Date: 26th August 2020
ASX Announcement (ASX: IHL)

Positive Results from *in vitro* Assessment of IHL-675A against Sepsis Associated Acute Respiratory Distress Syndrome

Highlights:

- The highest concentrations of Cannabidiol (20 μg/mL) and Hydroxychloroquine (50 μg/mL) each completely inhibited cytokine production by human peripheral blood mononuclear cells in response to bacterial lipopolysaccharide after 24 hours
- Cannabidiol and Hydroxychloroquine each displayed linear anti-inflammatory dose response curves
- Additional *in vitro* results from the experiment designed to assess the optimal fixed dose combination are expected soon, to be followed by Stage 2 *in vivo* testing
- SAARDS is a leading cause of mortality associated with lung, urinary tract, stomach, skin infections and COVID-19 coronavirus infection[5,6,7]

Clinical stage cannabinoid development company, Incannex Healthcare Limited (ASX: IHL, 'Incannex' or the 'Company'), is pleased to announce positive results on the anti-inflammatory activity of each constituent of IHL-675A against sepsis associated acute respiratory distress syndrome ('SAARDS').

An *in vitro* anti-inflammatory assay was performed to:

1. Define the dose response curves for both Cannabidiol ('CBD') and Hydroxychloroquine ('HCQ') and;
2. to define the range of study drug concentrations to inform assessment in the *in vitro* and *in vivo* combination studies.

In this assay, human peripheral blood mononuclear cells ('PBMCs') isolated from three different donors were each treated with CBD or HCQ in five different concentrations prior to the induction of an inflammatory response using bacterial lipopolysaccharide ('LPS'). An untreated control where only LPS was added was also included in the experiment.

After 24h incubation in the presence of the study drug and LPS, the culture medium was analysed for levels of key inflammatory cytokines using a Luminex based assay. Both CBD and HCQ displayed linear anti-inflammatory dose response curves. That is, with increasing concentrations of drug, the PBMCs produced less cytokines in response to stimulation with LPS.

The highest concentrations of CBD (20 μg/mL) and HCQ (50 μg/mL) each completely inhibited cytokine production by PBMCs in response to LPS. These results confirm the Company's expectations on the inflammation dampening effects of the study drugs, as extrapolated from other scientific literature[1,2]. The levels of three of the major inflammatory cytokines IL-1β, IL-6 and TNF-α are presented in the Appendix attached to this announcement.

The dose response curves identified in this experiment have allowed the Company to focus the combination assay on a narrower range of drug concentrations, which will permit IHL to attain more detailed data on the drug-drug interactions.

Chief Scientific Officer of Incannex Healthcare, Dr Mark Bleackley, said; "The potent anti-inflammatory activity of both CBD and HCQ is encouraging for the development of IHL-675A in prevention and treatment of sepsis associated ARDS.

Identifying the optimal combination of CBD and HCQ will contribute to the design of an IHL-675A fixed dose combination product whereby lower doses of drugs can achieve the same level of efficacy, minimising the potential for unwanted side effects and the creation of the defined IHL-675A product".

The next steps for the program include the receipt and assessment of the additional *in vitro* data, followed by the stage 2 *in vivo* study, which will assess the optimal fixed dose combination in an animal setting. Further details of the development plan are detailed in the announcement entitled "Positive Results from IHL-675 (ARDS) animal study" released to ASX platform on the 17th of July 2020.

IHL previously announced that it filed a provisional patent over IHL-675A for SAARDS on the on the 15th of April 2020. In that same announcement, IHL detailed that the clinical objective of SAARDS treatment is the reduction of the acute pulmonary inflammatory response, reversal of pulmonary oedema, and limitation of damage to the lung.

What is Sepsis Associated Acute Respiratory Distress Syndrome ('SAARDS')?

Sepsis occurs when the immune system overreacts to an infection, producing excessive levels of inflammatory cytokines, which are signalling molecules that attract immune cells[3]. Elevated levels of those cells secrete more cytokines, and this "cytokine storm" recruits even more immune cells, fuelling a cascading cycle that eventually damages host tissues and organs[4]. When the lungs are damaged by the cytokine storm hyperinflammatory response, SAARDS is said to be occurring. SAARDS is characterized by widespread inflammation of the lungs, often referred to as 'wet lung' or pneumonia, inhibiting the patient's ability to oxygenate blood[5].

SAARDS is a leading cause of mortality associated with COVID-19 coronavirus infection[5]. It is also a leading cause of mortality from other lung, urinary tract, stomach, and skin infections[6,7]. Existing patient outcomes are dismal meaning that there is significant unmet need in the treatment of SAARDS and has been for many decades. The best treatment continues to be the use of oxygen ventilators to treat symptoms of ARDS, but not the underlying inflammation feedback loop caused by the infection.

