Date: 05th November 2020
ASX Announcement (ASX: IHL)

Strong synergistic activity of IHL-675A to inhibit inflammation

***In vitro* preclinical examination provides evidence that IHL-675A exhibits stronger anti-inflammatory properties than cannabidiol alone**

Highlights:

- IHL-675A components, cannabidiol and hydroxychloroquine, act synergistically to inhibit production of key inflammatory cytokines in *in vitro* preclinical studies
- IHL-675A outperformed cytokine inhibition by CBD by 109% to 767% after 24 hours from drug administration
- IHL-675A outperformed the predicted cytokine inhibition by the combination by 87% to 767% after 24 hours
- Incannex will use *in vitro* data on the IHL-675A combination to refine the parameters of the *in vivo* anti-inflammatory study, which has already commenced
- As a result of the strong anti-inflammatory results, Incannex has expanded its provisional patent protection to cover a range of other inflammatory diseases that represent potential additional opportunities for Incannex
- CBD oil is currently being used for a range of inflammatory diseases and Incannex will continue to assess the benefit of IHL-675A over CBD only treatments in future studies.

Clinical stage cannabinoid development company, Incannex Healthcare Limited (ASX: IHL, 'Incannex' or the 'Company'), is pleased to announce that it has received positive results from Eurofins (USA) on the anti-inflammatory potency and synergistic activity of IHL-675A against sepsis associated acute respiratory distress syndrome ('SAARDS') in preclinical *in vitro* studies.

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 has sought patent protection on the drug combination due to potential implications in the treatment of SAARDS, which is a hyper-inflammatory response to infections with high patient mortality, and the leading cause of mortality in patients with COVID-19[1].

Methodology

To test the anti-inflammatory potential of IHL-675A, human peripheral blood mononuclear cells ('PBMCs') were stimulated with bacterial lipopolysaccharide ('LPS'). PBMCs were incubated with a range of concentrations of CBD and HCQ in combination or each drug alone and then stimulated with LPS to induce an inflammatory response. The inflammatory response was assessed by measuring cytokine levels in the culture medium after 24 hours. A reduction in cytokine levels in response to drug treatment is indicative of anti-inflammatory activity.

Cytokine levels were averaged across three replicates from two donors and normalised to maximum values to yield a relative inhibition value. A relative inhibition of 1 is complete inhibition of cytokine release whereas a value of 0 is no inhibition of cytokine release.

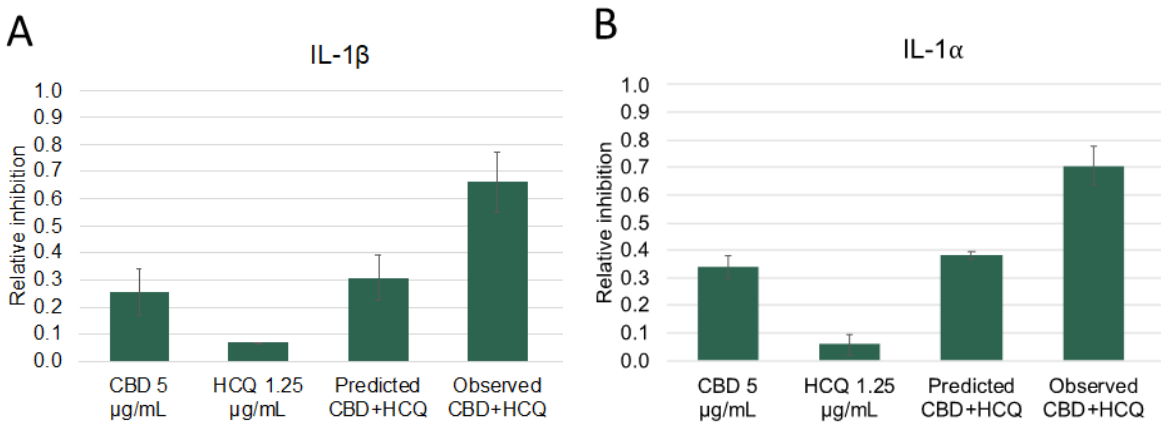
Anti-inflammatory synergy was determined using the standard scientific "Excess over Bliss" ('EOB') method where the predicted inhibition, as calculated using the formula $E_{pred\ A+B}=(E_A+E_B)-(E_AE_B)$, is subtracted from the observed inhibition to yield an EOB score. An EOB score of greater than zero indicates that the combination is synergistic.

