Date: February 28, 2023
Public Announcement (NASDAQ: IXHL) (ASX: IHL)

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

Highlights:

- Incannex has commenced a *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, and animal studies whereby IHL-675A was observed to reduce inflammatory disease scores to a greater extent than hydroxychloroquine, a common long standing prescription drug for rheumatoid arthritis.
- The trial will be managed by Avance Clinical, an Australian and US contract research organisation, who will engage 8-10 clinical trial sites across Australia and New Zealand, recruiting 120 patients in total.
- The trial will 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. There will be an option for trial participants to participate in an extension study following the trial.
- Patients, who meet the criteria for joint damage, may also be included in an magnetic resonance imaging assessment sub-study.
- The results of the trial will establish the safety and efficacy of IHL-675A and contribute to the combination rule assessment in a FDA505(b)2 new drug application dossier.

Sydney, Australia, February 28, 2023 – Incannex Healthcare Limited (Nasdaq: IXHL) (ASX: IHL), ('Incannex' or the 'Company') a pharmaceutical company developing proprietary medicinal cannabinoid products and psychedelic medicine therapies for unmet medical needs, is pleased to announce that it has commenced a Phase 2 clinical trial to assess the safety and efficacy of its proprietary anti-inflammatory combination drug IHL-675A in patients with rheumatoid arthritis ('RA'). IHL-675A is a proprietary fixed dose combination drug comprising cannabidiol (CBD) and hydroxychloroquine ('HCQ').

This Phase 2 clinical trial follows the successful Phase 1 clinical trial whereby IHL-675A was 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 than a standard dose of HCQ 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 a standard dose of HCQ, or equivalent dose of CBD.

The reduction in disease assessments achieved by IHL-675A were 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 of IHL-675A, particularly given that HCQ, marketed as Plaquenil and generic equivalents, is a common long-standing treatment prescribed for RA.

The Phase 2 trial now commenced 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 trial will be managed by Avance Clinical, an Australian and US CRO (Avance), who will identify and onboard 8-10 clinical trial sites with expertise in RA to conduct patient recruitment and assessments. Avance will manage the sites and study conduct, ensure that the data is of necessary quality and undertake analysis of data collected across all trial sites.

The Phase 2 trial will include 120 participants who meet the eligibility criteria. Participants will be randomised to one of four arms: either IHL-675A, CBD alone, HCQ alone or placebo. The primary endpoint of the trial 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 an electronic tablet).

The trial 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 magnetic resonance imaging ('MRI'). Subjects will be assessed for eligibility in the MRI study based on their Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) at screening.

Post completion of the 24-week randomisation period, there will be an option for trial participants to roll over into the open label extension study, where all eligible participants will receive IHL-675A for a further 24 weeks, regardless of the initial treatment arm allocated in the first 24 weeks.

The results of this study will establish the safety and efficacy of IHL-675A in rheumatoid arthritis 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: "This trial is a key milestone in the IHL-675A development program. We are excited to continue the development of this drug product to determine whether the remarkable preclinical efficacy we observed for IHL-675A in an animal disease model for arthritis is also seen to a similar extent in humans. Arthritis is a disease that negatively impacts the well-being of millions of people worldwide and this trial is a big step toward Incannex potentially improving quality of life for these patients. We look forward to continuing to build our research relationship with Avance Clinical, who did an outstanding job managing the Phase 1 clinical trial assessing the tolerability and pharmacokinetics of IHL-675A in healthy volunteers."

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.

Avance Clinical

Avance Clinical is the largest full-service Australian and US CRO specializing in delivering quality clinical trials, with globally accepted data, in Australia, New Zealand and the US. Avance Clinical, a Frost & Sullivan Asia-Pacific CRO Market Leadership Award recipient, has been providing CRO services in the region for the past 24 years. The company's clients are biotech companies in their early phases of drug development that need fast, agile, and adaptive solution-oriented clinical research services. Avance Clinical offers pre-clinical services with their experienced ClinicReady team from early to late phase leveraging significant Government incentive rebates of up to 43.5% and rapid start-up regulatory processes.

With experience across more than 110 indications the CRO can deliver world-class results and high-quality internationally accepted data for FDA and EMA review. Avance Clinical delivers customised solutions designed around specific client needs rather than a one size fits all approach.

[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

As a company, Avance Clinical has focused on state-of-the-art technology and systems across all functional areas to provide clients with the most effective processes. Medidata, Oracle, and Medrio are just some of Avance Clinical's trusted technology partners.

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 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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