Incannex

# IHL-675A

## Phase 1 clinical trial to assess safety and pharmacokinetics as a potential anti-inflammatory drug candidate

ASX Ticker: IHL | NASDAQ Ticker: IXHL

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Results Summary

# IHL-675A Phase 1 clinical trial

The 36 patient clinical trial demonstrates IHL-675A to be well tolerated, with no serious adverse events of concern.

About

# IHL-675A

IHL-675A is a cannabinoid combination drug comprising hydroxychloroquine sulphate ('HCQ') and cannabidiol ('CBD').

HCQ is a disease-modifying anti-rheumatic drug (DMARD) that works by calming a person's immune system.

CBD is a non-psychoactive phytocannabinoid derived from the cannabis plant, associated with anti-inflammatory and analgesic activity.

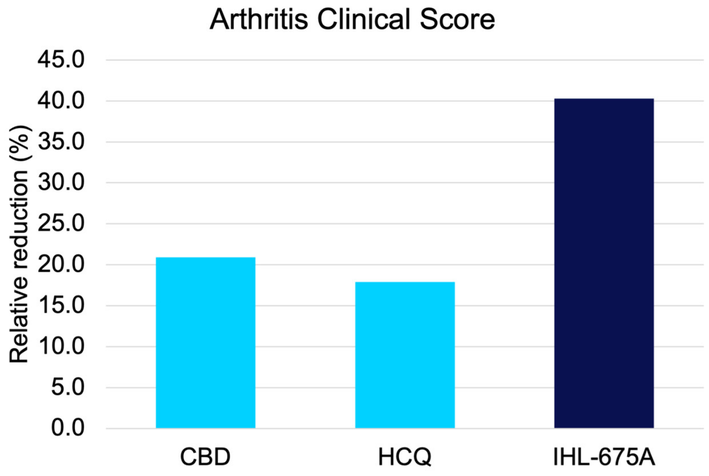
Incannex has demonstrated that IHL-675A components, HCQ and CBD act synergistically to inhibit production of inflammatory cytokines and reduce disease severity in animal models of:

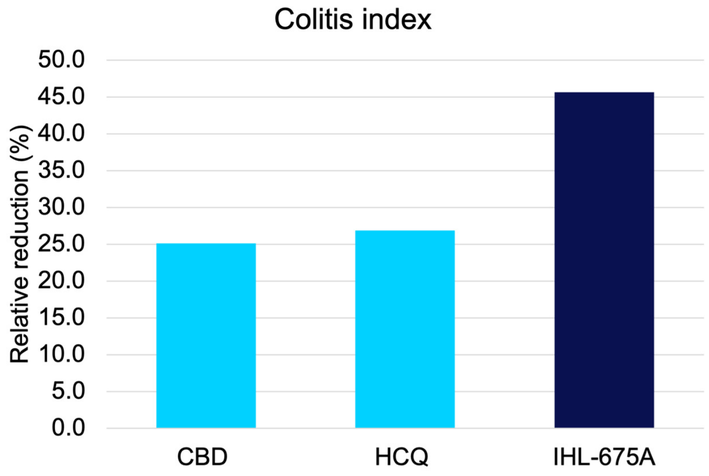
- Rheumatoid arthritis
- Inflammatory lung conditions
- Inflammatory bowel diseases

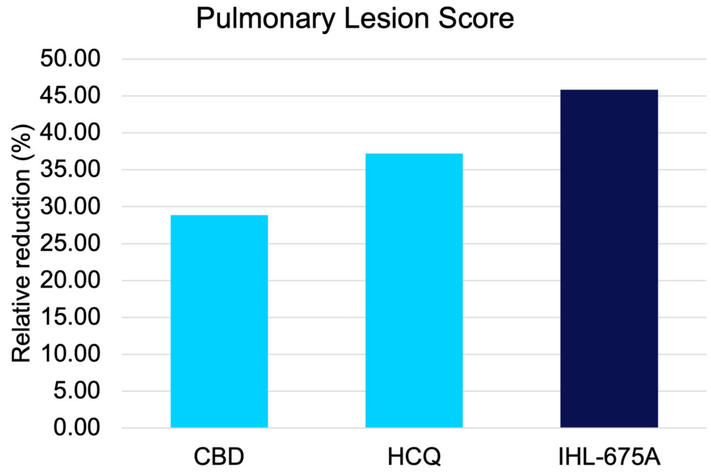
# IHL-675A
## Reducing disease severity in animal models



IHL-675A outperformed HCQ and CBD administered alone at reducing inflammatory disease scores — a strong efficacy signal demanding clinical assessment.