There is currently no registered pharmacotherapy (drug) treatment for SAARDS, however, the global medical community continues to investigate numerous drug treatments in its search for a new standard of care in response to COVID-19 coronavirus.

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:

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References:

[1] https://www.liebertpub.com/doi/10.1089/can.2018.0073
[2] https://pubmed.ncbi.nlm.nih.gov/9002011/?dopt=Abstract
[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6429642/
[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3294426/
[5] https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2930628-0
[6] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4823184/
[7] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30628-0/fulltext

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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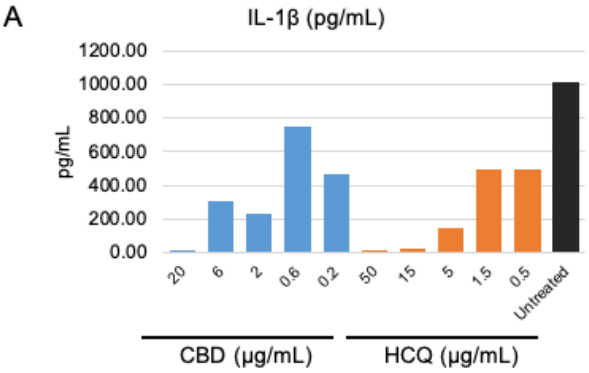
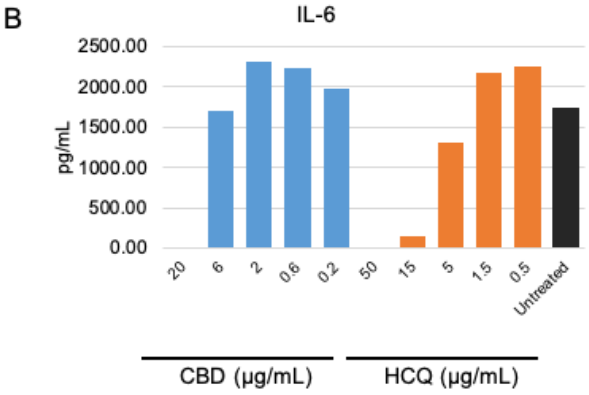
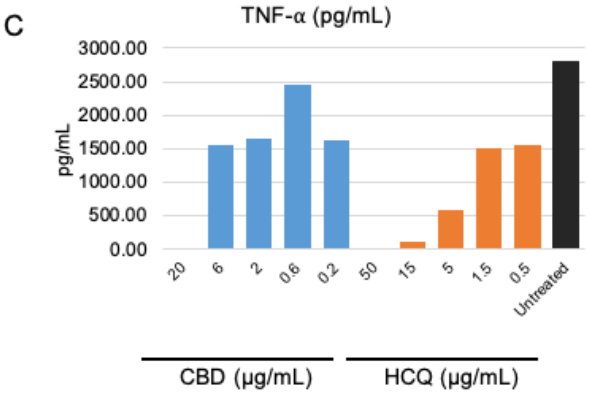
APPENDIX



		IL-1β (pg/mL)	SEM
CBD (μg/mL)	20	4.63	1.61
	6	306.49	118.68
	2	227.04	46.76
	0.6	749.07	242.72
	0.2	463.59	214.74
HCQ (μg/mL)	50	2.14	0.30
	15	18.58	10.23
	5	149.24	56.64
	1.5	494.90	248.86
	0.5	494.45	171.67
	Untreated	1004.16	568.96



		IL-6 (pg/mL)	SEM
CBD (μg/mL)	20	0.60	0.24
	6	1695.61	461.96
	2	2314.79	213.08
	0.6	2232.79	ND
	0.2	1974.98	21.89
HCQ (μg/mL)	50	6.33	1.88
	15	148.14	22.05
	5	1306.49	275.83
	1.5	2171.76	135.18
	0.5	2252.58	6.59
	Untreated	1727.11	38.82



		TNF-α (pg/mL)	SEM
CBD (μg/mL)	20	6.86	1.62
	6	1560.54	445.79
	2	1644.32	172.11
	0.6	2454.37	398.82
	0.2	1617.93	418.82
HCQ (μg/mL)	50	8.75	1.86
	15	109.17	37.94
	5	586.12	227.07
	1.5	1503.23	551.48
	0.5	1556.99	392.21
	Untreated	2787.73	1128.42

Figure 1. ***In vitro*** **anti-inflammatory activity of CBD and HCQ. Human PBMCs were incubated with CBD or HCQ at a range of concentrations and then stimulated with LPS to induce an inflammatory response. After 24 h, cytokine levels were assessed using a Luminex based assay. PBMCs from three donors were assessed independently. Data is the average cytokine level across the three PBMC donors for IL-1β and TNF-α but only two donors for IL-6 due to an error in data collection with one donor. (A) IL-1β, (B) IL-6 and (C) TNF-α.**