topical drug application. No psychogenic effects, such as hallucinations or dissociative phenomena, were experienced by any patient. To the contrary, patients indicated their thought processes were clearer, more focused, and that they were more keenly aware of surroundings."

What are the therapeutic areas where such brain-drug technologies can make a huge difference over current medicines in terms of patient outcomes, cost and length of treatment?
Dr Aric Logdson: Brain-drug technologies have the potential to revolutionise treatment in several therapeutic areas, including mental health disorders,

neurodegenerative diseases, and certain types of cancers.

Current drug development strategies have relatively low success rates due to the complexity of the brain and challenges in delivering drugs across the blood-brain barrier (BBB). Novel brain-drug technologies could significantly enhance the effectiveness of treatments for conditions like PTSD, Parkinson's disease, and Glioblastoma, thereby improving patient outcomes and potentially reducing side effects and expensive treatment costs.

Substance use disorders represent another area where brain-drug technologies can make a significant impact. Current treatment strategies often involve long-term medication use paired with behavioral counseling. However, innovative approaches could offer more effective and fast-acting solutions. For instance, targeted therapies could address the specific brain changes associated with addiction, enhancing recovery rates and preventing overdoses.

Brain-drug technologies could also transform how we treat brain tumors. Traditional chemotherapy often struggles to effectively target cancer cells in the brain, due to intrinsic BBB restrictions. However, new brain-drug technologies show promise in navigating the BBB to effectively treat brain cancer, while reducing side effects. One example is the combination use of advanced imaging and focused ultrasound to transiently open the BBB at the tumour site for chemotherapy. These innovative strategies may improve patient survival rates and reduce the need for traditional treatments that continuously prove to be inefficient.

As technology advances and our understanding of the brain continues to evolve, we can expect to become more efficient at treating the causes of these debilitating diseases.

Given the challenges, how many companies have similar development programmes around psychedelic compounds? What are some of the other promising drug delivery platforms in the discovery and preclinical phase?

Dr Aric Logdson: There are numerous companies in the psychedelic industry with drug development programmes. However, most are focused on attempting to modify the molecular structure of psychedelic compounds in order to remove the psychedelic effects. This would give them a novel psychedelic compound that they could then patent and control. Unfortunately, this process requires extensive FDA approvals and preclinical studies, leading to higher expenses and longer timelines. This process differs from Psycheceutical, where we are instead developing next-generation brain-drug technologies to safely deliver established psychedelic molecules with decades of supporting clinical data.

Give an overview of the leads in Psycheceutical's development pipeline.

Dr Aric Logdson: Our NeuroDirect ketamine topical for the treatment of PTSD is currently undergoing a Phase I trial in Australia. We recently announced the successful dosing of our first cohort of subjects, with key results from the study confirming that topical administration of NeuroDirect ketamine is safe and well-tolerated. Phase II clinical trials are planned for the beginning of 2024.

NeuroDirect ketamine topical is also being tested for the treatment of Complex Regional Pain Syndrome, currently in the preclinical stage. We are also in the preclinical stage of using the NeuroDirect delivery system for the treatment of addiction with an undisclosed psychedelic compound. We round out our drug pipeline with several drug candidates designed to treat Parkinson's disease and Traumatic Brain Injury (TBI).

Given the challenges of designing clinical trials for psychedelic drug candidates, how has the regulatory overview of such trials evolved over time? Has the US FDA's draft guidance, touted as the first psychedelic drug trial guidance, released this June, addressed these challenges adequately?

Dr Aric Logdson: We have seen a significant change in the regulatory landscape for psychedelic clinical trials. In the mid-20th century, research on psychedelic drugs quickly dismissed their therapeutic potential due to fears of their abuse liability. A dire need for innovative therapies for brain diseases has led to more public awareness of the potential benefits for psychedelic drugs, especially for treating mental health conditions like depression and PTSD.

Regulatory bodies have recently responded to this public acceptance, backed by scientific evidence. The US FDA, for example, has granted "breakthrough therapy" designation for several psychedelic substances, signaling a willingness to expedite their review process. This is a significant departure from previous attitudes, and reflects a revolutionary time to explore the therapeutic potential of these remarkable substances.

In June 2023, the FDA released its first draft guidance on psychedelic drug trials. This document aims to provide a clear framework for the design and execution of clinical trials involving psychedelic substances. It addresses key challenges, such as the need for rigorous safety protocols, the importance of set and setting, and the necessity of specialised training for clinicians who administer these substances.

While this guidance represents a major step forward, it's too early to determine its full impact. Further refinements will likely be needed as more data becomes available from ongoing and future psychedelic trials. However, the release of this guidance is a clear sign of the changing regulatory landscape for psychedelic medicines, and the growing public recognition of their therapeutic potential.

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