## Clinical development

# IHL-675A

- Animal disease model results were a major commercial signal: targeting the disruption of incumbent multi-billion dollar markets for diseases of inflammation.
- The addressable target markets exceed $125B per annum globally and include rheumatoid arthritis, COPD, asthma, bronchitis, colitis and Crohn's disease.
- IHL-675A Phase 2 clinical trial launched for patients with rheumatoid arthritis.
- Phase 2 trials for inflammatory lung conditions and inflammatory bowel disease are currently in planning.

## Addressable Market

**A$125B**

per annum globally

Including; Rheumatoid arthritis, COPD, Asthma, Bronchitis, Colitis and Crohn's disease

Phase 1 clinical trial

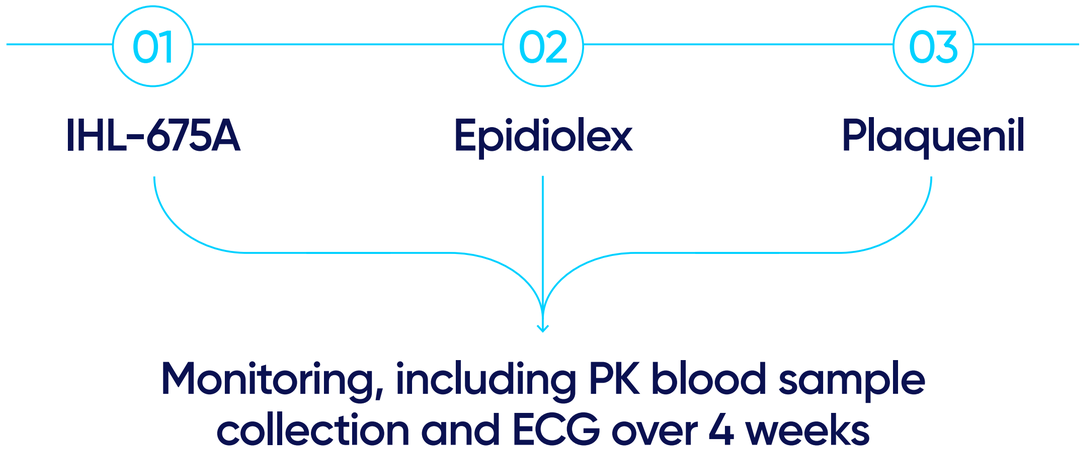
# IHL-675A
## First assessment in humans



### Aim

To assess the safety, tolerability and pharmacokinetics of IHL-675A compared to reference listed drugs for CBD and HCQ, marketed as Epidiolex and Plaquenil respectively, in healthy volunteers.

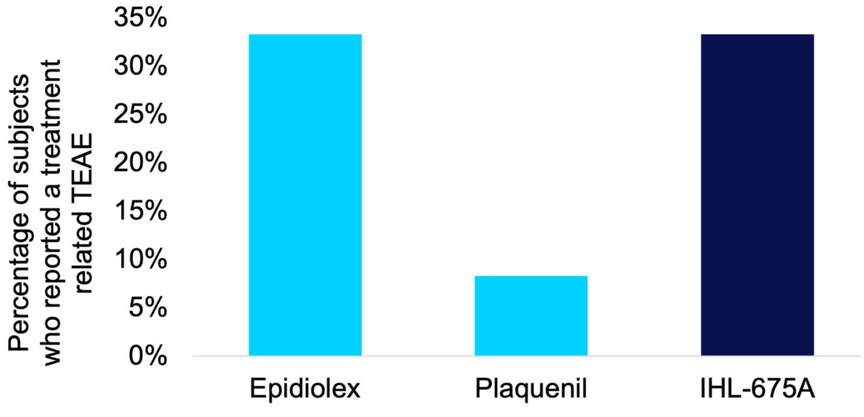
### Three-armed study with twelve patients per arm