Results

CBD and HCQ act synergistically to inhibit production of the assessed inflammatory cytokines IL-1β, IL-6, TNF-α, IL-1aα, and MIP-1α by PBMCs from the donors. The average EOB scores ranged from 0.32-0.57. IHL-675A outperformed CBD alone by 109% to 767% across the five cytokines IHL-675A outperformed the predicted cytokine inhibition based on the activity of each drug alone by 87% to 767% across the 5 cytokines.

The results in Figures A, B, C, D and E presented below, and Appendix 1, display the optimal fixed dose IHL-675A combination assessed for each cytokine. The bars noted as CBD+HCQ represent what our expectation was before the study commenced. The observed results from the study exceeded these in each inflammatory cytokine analysed.

Incannex will use this data to refine the parameters of the *in vivo* anti-inflammatory study that has already commenced. The results of the *in vivo* study will determine the next steps in the pursuit of an FDA "Emergency Use Authorisation" application.



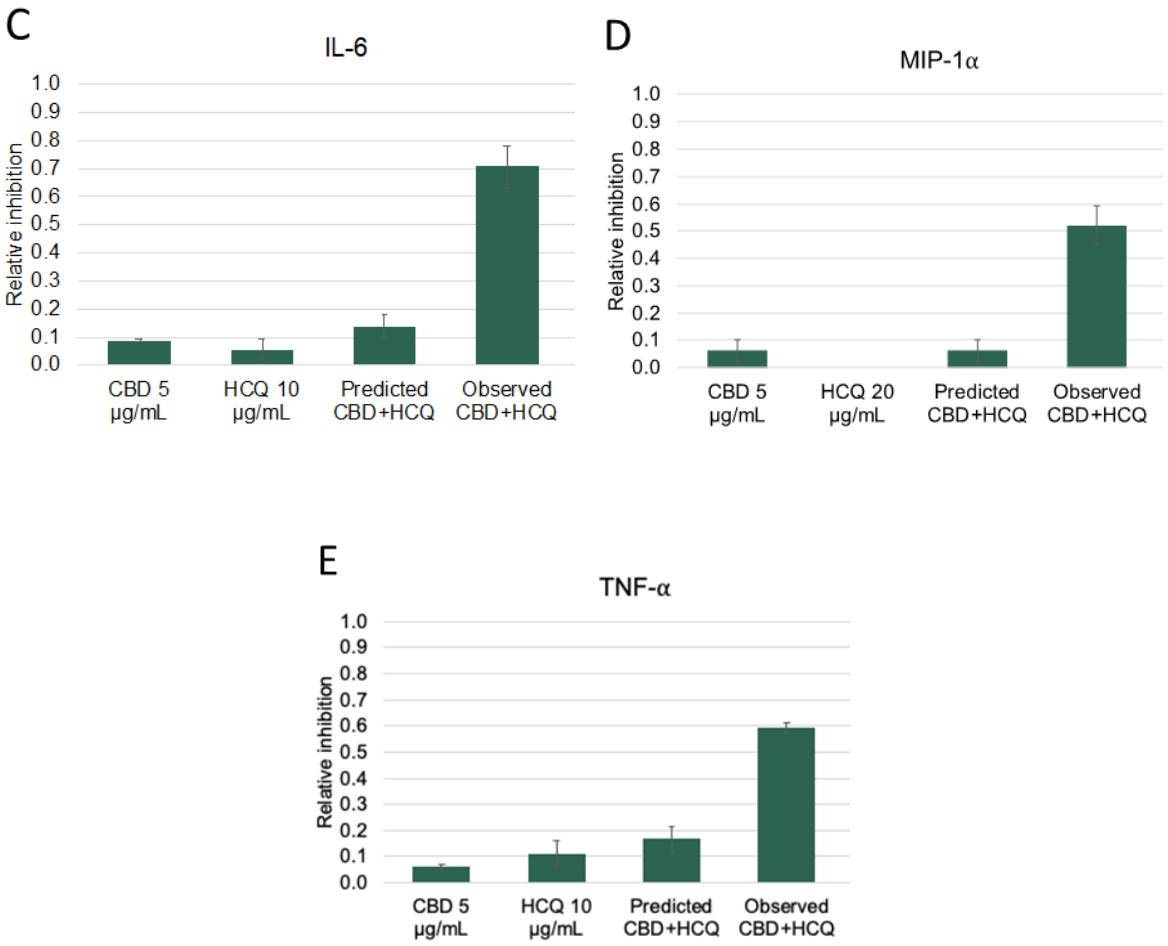


Figure 1. Inhibition of LPS-induced cytokine release from human PBMCs by CBD and HCQ. Data is presented is the average relative inhibition for the PBMC donors. Predicted inhibition by CBD+HCQ was calculated using the formula $E_{pred\ A+B}=(E_A+E_B)-(E_AE_B)$. Observed CBD+HCQ is the level of inhibition observed in the experiment. (A) IL-1b, (B) IL-1a, (C) IL-6, (D) MIP-1a, and (E) TNF-a. Error bars are standard error of the mean of the donors.

Expansion of Patent Position

As a result of the strong anti-inflammatory results, IHL has expanded its provisional patent protection to cover a range of other inflammatory diseases that represent potential additional opportunities for Incannex.

In vitro examination provides evidence that IHL-675A exhibits stronger anti-inflammatory properties than cannabidiol alone. CBD oil is currently being used for a range of inflammatory diseases and Incannex will continue to assess the benefit of IHL-675A over CBD only treatments in future studies.

