Date: July 13, 2023
Public Announcement (NASDAQ: IXHL) (ASX: IHL)

Incannex Receives HREC Approval for Phase 2 Clinical Trial Assessing IHL-675A for use in Treatment of Pain and Function in Rheumatoid Arthritis

Highlights:

- Incannex has received approval from HREC for the lead site, Emeritus Research, Camberwell, VIC for the *Phase 2, Blinded, Placebo Controlled Clinical Trial to Determine the Safety and Effect on Pain and Function of IHL-675A in Patients with Rheumatoid Arthritis.*
- The Phase 2 trial follows a successful Phase 1 trial where IHL-675A was observed to be well tolerated
- It follows animal study observations of IHL-675A substantially reducing inflammatory disease scores to a greater extent than hydroxychloroquine, a common long-standing prescription drug for rheumatoid arthritis with a considerable market profile
- This trial will be managed by Avance Clinical, an Australian and US CRO, who will engage 8-10 clinical trial sites across Australia and New Zealand, recruiting 128 patients in total.
- The trial will aim to assess the effect of IHL-675A on pain and function by utilising patient reported outcomes, disease scores and inflammatory biomarker analysis over a 24-week period.
- The results of the trial will establish the safety and efficacy of IHL-675A in rheumatoid arthritis patients and contribute to the combination rule assessment in a 505(b)2 new drug application dossier with FDA.

Melbourne, Australia, July 13, 2023 – 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 received approval from Bellberry Human Research Ethics Committee ('HREC') for the lead site, Emeritus Research, Camberwell, Victoria, for its Phase 2 clinical trial. The trial is pivotal in nature and will assess the safety and efficacy of IHL-675A, its proprietary anti-inflammatory combination drug product, in patients with rheumatoid arthritis ('RA').

The Phase 2 trial follows the successful Phase 1 clinical trial, results of which were released on 1 May, 2023, whereby both active pharmaceutical ingredients, cannabidiol ('CBD') and hydroxychloroquine sulphate ('HCQ') were absorbed from the Company's proprietary fixed dose combination product IHL-675A.

The drug product was also observed to be well tolerated, with no adverse events of concern. Prior to commencing clinical trials, Incannex observed positive results from an animal model of RA. IHL-675A was observed to be more effective at reducing arthritis across multiple assessments including clinical

score, paw volume, pannus score, total histology score and serum cytokine levels than the rodent equivalent of the standard dose of HCQ or equivalent doses of CBD.

The reduction in disease assessments achieved by IHL-675A was 1.06-3.52 times that observed for HCQ alone at the standard dose. These promising observations led the company to prioritise rapid clinical assessment, particularly given that HCQ, marketed as Plaquenil and generic equivalents, is a common long-standing treatment prescribed for RA with a considerable market profile.

The Phase 2 study, that has now been approved by HREC at the lead site Emeritus Research, Camberwell, Victoria, will assess the efficacy, safety and tolerability of IHL-675A compared to the respective component Active Pharmaceutical Ingredients (APIs), CBD and HCQ, and placebo. The treatments will be double blinded, meaning neither the investigators nor patients will know which treatment an individual is receiving.

The study will be managed by Avance Clinical, an Australian and US CRO (Avance). Recruitment of additional sites with experience in rheumatology clinical trials is ongoing, with the goal of 8-10 sites across Australia and New Zealand being included in the study.

The trial will include 128 participants who meet the eligibility criteria and 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.

The results of the trial will establish the safety and efficacy of IHL-675A in RA and will be a critical component of future regulatory applications, including contributing to the combination rule assessment in the FDA505(b)2 new drug application (NDA) dossier.

Incannex Chief Scientific Officer Dr Mark Bleackley said: "HREC approval for the Phase 2 clinical trial is a key step in the development of IHL-675A for treatment of pain and reduced function associated with rheumatoid arthritis. We look forward to working with Emeritus and Avance to assess the effect of IHL-675A in this patient population."

About IHL-675A

IHL-675A comprises a combination of HCQ, an expired 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.

A Phase 1 clinical trial assessing the tolerability and pharmacokinetics has completed patient dosing with no adverse events of concern reported. The pharmacokinetic data is currently being analysed.

The treatment of these indications has a combined global annual market size of exceeding US$125B per annum[1]. IHL has completed a pre-IND meeting with the FDA to discuss the regulatory pathway for the development of IHL-675A in the United States and plan to open INDs for each of the three indications. FDA agreed that marketing applications for IHL-675A should be 505(b)(2) applications due to the existence of certain safety and efficacy information on the active ingredients of IHL-675A originating from historical studies that we are entitled to use in a new drug application.

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 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.

Emeritus Research

Emeritus Research is a group of private clinical trials sites that successfully delivers clinical trials in all therapeutic areas outside of oncology, currently based in Melbourne Victoria and Sydney New South Wales. All Emeritus Research sites conduct First in Human (FIH) Phase I to Phase IV trials in their out-patient facilities. With versatile private sites Emeritus Research can quickly scale up or down resourcing, implement new procedures and determine the best approach to successfully execute clinical trials. Each site within the Emeritus group is centrally managed to provide continuity between site quality, start-up, recruitment, and trial conduct.

Avance Clinical

Avance Clinical is the largest premium full-service Australian and North American CRO delivering quality clinical trials, with globally accepted data, in Australia, New Zealand and the US for international biotechs. The company's clients are biotechs in their drug development phases that need fast, agile, and adaptive solution-oriented clinical research services.

Frost & Sullivan Awards

Avance Clinical, a Frost & Sullivan Asia-Pacific CRO Market Leadership Award recipient for the past three years, has been providing CRO services in the region for more than 26 years.

Pre-clinical through to Phase I and Beyond

Avance Clinical offers pre-clinical consultancy services with their experienced ClinicReady team right through to Phase I and beyond clinical services leveraging significant Government incentive rebates of up to 43.5% and rapid start-up regulatory processes that are available in Australia.

With experience across more than 110 therapeutic indications, Avance Clinical can deliver world-class, high-quality, internationally accepted data suitable for FDA and EMA review.

Technology

Avance Clinical uses state-of-the-art technology and gold-standard systems across all functional areas to provide clients with the most effective processes. Medidata, Oracle, Zelta, Veeva and Medrio are just some of Avance's technology partners.

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

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Reference:

[1]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

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 30 pending patent applications. Incannex is listed on the Australian Stock Exchange (ASX) with stock code “IHL” and 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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