# IHL-675A ⟶
# Safety/tolerability results

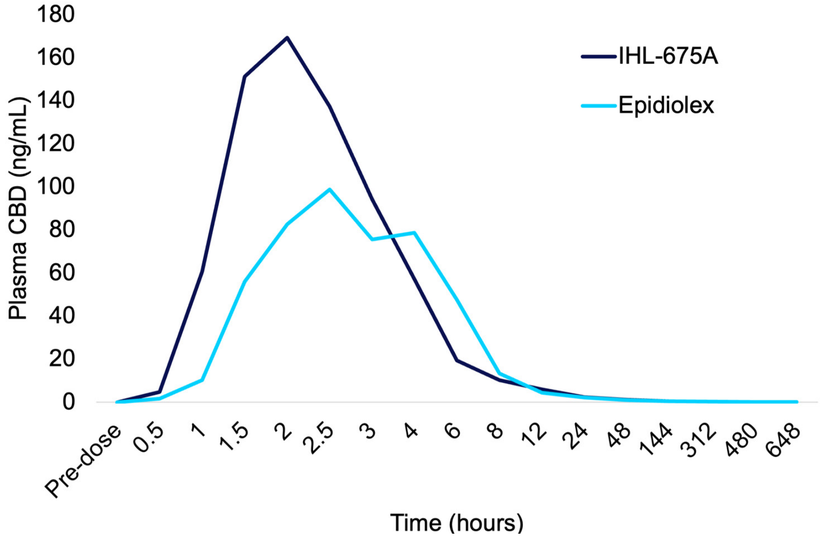


- No adverse events of concern.
- Adverse events were consistent with public reports for Epidiolex and Plaquenil.
- Treatment-related treatment emergent adverse events (TEAEs) included abdominal pain, dizziness, fatigue, frequent bowel movements, headache and somnolence.
- The number of TEAEs for IHL-675A was the same as Epidiolex.
- All TEAEs were mild in severity with the exception of one incident of abdominal cramps of moderate severity in the IHL-675A group, which resolved soon after onset.
- No cardiac related TEAEs were reported.



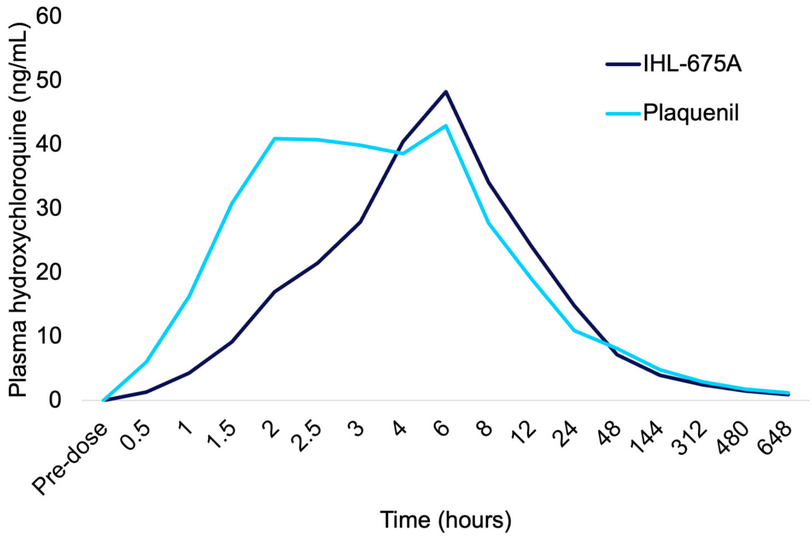
# Pharmacokinetics: CBD ⟶

- Compared to Epidiolex, CBD dosed in IHL-675A:
  - Reached a greater maximum concentration ($C_{max}$), 1.57 times higher
  - Was taken up more rapidly ($T_{max}$), 26 % faster
  - Was cleared more quickly ($T_{1/2}$), 13 % faster
  - Had a similar level of total exposure ($AUC_{inf}$)
- These differences are only trends at this point (p>0.05).
- Similar patterns were observed for major CBD metabolites 7-COOH-CBD and 7-OH-CBD.



