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UNIVERSITY OF WESTERN AUSTRALIA DISCOVERS NEW LSD COMPOUNDS

Woke Pharmaceuticals, investor into the largest and most diverse portfolio of psychedelic research projects in Australia, is pleased to announce strong progress from its funded project with The University of Western Australia to discover novel active analogues of Lysergic Acid Diethylamide (LSD).

LSD is a classic hallucinogen that has some similar biological properties to psilocybin (the active ingredient in magic mushrooms) and dimethyltryptamine (DMT). It was widely studied from the 1950s to 1970s, including by various governments and research bodies. It is considered non-addictive with a low potential for abuse.

On March 7, 2024 it was announced that an LSD analogue (MM120) had achieved 'breakthrough status' by the US Food and Drug Administration (FDA). The status was granted after positive results from a trial to treat generalised anxiety disorder that saw a single dose of MM120 led to a 48% rate of remission 12 weeks after the drug's administration.

As a complex and expensive drug to manufacture, nearly two years ago Woke Pharmaceuticals and The University of Western Australia signed an agreement to undertake a program aimed at identifying and synthesising a library of novel compounds that are structurally similar to LSD. The objective was to discover molecules that maintain or enhance the potency of LSD to bind with key neuroreceptors but also to minimise the risk of side-effects while being simpler and thus more cost-effective to produce.

A key consideration of the drug discovery program was to produce easy-to-synthesise analogues of LSD with high potency at the serotonin receptor required for psychedelic effects (5-HT_{2A}), but with reduced, or ideally abolished, activity at an important but unwanted off-target cardiac receptor (5-HT_{2B}), which with chronic use is associated with life-threatening side effects including heart valve failure.

This cardiac toxicity liability is currently shared by all classical psychedelics in use, and engineering new compounds without activity at 5HT_{2B} is a top priority for next-generation drugs. This is especially true if micro-dosing regimes are desired (due to the increased frequency of drug administration).

Associate Professor Scott Stewart at the School of Molecular Sciences at the University of Western Australia and Lead Researcher of the Program, said, "To date, we have developed a total of 24 novel LSD analogues and performed *in vitro* assays for activity against both the desired (5HT_{2A}) and undesired (5-HT_{2B}) serotonin receptor types, and identified a group of highly selective new compounds.

"These compounds are more potent at the psychedelic 5HT_{2A} receptor than the approved drug psilocin, but with over 100-fold selectivity over the off-target 5-HT_{2B} receptor. In fact, our initial data indicate some compounds from this series may be completely inactive against this off-target cardiac receptor.

"I am extremely excited by our easy-to-synthesise compounds based on LSD that show high potency at the serotonin (5-HT_{2A}) receptor and reduced activity at the unwanted (5-HT_{2B}) receptor. With this goal met, we hope to now optimize the metabolic stability of our drug candidates, with the intent of fine-tuning their duration of action in the hopes of offering psychedelic experiences more suited to use in the clinic. I look forward to developing these compounds further with Woke," said Associate Professor Scott Stewart.

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While Woke Pharmaceutical's primary focus has been on the development and commercialisation of its novel psychedelic candidates based on synthetic psilocybin, the company has also believed that LSD, and variations of LSD, may hold enormous potential for the treatment of mental health disorders.

Matthew Hayne, Managing Director of Woke Pharmaceuticals said: "We welcome the discoveries and progress by The University of Western Australia in this high potential field.

"The recent announcement by the FDA further legitimises this field of study and Associate Professor Scott Stewart and his team are at the global forefront of identifying and developing new forms of LSD that may better suit patients through customised psychedelic experiences with reduced risk profiles. Such compounds may be better received by Governments and regulators should they be inherently lower risk compared to other psychedelic drugs seeking approval.

"Woke Pharmaceuticals is currently working with The University of Western Australia to develop and execute an Intellectual Property strategy in relation to their discoveries. We hold great hope that some of these novel compounds will be used in clinics in the future," said Matthew Hayne.

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ABOUT WOKE PHARMACEUTICALS

Woke Pharmaceuticals Pty Ltd is an Australian-based company focused on the development and commercialisation of novel psychedelic therapies for the treatment of mental health disorders. The Company's lead candidates are based on synthetic psilocybin, which is a naturally occurring psychedelic prodrug compound produced by more than 200 species of fungi. Clinical trials have shown its safety and efficacy in the treatment of mental health disorders. Woke Pharmaceuticals is developing two dose forms with rapid release capabilities. The Company is also conducting a novel drug discovery programme to identify pharmacologically optimised analogues of LSD with The University of Western Australia.