Date: 23rd November 2020
ASX Announcement (ASX: IHL)

Positive *In vivo* results confirm strong synergistic activity of IHL-675A to inhibit inflammation

***In vivo* examination confirms previously announced *in vitro* data demonstrating that IHL-675A exhibits stronger anti-inflammatory properties than cannabidiol alone; engages Camargo Pharmaceutical Services to call a Pre-IND meeting with the FDA**

Highlights:

- IHL-675A components, cannabidiol and hydroxychloroquine, act synergistically to inhibit production of key inflammatory cytokines in *in vivo* studies
- IHL-675A outperformed CBD alone significantly as presented in Appendix 1, Table 1
- IHL-675A outperformed the predicted cytokine inhibition based on the activity of each drug alone by 26% to 81% across the five analysed cytokines after 2 hours
- Incannex and Camargo Pharmaceutical Services LLC will conduct a Pre-IND meeting with the FDA to explore the fastest pathway for registration of IHL-675A
- Incannex anticipates to be granted an expedited Pre-IND meeting due to the Company's intention to submit a FDA Emergency Use Authorisation request for patients with COVID-19
- Incannex has expanded its provisional patent protection to cover the treatment of a range of other inflammatory diseases that represent broad potential market opportunities for the Company, which are currently being evaluated.

Clinical stage cannabinoid development company, Incannex Healthcare Limited (ASX: IHL, 'Incannex' or the 'Company'), is pleased to announce that it has received further positive results from Eurofins (Taiwan) in relation to the anti-inflammatory potency and synergistic activity of IHL-675A in preclinical *in vivo* (animal) studies. The potent anti-inflammatory activity of IHL-675A makes it an excellent candidate for prevention and treatment of sepsis associated acute respiratory distress syndrome ("SAARDS").

SAARDS is caused by a hyper-inflammatory response to infections and has high patient mortality. It is a leading cause of mortality in patients with COVID-19[1]. Other common infections that can lead to sepsis and SAARDS are, lung (e.g. influenza), kidney, gut and skin infections.

Overview

IHL-675A comprises cannabidiol ('CBD') and hydroxychloroquine ('HCQ') and various fixed dose combinations of CBD and HCQ were used to assess the anti-inflammatory potency of IHL-675A. Incannex previously reported the synergistic anti-inflammatory activity of CBD and HCQ *in vitro* using human peripheral blood mononuclear cells from two donors. In those studies, IHL-675A outperformed cytokine inhibition by CBD by 109% to 767% after 24 hours from drug administration across a range of inflammatory cytokines. These *in vitro* results (released in announcement titled, "Strong anti-

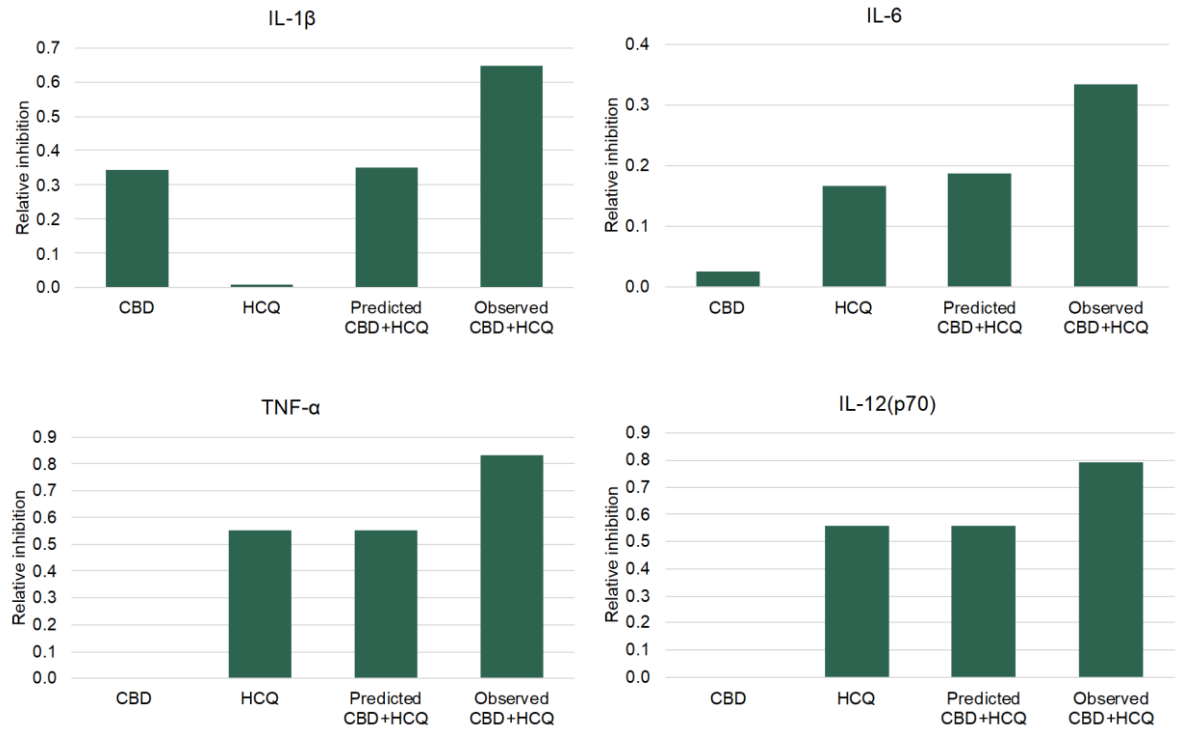
inflammatory action from IHL-675A" on 05 November 2020) have been validated *in vivo*; studies that were conducted to assess the method of action of IHL-675A in a complex living organism.

