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NEWS RELEASE

Orphan Drug Designation Granted for the Treatment of Complex Regional Pain Syndrome with Ketamine to iX Biopharma

Singapore, 17 May 2021 – Specialty pharmaceutical company **iX Biopharma Ltd** (SGX:42C) ("iX Biopharma" or, "the Company") is pleased to announce that the United States Food and Drug Administration (US FDA) has granted the Company an orphan drug designation for treatment of patients with Complex Regional Pain Syndrome (CRPS) with ketamine. CRPS is a rare disorder of a body region, usually of the distal limbs, which is characterised by excess and prolonged pain and inflammation typically occurring after a fracture, soft tissue injury, or surgery.

The US FDA's Office of Orphan Drug Products grants special orphan status to support development of medicines for rare diseases or conditions that impact fewer than 200,000 people in the United States. Orphan drug designation provides to iX Biopharma certain benefits, including market exclusivity of 7 years upon regulatory approval, tax credits for qualified clinical trials and waiver of US FDA's New Drug Application filing fee of approximately US$2.9 million.

Dr Janakan Krishnarajah, Chief Operating Officer and Chief Medical Officer at iX Biopharma, said, "*There is no approved drug for the treatment of CRPS, which in severe cases can result in chronic and profound disability. Ketamine is a compelling therapeutic candidate due to its action on the NMDA receptor and scientific research suggests that ketamine infusions over a period of up to 14 days shows strong promise for the treatment of CRPS. Delivery via sublingual route, using our novel sublingual ketamine, **Wafermine**, has significant potential benefits including avoidance of infusion related adverse events, reduction in administration costs, ease of use, and improved compliance."*

The inclusion of CRPS adds to an already valuable Wafermine asset, which is currently being developed for acute moderate to severe pain and potentially major depressive disorder. CRPS opens up a new market with significant unmet medical need. This increases the attractiveness of the Wafermine asset to licensees, who will be able to unlock substantially more value across multiple conditions.

About Orphan Drug Designation

The Orphan Drug Act (ODA) provides for granting special status to a drug or biological product to treat a rare disease or condition upon request of a sponsor. This status is referred to as orphan designation (or sometimes "orphan status"). For a drug to qualify for orphan designation both the drug and the disease or condition must meet certain criteria specified in the ODA and FDA's implementing regulations at 21 CFR Part 316. Orphan designation qualifies the sponsor of the drug for various development incentives of the ODA, including tax credits for qualified clinical testing. A marketing application for a prescription drug product that has received orphan designation is not subject to a prescription drug user fee unless the application includes an indication for other than the rare disease or condition for which the drug was designated. (https://www.fda.gov/industry/developing-products-rare-diseases-conditions)

About Complex Regional Pain Syndrome (CRPS)

CRPS is a debilitating chronic neurologic condition affecting the limbs, with a prevalence of approximately 5.4[1]–26.2[2] per 100,000 person years. It is a syndrome characterised by a continuing (spontaneous and/or evoked) regional pain that is disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor, edema and/or trophic findings. The syndrome shows variable progression over time and is difficult to treat effectively. It can occur after surgery or trauma including a noxious event, or brain or spinal cord injury.

About Ketamine

The principal pharmacological action of ketamine is inhibition of NMDA receptors. NMDA receptors are a likely participant in central sensitization, a process resulting in the amplification of pain signals to the brain. *T*he pathogenesis of CRPS and its cause by multifactorial processes involving both peripheral and central mechanisms with several contributors has been established. The role of glutamate in central sensitization through its activation of spinal NMDA receptors is clearly established in CRPS. Numerous clinical studies have been performed to establish the role of ketamine in the treatment of CRPS, leading to the conclusion that ketamine has shown to provide a clinically relevant reduction in the pain associated with CRPS.

