

Incannex initiates fifth research program following further positive *in vivo* results; IHL-675A for Inflammatory Bowel Disease

IHL-675A has been demonstrated to outperform CBD for anti-inflammatory properties in a pre-clinical in vivo study of inflammatory bowel disease; potential for IHL-675A to become a multi-use medication.

Highlights:

- IHL reports positive results from another *in vivo* study that has further assessed the anti-inflammatory capability of its proprietary IHL-675A; synergy between CBD and HCQ has yet again been demonstrated
- Results indicate that IHL-675A has superior anti-inflammatory activity compared to CBD and HCQ in a mouse model of Colitis; a form of inflammatory bowel disease
- IHL-675A demonstrated a reduction in the Colitis Index of 46%; CBD-only treatment achieved a reduction of 25% (Appendix 1, Table 1)
- Incannex has expanded target indications for IHL-675A to include Inflammatory bowel disease, as well as SAARDS, COPD, asthma and bronchitis
- Potential for IHL-675A to become a multi-use medication
- Incannex will now expand its discussions with research organisations and regulators to continue a clinical and regulatory strategy and these negotiations are ongoing.
- Inflammatory bowel disease is a growing patient problem that requires new, cost effective treatments¹.

Clinical stage pharmaceutical development company, Incannex Healthcare Limited (ASX: IHL, 'Incannex' or the 'Company'), is pleased to announce that it has received positive results from another *in vivo* (animal) study that has further assessed the anti-inflammatory capability of its proprietary IHL-675A, which is a drug that combines cannabidiol ('CBD') and hydroxychloroquine ('HCQ'). The discovery triggers the launch of a fifth clinical program to target inflammatory bowel disease ('IBD'); a new indication for Incannex with a global yearly addressable market size of more than US\$20B¹.

Incannex have demonstrated potent anti-inflammatory activity of IHL-675A in pulmonary conditions, making it an excellent candidate for prevention and treatment of inflammatory lung conditions, including sepsis associated acute respiratory distress syndrome ('SAARDS'), COPD, asthma and bronchitis.

Incannex's discovery that CBD and HCQ have synergistic anti-inflammatory activity increased the potential for IHL-675A beyond these conditions and into other inflammatory indications.

Incannex has assessed the anti-inflammatory effect of IHL-675A on IBD, using a mouse model of colitis. In this model, colitis is induced by intracolonic installation of 2,4,6-trinitrobenzene sulfonic acid (TNBS) in 50 % ethanol². The ethanol disrupts the intestinal barrier, permitting TNBS to interact with colon proteins.

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Interaction of TNBS with high molecular weight proteins renders them immunogenic. Administration of a single dose of TNBS in ethanol leads to an immune response and Th1 mediated inflammation. Inflammation in the colon causes damage that manifests in inconsistent stool formation and blood in the faeces.

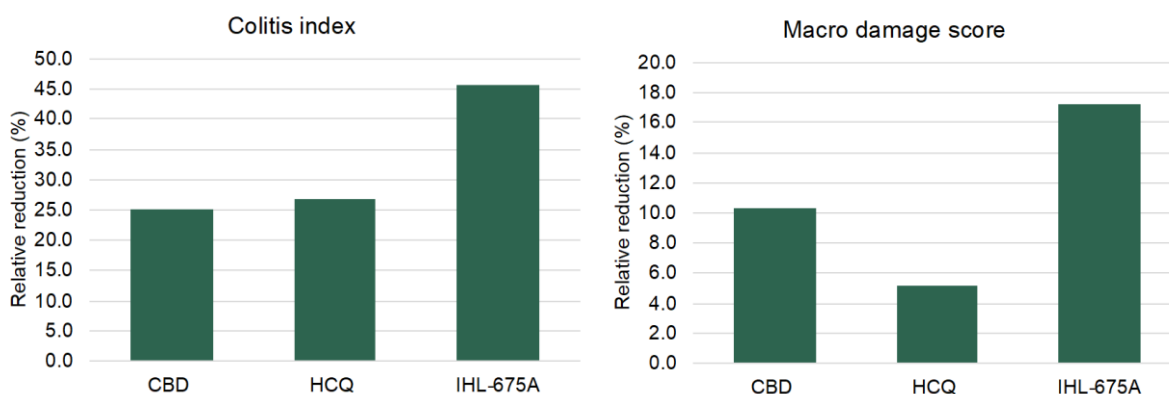
Overview

The experiment to assess the potential benefit of IHL-675A in the model of colitis used eleven groups of six mice. Mice were treated with IHL-675A, CBD or HCQ for four consecutive days after administration of TNBS/ethanol to induce ulcerative colitis. A vehicle treated group and sham group were included in the study. Stool consistency was monitored over the course of the experiment. On Day 5 mice were sacrificed, blood collected for cytokine analysis and the colon removed for analysis.

Endpoint measurements include stool consistency score (an ordinal scale that measures stool consistency with a higher number indicative of looser stools), colon weight, colon macroscopic damage score (an ordinal scale that combines adhesions, strictures, ulcers/inflammations and instances of wall thickening), colitis index³ (a composite scale from the histological examination of colon sections) and myeloperoxidase⁴ (an enzyme abundantly expressed in neutrophil granulocytes that contributes to inflammatory damage in IBD) levels in the colon tissue at day 5. The results from each of these endpoints were sham subtracted and the relative reduction was calculated.

