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## NEWS RELEASE

### FIRST SUBLINGUAL KETAMINE DRUG FOR TREATMENT OF ACUTE PAIN TO BE EVALUATED IN END-OF-PHASE 2 MEETING WITH FDA

- ✓ **Racemic sublingual ketamine, *Wafermine*, is the first sublingual ketamine drug seeking FDA approval for the treatment of moderate to severe acute pain**
- ✓ ***Wafermine* is a Phase 2-ready drug for treatment resistant depression**

**Singapore, 21 May 2019** – iX Biopharma Ltd (SGX:42C) announced today that following the completion of its Phase 2 clinical study on **Wafermine**, a sublingual racemic ketamine wafer for the treatment of acute moderate to severe pain, the U.S. Food and Drug Administration (FDA) has scheduled the End-of-Phase 2 (EOP2) meeting with the Company in the third quarter of 2019.

The results of the Phase 2b randomized, double-blind, placebo-controlled study on *Wafermine* demonstrated strong analgesic efficacy, safety and tolerability in participants experiencing moderate to severe acute, post-operative pain after undergoing either abdominoplasty or bunionectomy surgery.

*“Wafermine demonstrated strong, consistent effect sizes in Phase 2 clinical trials,”* said Dr. Neil Singla, Chief Scientific Officer at Lotus Clinical Research in the U.S. where the Phase 2b study was conducted. *“This Phase 2 program not only provided evidence that Wafermine is effective for acute postoperative pain, but also contributed guidance on the best experimental design choices to demonstrate Wafermine’s efficacy in both bunionectomy and abdominoplasty moving forward. This program paves the way for a strong likelihood of success in Phase 3 pivotal trials.”* Dr. Singla is a board-certified anaesthesiologist and a nationally recognized key opinion leader in analgesic protocol design and implementation<sup>1</sup>.

More information about this Phase 2b study of *Wafermine* can be found at the link below:  
[\[http://www.ixbiopharma.com/resources/ck/files/180905-press-release.pdf\]](http://www.ixbiopharma.com/resources/ck/files/180905-press-release.pdf)

#### **Novel mechanism of action for the treatment of pain**

*Wafermine* works through a novel mechanism of action compared to currently approved therapies for acute pain. It is thought that much of ketamine’s analgesic effects result from its inhibition of the NMDA receptor channels.

In the backdrop of the opioid crisis, there is an urgent medical need for effective and safe non-opioid alternatives to treat moderate to severe acute pain. Unlike opioid analgesics, low dose ketamine is not associated with the negative side effect of respiratory depression, which can lead to overdose deaths. *Wafermine* is expected to be used in substitution, or as an adjunct to opioids. This will provide medical practitioners with a viable alternative to prescription opioids.

## Phase 2-ready for treatment resistant depression

In addition to the treatment of pain, iX Biopharma is evaluating Wafermine for a second indication of treatment resistant depression. Wafermine is ready to start Phase 2 studies in this indication.

Today, over 300 million people suffer from depression globally<sup>2</sup>. Amongst this demographic, one in three patients are considered to have treatment resistant depression<sup>3</sup>. The FDA approval of Spravato® (intranasal esketamine) in March 2019 established drugs targeting the NMDA receptor as an exciting new class of antidepressants. Unlike Spravato®, which is the single isomer (the S isomer) of ketamine, Wafermine is a racemic ketamine containing both the R and S isomer in equal proportions. IV racemic ketamine trials have in the past shown rapid antidepressant effects in patients<sup>4,5</sup> and to effectively treat between 50-70% of patients with treatment resistant depression<sup>4,5,6</sup>.

### WaferiX™, patented sublingual wafer

Wafermine, which utilises iX Biopharma's patented sublingual wafer technology, known as WaferiX™, disintegrates under the tongue rapidly for faster therapeutic action and predictable dosing. In pharmacokinetic studies, sublingual delivery using WaferiX™ increased bioavailability of active compounds when compared to oral administration, while avoiding excessively high peak plasma concentrations typical of IV bolus dosing. In addition, sublingual delivery is cost-effective, convenient and well-tolerated compared to intravenous or intranasal administration.

*“Wafermine provides an attractive non-opioid approach for the treatment of acute pain by targeting the NMDA receptor and would represent the first ketamine drug for the indication of pain. Additionally, racemic ketamine's novel mechanism of action has been demonstrated to have a strong and rapid anti-depressant effect in patients with treatment-resistant depression. We believe Wafermine has tremendous prospects given its potential to address these two prevalent conditions with significant medical need”,* said **Dr Janakan Krishnarajah, Chief Medical Officer of iX Biopharma**. iX Biopharma intends to partner with suitable pharmaceutical companies to advance Wafermine's clinical development program for the indications of pain and depression.

- The End -

### About iX Biopharma Ltd

iX Biopharma is a specialty pharmaceutical and nutraceutical company listed on the Catalist board of the Stock Exchange of Singapore (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.

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1. Dr. Neil Singla, a board-certified anesthesiologist, is the founder and Chief Scientific Officer of Lotus Clinical Research. He currently chairs the Analgesic Clinical Trials Shared/Special Interest Group at both the American Pain Society (APS) and the International Association for the Study of Pain (IASP). He also chairs the annual APS Conference on Analgesic Clinical Trials (APS-CAT).
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6. Wan, L. B. et al. Ketamine safety and tolerability in clinical trials for treatment-resistant depression. *J. Clin. Psychiatry* 76, 247–252 (2015). Available at: <https://pdfs.semanticscholar.org/4495/7147ba1a7f3eb6564c1105935e411d3780b5.pdf> Accessed May 2019.

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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.

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