After receiving positive *in vitro* and *in vivo* results, Incannex has expanded its IP strategy to pursue patent protection for the treatment of broad range of other inflammatory diseases that represent broad potential market opportunities for IHL that are currently being evaluated.

Results

The results of the *in vivo* study are presented in Figure 1, and Appendix 1, showing the optimal fixed dose IHL-675A combination assessed for each cytokine in 11 groups of 10 mice. The bars noted as 'Predicted CBD + HCQ' represent IHL's expectation based on the activity of each drug alone. The observed results from the study significantly exceeded the predicted results across the inflammatory cytokines analysed.

CBD and HCQ synergise to inhibit the production of inflammatory cytokines IL-1β, IL-6, TNF- α, IL-12(p70), and IFN- γ in a mouse model of LPS induced sepsis. The average Excess over Bliss ('EOB') scores ranged from 0.15-0.30. IHL-675A outperformed CBD alone significantly (as presented in Appendix 1, Table 1), across the five inflammatory cytokines. IHL-675A outperformed the predicted cytokine inhibition based on the activity of each drug alone by 26% to 81% across the five analysed cytokines after 2 hours.



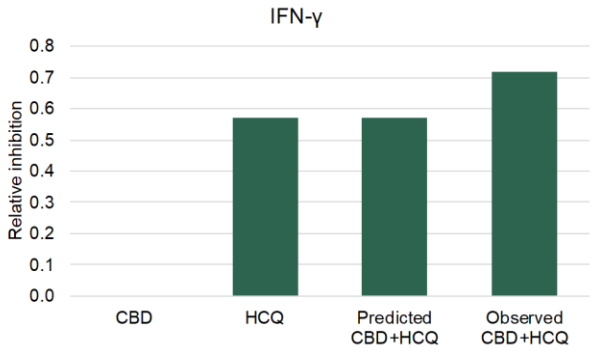


Figure 1. Synergistic anti-inflammatory activity of CBD and HCQ in a mouse sepsis model. The anti-inflammatory activity of the combination of CBD and HCQ was greater than that predicted using the Excess over Bliss method. The CBD+HCQ combination was synergistic at inhibiting release of IL-1β, IL-6, TNF- α, IL-12(p70), and IFN- γ.

*** See Appendix 1 for Methodology

Next Steps: Pre-IND meeting with the FDA regarding clinical trial development program

IHL has engaged Camargo Pharmaceutical Services LLC ('Camargo') to assist Incannex to conduct a Pre-Investigational New Drug (Pre-IND) meeting with the US Food and Drug Administration ('FDA') for the use of IHL-675A in the treatment of patients with SAARDS.

Since June 2020, IHL has announced successful results on the anti-inflammatory potency of IHL-675A from four separate preclinical studies. Camargo will report these results to FDA in a comprehensive information package, which will also outline future clinical development plans for IHL-675A.

The Pre-IND meeting will provide Incannex the ability to seek advice from the FDA on the most efficient development plan required to submit an IND application and initiate clinical studies in the United States. Specifically, Camargo will assist IHL to develop the nonclinical, clinical, pharmacological, and biopharmaceutical strategy to be proposed to FDA.

Camargo has previously advised that IHL-675A is a potential candidate for FDA Emergency Use Authorisation ('EUA') resulting from the COVID-19 Pandemic. At the Pre-IND meeting, Incannex and Camargo will seek guidance on its development plan necessary for an EUA request with FDA for the treatment of patients with SAARDS caused by COVID-19 viral infections (*SARS-CoV-2 viral infections)* in the United States. Furthermore, Incannex anticipates to be granted an expedited Pre-IND meeting due to the Company's intention to submit a FDA Emergency Use Authorisation request for patients with COVID-19.