CEO and Managing Director of Incannex Healthcare, Mr Joel Latham said; "As a company, we set out to gain evidence that our proprietary combination of CBD and HCQ would exhibit significant synergistic outperformance against the individual constituents.

Not only have we managed to achieve this, but we have significantly outperformed against our predictions of anti-inflammatory activity in the IHL-675A combination drug. Potentially, this could mean that IHL-675A is a better alternative to CBD oil products for inflammatory diseases, subject to further examination. Incannex has commenced its IHL-675A combination *in vivo* experiments as the next step in pursuit of our eventual ambition of FDA drug registration".

ENDS

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

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:

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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.

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Appendix 1

Table 1. Inhibition of cytokine release in LPS stimulated human PBMCs treated with CBD, HCQ and CBD+HCQ (IHL-675A)

		CBD 5 µg/mL	HCQ 1.25 µg/mL	Predicted IHL-675A	Observed IHL-675A	% over Predicted	EOB
IL-1β	Average	0.26	0.07	0.31	0.66	113%	0.35
	SEM	0.09	0.00	0.08	0.11		0.03
		CBD 5 µg/mL	HCQ 10 µg/mL	Predicted IHL-675A	Observed IHL-675A	% over Predicted	EOB
IL-6	Average	0.09	0.05	0.14	0.71	407%	0.57
	SEM	0.01	0.04	0.04	0.07		0.11
		CBD 5 µg/mL	HCQ 10 µg/mL	Predicted IHL-675A	Observed IHL-675A	% over Predicted	EOB
TNF-α	Average	0.06	0.11	0.17	0.59	247%	0.43
	SEM	0.01	0.05	0.05	0.02		0.07
		CBD 5 µg/mL	HCQ 1.25 µg/mL	Predicted IHL-675A	Observed IHL-675A	% over Predicted	EOB
IL-1α	Average	0.34	0.06	0.38	0.71	87%	0.32
	SEM	0.04	0.04	0.01	0.07		0.06
		CBD 5 µg/mL	HCQ 20 µg/mL	Predicted IHL-675A	Observed IHL-675A	% over Predicted	EOB
MIP-1α	Average	0.06	0.00	0.06	0.52	767%	0.46
	SEM	0.04	0.00	0.04	0.07		0.11

EOB- "Excess over Bliss" value (Observed CBD+HCQ – Predicted CBD+HCQ)
SEM- Standard error of the mean