Incannex Completes Positive Pre-IND Meeting with US FDA on IHL-675A for Treatment of Rheumatoid Arthritis

Melbourne, Australia, July 26, 2022 – Incannex Healthcare Limited (Nasdaq: IXHL) (ASX: IHL), ('Incannex' or the 'Company') a clinical-stage pharmaceutical company developing unique medicinal cannabinoid pharmaceutical products and psychedelic medicine therapies for unmet medical needs, is pleased to announce that it has completed a constructive pre-Investigational New Drug Application ('pre-IND') meeting with the U.S. Food and Drug Administration ('FDA') for its proprietary drug product IHL-675A for treatment of rheumatoid arthritis ('RA').

IHL-675A is Incannex's proprietary combination product containing cannabidiol ('CBD') and hydroxychloroquine sulfate ('HCQ') for treatment of inflammatory disorders including RA. Incannex submitted a pre-IND meeting package to the FDA in June 2023. The meeting package included a description of the unique formulation developed by Incannex, an overview of the proposed clinical development plan and specific questions Incannex submitted on the regulatory requirements for opening an Investigational New Drug ('IND') application. Opening an IND is required to conduct trials in the United States and ensures that trials are designed so that they meet the data requirements necessary for FDA marketing approval.

In the written correspondence, FDA provided valuable, multidisciplinary feedback on the proposed clinical development of IHL-675A. Importantly, the FDA confirmed that no further nonclinical studies are needed for the IND application. The FDA also provided specific guidance on what is required for Incannex to submit an NDA via the 505(b)(2) pathway, whereby some of the information required for marketing approval is derived from published studies on the components of IHL-675A and/or the Agency's findings on safety and/or effectiveness for relevant listed drugs.

The FDA provided critical guidance on the proposed clinical development plan for IHL-675A. Incannex is incorporating this guidance into clinical trial designs and the overarching strategy for development of IHL-675A.

Chief Scientific Officer of Incannex, Dr. Mark Bleackley, said; "Feedback received from the FDA in the pre-IND meeting is highly valuable for the continued development of IHL-675A for treatment of rheumatoid arthritis. The agency's responses covered multiple aspects of our development strategy that will be incorporated into our clinical trial designs and research plans. We look forward to continuing to work with the FDA to ensure that the IHL-675A development program generates high quality data that addresses the requirements set forth by the agency."

About IHL-675A

IHL-675A comprises a combination of HCQ, an off-patent registered pharmaceutical drug, and CBD. HCQ is a disease modifying anti-rheumatic drug that regulates the activity of the immune system, which may be overactive in some conditions. HCQ can modify the underlying disease process, rather than simply treating the symptoms. Incannex has demonstrated that IHL-675A components, CBD and HCQ, act synergistically to inhibit production of key inflammatory cytokines in an *in vitro* study of human cells and in four distinct successful *in vivo* experiments using established models of inflammation.

Incannex has evaluated the results of these experiments and believe IHL-675A to be a multi-use drug candidate suitable for the prevention and treatment of inflammation, with an initial focus on rheumatoid arthritis, inflammatory lung conditions (acute respiratory distress syndrome, COPD, asthma, and bronchitis), and inflammatory bowel disease. The treatment of these indications has a combined global annual market size of exceeding US$125B per annum[1].

A Phase 1 clinical trial assessing the tolerability and pharmacokinetics has been completed. IHL-675A was well tolerated, with similar number of adverse events reported as for the reference listed drugs for CBD and HCQ, and no adverse events of concern. Analysis of blood samples collected from trial participants demonstrated that both CBD and HCQ are absorbed from IHL-675A with favourable pharmacokinetic profiles.

Incannex are currently conducting a Phase 2 clinical trial assessing IHL-675A in patients with rheumatoid arthritis at 8-10 sites in Australia and New Zealand. The trial will include 128 participants who meet the eligibility criteria. The study is designed to include patients who have on-going pain and reduced function while on stable treatment for their RA. Participants will be randomised to one of 4 arms: either IHL-675A, CBD alone, HCQ alone or placebo. The primary endpoint for the study is pain and function relative to baseline determined via the score on the RAPID3 assessment at 24 weeks. Participants will also record their pain and function outcomes daily, by completing questionnaires on pain, fatigue, joint stiffness and quality of life, using an electronic Patient Reported Outcomes device (similar to completing a questionnaire on a smart phone or tablet). The participants will attend monthly visits at the clinical trial site, where blood tests, and physical examinations will monitor additional safety and efficacy outcomes including inflammatory biomarkers. The trial will also include a sub-study examining joint damage via MRI. Subjects will be assessed for eligibility in the MRI study based on their Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) at screening.

HCQ is approved for treatment of rheumatoid arthritis and is used by a significant cohort of patients with the disease. Many patients are also reportedly using non-cGMP grade CBD to ameliorate their symptoms. The intention of Incannex is to undertake clinical trials for its proprietary fixed dose

[1] https://www.alliedmarketresearch.com/asthma-COPD-drug-market
https://www.alliedmarketresearch.com/rheumatoid-arthritis-RA-drugs-market#:~:text=The%20global%20rheumatoid%20arthritis%20drugs,pain%20and%20inflammation%20in%20joints
https://www.grandviewresearch.com/industry-analysis/inflammatory-bowel-disease-ibd-treatment-market#:~:text=The%20global%20inflammatory%20bowel%20disease,market%20over%20the%20forecast%20period

combination of HCQ and CBD to achieve FDA marketing approval for a pharmaceutical grade IHL-675A product that can be prescribed by a patient's doctor.

This announcement has been approved for release to ASX by the Incannex Board of Directors.

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About Incannex Healthcare Limited

Incannex is a clinical stage pharmaceutical development company that is developing unique medicinal cannabis pharmaceutical products and psychedelic medicine therapies for the treatment of obstructive sleep apnoea (OSA), traumatic brain injury (TBI) and concussion, lung inflammation (ARDS, COPD, asthma, bronchitis), rheumatoid arthritis, inflammatory bowel disease, anxiety disorders, addiction disorders, and pain, among other indications.

U.S. FDA approval and registration, subject to ongoing clinical success, is being pursued for each drug and therapy under development. Each indication under investigation currently has no, or limited, existing registered pharmacotherapy (drug) treatments available to the public and represent major global economic opportunities to Incannex and its shareholders.

Incannex has a strong patent filing strategy in place as it develops its products and therapies in conjunction with its medical and scientific advisory board and partners. The Company holds 19 granted patents and 29 pending patents. Incannex is listed on the Australian Stock Exchange (ASX) with stock code "IHL" and also has American Depository Shares listed on NASDAQ under code "IXHL".

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Forward-looking statements

This press release contains "forward-looking statements" within the meaning of the "safe harbor" provisions of the U.S. Private Securities Litigation Reform Act of 1995. These forward-looking statements are made as of the date they were first issued and were based on current expectations and estimates, as well as the beliefs and assumptions of management. The forward-looking statements included in this press release represent Incannex's views as of the date of this press release. Incannex anticipates that subsequent events and developments may cause its views to change. Incannex undertakes no intention or obligation to update or revise any forward-looking statements, whether as of a result of new information, future events or otherwise. These forward-looking statements should not be relied upon as representing Incannex's views as of any date after the date of this press release.

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