# Pharmacokinetics: HCQ ⟶

- Compared to Plaquenil, HCQ from IHL-675A was:
  - Taken up more slowly ($T_{max}$), 46% slower
  - Reached a similar maximum concentration ($C_{max}$)
  - Had a similar rate of clearance ($T_{1/2}$)
  - Had a similar total exposure ($AUC_{inf}$)
- These differences are only trends at this point (p>0.05).
- Only low (average < 2 ng/mL) concentrations of HCQ metabolites desethylhydroxychloroquine, bisdesethylhydroxychloroquine and desethylchloroquine were detected at all points in the study.



# Conclusions

**01.**
IHL-675A is well tolerated in healthy volunteers.

**02.**
Adverse events for IHL-675A were consistent with what was observed, and has been publicly reported for Epidiolex and Plaquenil.

**03.**
Both active pharmaceutical ingredients, CBD and HCQ, are absorbed from IHL-675A.

**04.**
Trends in PK profiles indicate that the uptake of CBD may be more rapid for IHL-675A than Epidiolex and the uptake of HCQ may be slower for IHL-675A than Plaquenil.

**05.**
This could be advantageous for IHL-675A. CBD provides immediate relief for inflammation and pain whereas HCQ is a slower acting molecule and provides extended relief.

Next Steps

# Phase 2 Clinical Trials

01 **Commencement**

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.

02 **Engagement**

The trial is engaging up to 10 trial sites and recruiting 120 patients in total.

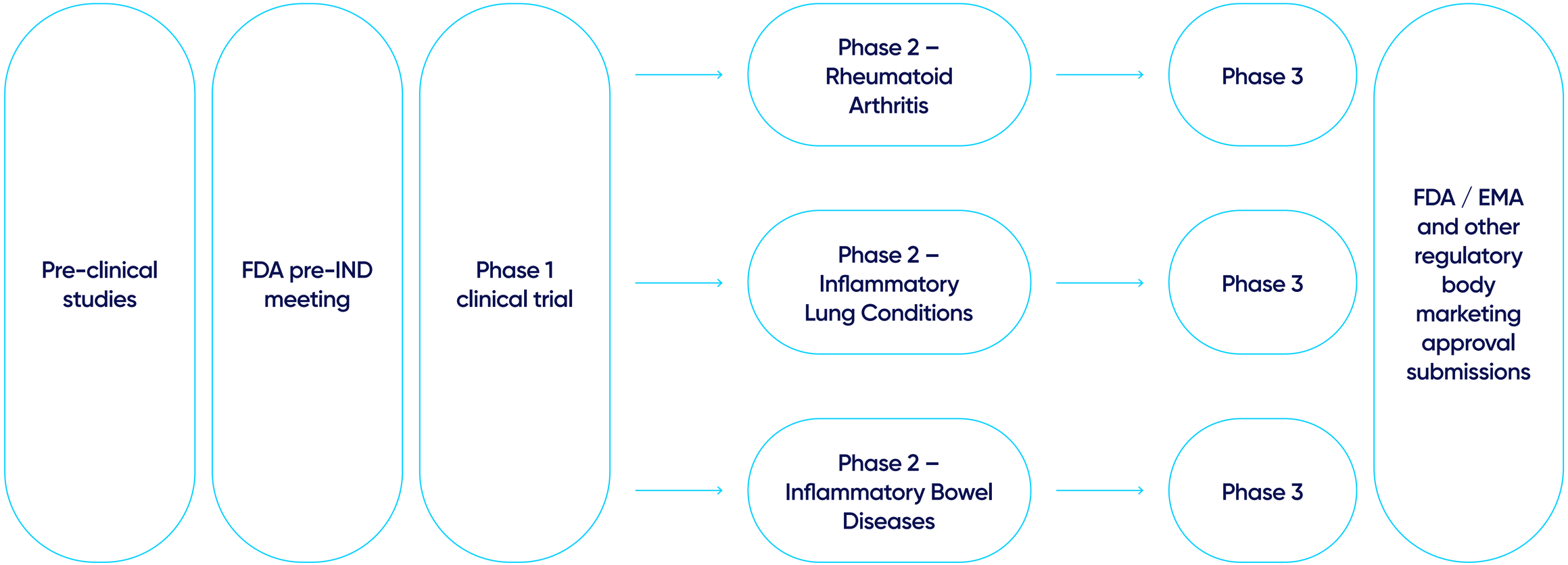
03 **Planning**

Planning of Phase 2 studies in patients with inflammatory bowel disease and lung inflammation is underway.