Results

IHL-675A outperformed both CBD and HCQ at reducing the colitis index, macroscopic damage score, stool consistency score, colon to body weight ratio and myeloperoxidase (MPO) levels. These results indicate that IHL-675A has a benefit in a mouse model of ulcerative colitis greater than that of CBD or HCQ alone. In turn, this indicates that IHL-675A has potential for treating inflammatory bowel disease in humans.





IHL-675A potential

IHL-675A has outperformed CBD for its ability to dampen inflammation in four separate preclinical models of evaluation that are relevant to various indications in humans (SAARDS, COPD, asthma, bronchitis, IBD).

The Company continues to evaluate IHL-675A’s potential for use in other inflammation-based conditions and specifically for conditions over which some patients are using CBD as a primary or supplemental treatment to their condition. Any additional positive preclinical evaluations relevant to other diseases will also trigger additional programs.

As such, Incannex will now expand its discussions with research organisations and regulators to continue a clinical and regulatory strategy and these negotiations are ongoing. In particular, it is anticipated that the US Food and Drug Administration (‘FDA’) 505(b)(2) new drug application pathway will be applicable to the IBD indication. This is in addition to the FDA pre-IND submission undertaken for the SAARDS indication, as detailed in the announcement titled “Positive IHL-675A in vivo results and FDA Pathway” released on the 23rd of November 2020.

IHL has developed a global IP strategy to support its commercial objectives. IHL is continuously monitoring the results of its research and development program, with a view to identifying and protecting new IP that aligns with those commercial objectives.

By taking a global approach to its IP strategy, IHL intends to pursue patent protection in key global markets, including the US, Europe, Japan and Israel. This approach aligns with IHL’s regulatory strategy, including the proposed submission of a pre-IND meeting request to the FDA for IHL-675A products.

Inflammatory Bowel Disease

IBD is an umbrella term used to describe disorders that involve chronic inflammation of your digestive tract. Significant types of IBD include:

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- Ulcerative colitis. This condition involves inflammation and sores (ulcers) along the superficial lining of your large intestine (colon) and rectum.
- Crohn's disease. This type of IBD is characterized by inflammation of the lining of your digestive tract, which often can involve the deeper layers of the digestive tract.

Both ulcerative colitis and Crohn's disease are usually characterized by diarrhea, rectal bleeding, abdominal pain, fatigue and weight loss. IBD can be debilitating and sometimes leads to life-threatening complications.

The precise cause of inflammatory bowel disease remains unknown. Previously, diet and stress were suspected, but now doctors know that these factors may aggravate, but are not the cause, of IBD. One possible cause is an immune system malfunction. When your immune system tries to fight off an invading virus or bacterium, an abnormal immune response causes the immune system to attack the cells in the digestive tract, too.

The global IBD market is expected to reach US\$22.4B by 2026, growing at an expected CAGR of 4.4% from 2018 to 2026¹.

CEO and Managing Director of Incannex Healthcare, Mr Joel Latham said; “We know that CBD has been the focus of academic studies in relation to inflammation for some time. After a variety of our own pre-clinical studies, our proprietary IHL-675A combination CBD and HCQ drug may have the potential to be clinically relevant to a large variety of conditions, including those for which CBD has previously been a research target molecule for their treatment”.

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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About Incannex Healthcare Limited (ASX: IHL)

Incannex Healthcare Limited (IHL.ASX) is a clinical stage pharmaceutical development company developing unique medicinal cannabis pharmaceutical products and psychedelic medicine therapies for the treatment of Generalised Anxiety Disorder (GAD), Obstructive Sleep Apnoea (OSA), Traumatic Brain Injury (TBI)/Concussion and Acute Respiratory Distress Syndrome (ARDS). FDA registration, subject to ongoing clinical success, is being pursued for each product and therapy under development.

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

IHL has a strong IP 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) is continuously monitoring the results of its research and development program, with a view to identifying and protecting new IP that aligns with those commercial objectives as it develops its products and therapies 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 Incannex.

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Investors: investors@incannex.com.au

References:

¹<https://www.grandviewresearch.com/industry-analysis/inflammatory-bowel-disease-ibd-treatment-market#:~:text=The%20global%20inflammatory%20bowel%20disease,market%20over%20the%20forecast%20period>

²Antoniou E, Margonis GA, Angelou A, Pikouli A, Argiri P, Karavokyros I, Papalois A, Pikoulis E. 2016. The TNBS-induced colitis animal model: An overview. *Ann Med Surg* 11:9–15.

³Dieleman LA, Palmen MJ, Akol H, Bloemena E, Peña AS, Meuwissen SG, Van Rees EP. 1998. Chronic experimental colitis induced by dextran sulphate sodium (DSS) is characterized by Th1 and Th2 cytokines. *Clin Exp Immunol* 114:385–391.

⁴Chami B, Martin NJJ, Dennis JM, Witting PK. 2018. Myeloperoxidase in the inflamed colon: A novel target for treating inflammatory bowel disease. *Arch Biochem Biophys* 645:61–71.

Appendix 1

Table 1. Relative reduction in colitis assessments by IHL-675A, CDB and HCQ.

	Relative colon weight	Stool consistency score	Macro damage score	Colitis index	MPO
CBD	37	17	10	25	34
HCQ	29	0	5	27	0
IHL-675A	39	33	17	46	46
IHL-675A > CBD*	1.05x	1.94x	1.70x	1.84x	1.35x

*IHL-675A multiple of outperformance relative to CBD only treatment

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