

NEWS RELEASE

IX BIOPHARMA TO PARTICIPATE IN STUDY WITH WAFERMINE FOR TREATMENT OF BREAKTHROUGH PAIN IN ADVANCED CANCER PATIENTS

- ✓ Study is sponsored by Chris O'Brien Lifehouse cancer centre in Sydney, Australia
- ✓ Unlocks Wafermine's potential to address the global cancer pain market, estimated at US\$5.5B

Singapore, 15 June 2021 – Specialty pharmaceutical company **ix Biopharma Ltd** (SGX:42C) ("ix Biopharma" or, "the Company") is pleased to announce that it will supply its novel Wafermine sublingual ketamine wafers in a pilot study funded by Chris O'Brien Lifehouse, one of Australia's leading comprehensive cancer hospitals in Camperdown, Sydney. The study will evaluate the efficacy, acceptability, safety and tolerability of Wafermine administered as a first-line treatment for patients with advanced cancer suffering from moderate to severe pain.

The study is a prospective double-blind randomised placebo-controlled repeated cross-over trial and will be carried out at 2 sites, Chris O'Brien Lifehouse cancer centre and Royal Prince Alfred Hospital. It will enrol 32 adult patients with locally advanced or metastatic cancer who experience moderate to severe pain associated with cancer diagnosis requiring ongoing opioid analgesia. The study objectives include the measurement of pain severity, pain impact, side effects and quality of life.

The study will be led by Dr Yi-Ching Lee, Consultant Pain Specialist in Chris O'Brien Lifehouse & Royal Prince Alfred Hospital. **Dr Lee said**, "*We have been using sublingual ketamine at Royal Prince Alfred Hospital to treat patients with refractory pain effectively. After reviewing Wafermine's study data to-date and our own clinical experience with sublingual ketamine, we believe that Wafermine has the potential to be used effectively to treat breakthrough cancer pain. The results of this study will assist in the conduct of a definitive trial in guiding physicians on the use of Wafermine to treat cancer pain, which is a condition with significant unmet medical need.*"

A large number of patients in the community suffer from poorly controlled pain associated with advanced cancer. Opioid based medication has been the main treatment for pain, however studies show that more than one third of patients, particularly those with advanced cancer, still experience moderate to severe pain^{1,2}.

Ketamine is clinically well established in the management of moderate to severe acute pain, with good evidence for reduction in pain scores, opioid requirements and postoperative nausea and vomiting. Ketamine is currently used as an off-label treatment for breakthrough cancer pain in Australia. However, the current intravenous (IV) route of administration of ketamine limits the drug's broader use in the community. In addition, IV ketamine may result in a severe side effect profile and hence be intolerable to cancer patients. By way of comparison, the benefit of using Wafermine, a sublingual ketamine wafer, is that it is easy to administer and has the potential for a better side effect profile, and therefore it may be better tolerated and more accessible by patients in the community setting.

¹ Portenoy, R. K. Treatment of cancer pain. The Lancet 377, 2236–2247 (2011).

² Van den Beuken-van Everdingen, M. H. J., Hochstenbach, L. M. J., Joosten, E. A. J., Tjan-Heijnen, V. C. G. & Janssen, D. J. A. Update on Prevalence of Pain in Patients With Cancer: Systematic Review and Meta-Analysis. J. Pain Symptom Manage. 51, 1070-1090.e9 (2016)

Based on the Australian Institute of Health and Welfare, the estimated number of cancer diagnosis in 2020 is close to 150,000³. 50% of these cancer patients and 66% of those with advanced cancer experience pain⁴. Globally, estimates from the International Agency for Research on Cancer (IARC), in 2018 put new cancer cases at 17 million⁵. The global cancer pain market generated US\$5.5 billion in 2018 and is projected to reach US\$7.5 billion by 2025, growing at a CAGR of 4.5% from 2018 to 2025⁶.

About Wafermine

Wafermine is a novel sublingual ketamine wafer developed using the Group's patented WaferiX sublingual delivery technology for the treatment of acute moderate to severe pain. It is estimated that there were approximately 120 million acute pain cases in the US, EU5 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 cases⁷.

Ketamine is a non-opioid drug which offers a valuable alternative to opioids for the treatment of pain. Ketamine is a NMDA antagonist which, unlike opioids, does not cause respiratory depression leading to death if misused. Wafermine has the potential to be used in substitution or as an adjunct to opioids addressing a large unmet clinical need.

Wafermine also has the potential to be developed for the treatment of depression. Ketamine is gaining ground as a rapidly acting treatment for major depression, which is the leading cause of disability worldwide. IV ketamine is currently used off-label to treat depression when other antidepressants are not effective.

About Chris O'Brien Lifehouse and Royal Prince Alfred Hospital

The Chris O'Brien Lifehouse in Sydney is a not-for-profit organisation, purpose built 125-bed comprehensive cancer centre located in Sydney, Australia and working in close partnership with Royal Prince Alfred Hospital and University of Sydney, caring for cancer patients independent of their private or public healthcare status. The hospital opened its doors to outpatients in November 2013 and inpatients in February 2015. The hospital provides a busy outpatient service and overall services approximately 60,000 patients per year. The hospital also houses a Clinical Trials Unit and a Psycho-oncology Research Unit of the local University, currently running over 100 clinical trials. It provides integrative oncology services offering complementary therapies and exercise programmes through already-established disciplines within the multi-disciplinary team.

³ Australian Institute of Health and Welfare. Australia's health 2020. (2020)

⁴ Shapiro, C. L. Cancer Survivorship. *N. Engl. J. Med.* 379, 2438–2450 (2018); and Haumann, J., Joosten, E. (Bert) A. & Everdingen, M. H. J. van den B. Pain prevalence in cancer patients: status quo or opportunities for improvement? *Curr. Opin. Support. Palliat. Care* 11, 99–104 (2017).

⁵ Global Cancer Facts and Figures, American Cancer Society, accessed at <https://www.cancer.org/research/cancer-facts-statistics/global.html#:~:text=According%20to%20estimates%20from%20the,9.5%20million%20cancer%20deaths%20worldwide>

⁶ "Cancer Pain Market by Type and Application: Global Opportunity Analysis and Industry Forecast 2018-2025", Allied Market Research, accessed at <https://www.alliedmarketresearch.com/press-release/cancer-pain-market.html>

⁷ Acute Pain - Market Insights, Epidemiology and Market Forecast to 2028, Research and Markets, 30 September 2019

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'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.

Contact for media:

Yee Chia Hsing

Director of Corporate Affairs

T: +65 6235 2270

E: chiahsing.yee@ixbiopharma.com

Eva Tan

Chief Commercial Officer

T: +65 62353212

E: eva.tan@ixbiopharma.com

Investor relations

Alvina Tan

Media & Investor Relations Consultant

T: +65 9787 7267

E: alvina.tan@arkadvisors.com.sg

This announcement has been prepared by the Company and its contents have been reviewed by the Company's Sponsor, UOB Kay Hian Private Limited (the "**Sponsor**"), for compliance with the relevant rules of the Singapore Exchange Securities Trading Limited (the "**SGX-ST**") Listing Manual Section B: Rules of Catalist.

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The contact person for the Sponsor is Mr. Lance Tan, Senior Vice President. The contact particulars are 8 Anthony Road, #01-01, Singapore 229957, telephone: (65) 6590 6881.