04 **Treatment**

The treatment of these three indications has a combined global addressable annual market size exceeding US$125B per annum.

# Clinical and Regulatory Progression



# CBD and metabolite PK results

| | | IHL-675A | | | | Epidiolex | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $C_{max}$ | $T_{max}$ | $AUC_{inf}$ | $T_{1/2}$ | $C_{max}$ | $T_{max}$ | $AUC_{inf}$ | $T_{1/2}$ |
| | | (ng/mL) | (hr) | (hr*ng/mL) | (hr) | (ng/mL) | (hr) | (hr*ng/mL) | (hr) |
| **CBD** | Mean | 207.04 | 2.13 | 841.08 | 220.17 | 131.89 | 2.88 | 725.9 | 231.22 |
| | SD | 117.44 | 0.91 | 358.63 | 53.85 | 61.92 | 1.21 | 223.98 | 56.45 |
| | Min | 72.6 | 1.02 | 391 | 113.84 | 45.6 | 1.5 | 355 | 144.41 |
| | Max | 472 | 4 | 1699 | 301.17 | 241 | 6 | 1121 | 305.88 |
| **7-OH-CBD** | Mean | 55.24 | 2.17 | 389.18 | 40.54 | 21.06 | 3 | 262.27 | 21.15 |
| | SD | 34.58 | 0.94 | 214.49 | 52.79 | 9.15 | 1.22 | 103.95 | 10.05 |
| | Min | 14.9 | 1.02 | 220 | 10.78 | 7.7 | 1.5 | 149 | 10.54 |
| | Max | 116 | 4 | 950 | 202.58 | 38.4 | 6 | 448 | 49.36 |
| **7-COOH-CBD** | Mean | 479.75 | 2.83 | 18753.9 | 167.87 | 362.17 | 4.97 | 16268 | 153.68 |
| | SD | 218.74 | 1.2 | 8979.02 | 95.47 | 299.63 | 1.3 | 11069.2 | 92.41 |
| | Min | 209 | 1.5 | 11445 | 46.03 | 116 | 2.5 | 4475 | 18.47 |
| | Max | 921 | 6 | 43714 | 332.65 | 1180 | 6.05 | 42018 | 317.68 |

# HCQ and metabolite PK results

*NA - metabolite not detected at levels sufficient to calculate PK parameter*

| | | IHL-675A | | | | Epidiolex | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $C_{max}$ | $T_{max}$ | $AUC_{inf}$ | $T_{1/2}$ | $C_{max}$ | $T_{max}$ | $AUC_{inf}$ | $T_{1/2}$ |
| | | (ng/mL) | (hr) | (hr*ng/mL) | (hr) | (ng/mL) | (hr) | (hr*ng/mL) | (hr) |
| HCQ | Mean | 54.71 | 5.59 | 2986 | 182.62 | 55.52 | 3.46 | 3430.8 | 251.6 |
| | SD | 23.85 | 2.51 | 1244.46 | 93.7 | 24.81 | 1.94 | 1104.38 | 73.65 |
| | Min | 22 | 2 | 800 | 35.68 | 26.1 | 1 | 2073 | 163.92 |
| | Max | 105 | 12.03 | 4217 | 311.57 | 124 | 6 | 5888 | 421.51 |
| DESETHYL-HYDROXY-CHLOROQUINE | Mean | 1.38 | 81.08 | NA | NA | 1.29 | 17.46 | NA | NA |
| | SD | 1.24 | 183.01 | NA | NA | 1.04 | 35.04 | NA | NA |
| | Min | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Max | 4.4 | 673.83 | 0 | 0 | 3.3 | 123.93 | 0 | 0 |
| THYL-CHLOROQUINE | Mean | 0.8 | 7.77 | NA | NA | 0.42 | 5.59 | NA | NA |
| | SD | 0.72 | 13.03 | NA | NA | 0.84 | 13.58 | NA | NA |
| | Min | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Max | 2 | 49.05 | 0 | 0 | 2.9 | 49.07 | 0 | 0 |
| BISDESETHYL-HYDROXY-CHLOROQUINE | Mean | 0 | 0 | NA | NA | 0 | 0 | NA | NA |
| | SD | 0 | 0 | NA | NA | 0 | 0 | NA | NA |
| | Min | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Max | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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