About Wafermine

Wafermine is a novel sublingual ketamine wafer developed using iX Biopharma's patented WaferiX sublingual delivery technology. The Company is developing Wafermine for the treatment of acute moderate to severe pain. There were approximately 120 million acute pain cases in the US, EU5

[1] Sandroni, Benrud-Larson, McClelland, & Low, 2003 Sandroni, P., Benrud-Larson, L. M., McClelland, R. L., & Low, P. A. (2003). Complex regional pain syndrome type I: incidence and prevalence in Olmsted county, a population-based study. Pain, 103(1-2), 199-207. doi:10.1016/s0304-3959(03)00065-4

[2] Misidou, C., & Papagoras, C. (2019). Complex Regional Pain Syndrome: An update. Mediterr J Rheumatol, 30(1), 16-25. doi:10.31138/mjr.30.1.16; Sigtermans, M. J., van Hilten, J. J., Bauer, M. C. R., Arbous, S. M., Marinus, J., Sarton, E. Y., & Dahan, A. (2009). Ketamine produces effective and long-term pain relief in patients with Complex Regional Pain Syndrome Type 1. Pain, 145(3), 304-311. doi:10.1016/j.pain.2009.06.023

countries (Germany, France, Italy, Spain, and the United Kingdom) and Japan in 2017. Moderate to severe pain accounted for the largest share of the acute pain cases[3].

The Company's Phase 3 programme to support the registration of Wafermine for the treatment of acute moderate to severe pain has been agreed with the FDA and EMA following the successful conclusion of the End-of-Phase 2 meeting with the FDA and the Scientific Advice from the EMA.

Unlike opioids, Wafermine does not cause respiratory depression which may lead to death. Wafermine has the potential to be used in substitution or as an adjunct to opioids addressing a large unmet clinical need.

About iX Biopharma Ltd

iX Biopharma is a specialty pharmaceutical and nutraceutical company listed on the Catalist board of the Singapore Exchange Securities Trading Limited (SGX-ST), operating a fully integrated business model from drug development to manufacturing and supply, with facilities in Australia. The Group is focused on the development and commercialisation of therapies for diseases of the central nervous system using novel, patent-protected formulations for sublingual delivery.

iX Biopharma has developed a patented drug delivery platform technology, WaferiX. WaferiX delivers drug sublingually via the mucosa for better absorption, faster onset of action and predictable effect. The WaferiX delivery platform is particularly useful for drug repurposing which is a growing trend with a global market worth over US$30 billion[4]. Drug repurposing is where existing approved drugs are developed into new drugs targeting different indications or a different route of administration, at a lower development cost and risk.

iX Biopharma's pipeline of products under development includes Wafermine (ketamine wafer) and BnoX (buprenorphine wafer) for pain management. iX Biopharma's drugs for the treatment of erectile dysfunction, Wafesil, a sublingual sildenafil wafer, and Silcap, have been registered in Australia and Singapore. iX Biopharma has developed Xativa, the world's first freeze-dried sublingual medicinal cannabis wafer.

The Group's nutraceuticals division, Entity Health Limited, is engaged in the development and commercialisation of nutraceutical products that address specific conditions and improve quality of life. It distributes its Entity line of nutraceutical products in Australia through more than 250 pharmacies and health food shops, in China through its flagship stores on Tmall Global and JD Worldwide, and globally through its online store.

[3] *Acute Pain - Market Insights, Epidemiology and Market Forecast to 2028, Research and Markets, 30 September 2019*

[4] *https://www.intechopen.com/books/drug-repurposing-hypothesis-molecular-aspects-and-therapeutic-applications/drug-repurposing-dr-an-emerging-approach-in-drug-discovery*

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This announcement has been reviewed by the Company's sponsor, CIMB Bank Berhad, Singapore Branch ("Sponsor") in accordance with Rule 226(2)(b) of the Catalist Rules. This announcement has not been examined or approved by the SGX-ST and the SGX-ST assumes no responsibility for the contents of this announcement, including the correctness of any of the statements or opinions made or reports contained in this announcement. The contact person for the Sponsor is Mr. Eric Wong, Director, Investment Banking, Singapore. The contact particulars are 50 Raffles Place, #09-01 Singapore Land Tower, Singapore 048623, telephone: (65) 6337-5115.