About Camargo

Camargo is a leading global strategy, regulatory, and development partner for emerging to mid-tier biopharma companies. Camargo specialises in complex development programs where no playbook exists,

with integrated solutions to reach milestones with speed and capital efficiency. Camargo has experience in complex development programs and accelerated approval pathways, leveraging core expertise in areas such as the FDA 505(b)(2) new drug application pathway, oncology, rare disease, combination products, and digital therapeutics.

Founded in 2003, Camargo is proud to support clients in more than 35 countries around the world. For more about Camargo, visit camargopharma.com.

Camargo's accomplishments include:

- Over 200 FDA drug approvals
- Participation in 3-6 FDA meetings every month
- Participation in 1 in 5 recent 505(b)(2) NDAs
- 98%+ FDA concurrence rate for fulfilling NDA requirements
- Global reach of 25+ countries, excelling at providing guidance for the hybrid approval scheme in the European Union.

ENDS

The release of this announcement has been approved for issue by IHL's Board of Directors. For further details on the announcement, interested parties should contact:

Mr Joel Latham, Managing Director and Chief Executive Officer
P: +61 409 840 786
E: joel@incannex.com.au

References:

[1]https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2930628-0

About Incannex Healthcare Limited (ASX: IHL)

Incannex Healthcare Limited (IHL.ASX) is developing unique medicinal cannabis products for the treatment of Obstructive Sleep Apnoea (OSA), Traumatic Brain Injury (TBI)/Concussion, Acute Respiratory Distress Syndrome (ARDS) and Temporomandibular Joint Disorder (TMD). FDA registration, where being sought, is subject to clinical success.

Each indication represents major global markets and currently have no existing registered pharmacotherapy (drug) treatment, raising the possibility of patients receiving Government subsidies for products that demonstrate suitable safety and efficacy profiles in clinical trials.

There is an established body of research validating the hypothesis for the cannabinoids being used in Incannex's chosen therapeutic areas and IHL has a strong patent filing strategy (as announced "IHL files cannabinoid patent over IHL-216A for TBI" 04th October, 2019 and "IHL Files Patent over IHL-42X for OSA" 06th of December, 2019) as it develops its products in conjunction with its medical advisory board.

Further to its clinical programs, Incannex has its Australian license to import, export and distribute medicinal cannabis products and has launched a line of cannabinoid oil products. The cannabis-based oils are sold under Incannex's product supply and distribution agreement with Cannvalate Pty Ltd, which is the largest network of cannabis medicine prescribers in Australia and a major shareholder of IHL.

Website: www.incannex.com.au

Investors: investors@incannex.com.au

Appendix 1

Methodology

To determine whether CBD and HCQ synergise *in vivo,* a mouse sepsis model was employed. Mice from 11 groups of 10 mice, weighing 18-20 g were injected with CBD and HCQ both alone and in combination. After 1 hour the mice were injected with LPS to induce an inflammatory response. Each mouse in every cohort were assessed for each of the 5 inflammatory cytokines.

Two hours after LPS injection, blood was collected from the mice by cardiac puncture. Sera were processed and analysed for cytokine levels using a Luminex based assay. For synergy analysis, data was baseline subtracted using sham treated (no LPS injection) cytokine levels and then the values for each cytokine were normalized relative to maximum values across the groups.

The normalised values were used to calculate the relative inhibition where a value of 1 is complete inhibition and a value of 0 is no inhibition. Synergy was calculated using the Excess over Bliss (EOB) method, or the difference between the observed and predicted inhibition between the combination of drug concentrations where the predicted inhibition is determined using the equation $E_{pred\ A+B}=(E_A+E_B)-(E_AE_B)$. An EOB score of greater than 0 is indicative of synergy.

Table 1. Inhibition of cytokine production by CBD, HCQ and CBD+HCQ (IHL-675A) in a mouse model of sepsis.

	IL-1β	IL-6	TNF-α	IL-12(p70)	IFN-γ
CBD	0.34	0.03	0.00	0.00	0.00
HCQ	0.01	0.17	0.55	0.56	0.57
Predicted CBD+HCQ	0.35	0.19	0.55	0.56	0.57
Observed CBD+HCQ	0.65	0.33	0.83	0.79	0.72
EOB	0.30	0.15	0.28	0.24	0.15
% over Predicted	85.7%	73.7%	50.9%	41.1%	26.3%

EOB- "Excess over Bliss" (Observed CBD+HCQ – Predicted CBD+HCQ)