



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:

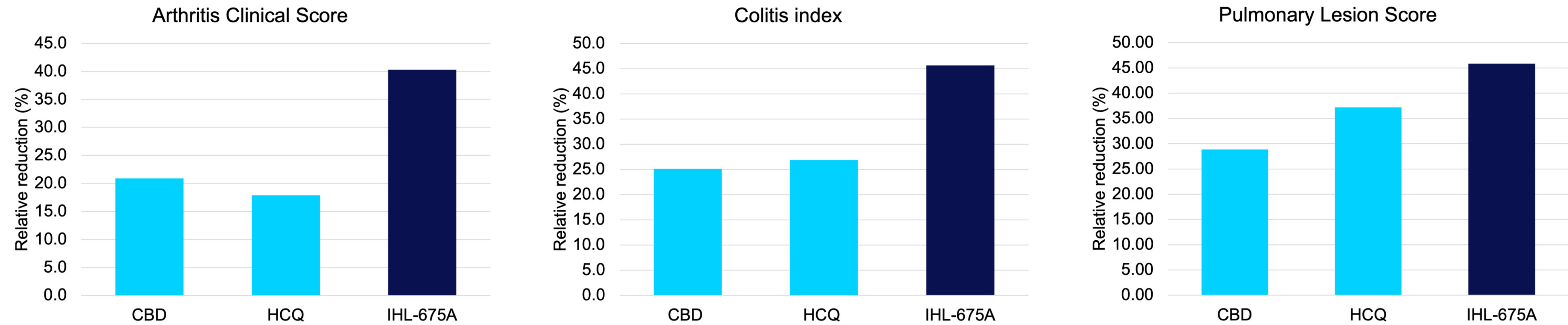
- Rheumatoid arthritis
- Inflammatory lung conditions
- Inflammatory bowel diseases

Performance Results

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

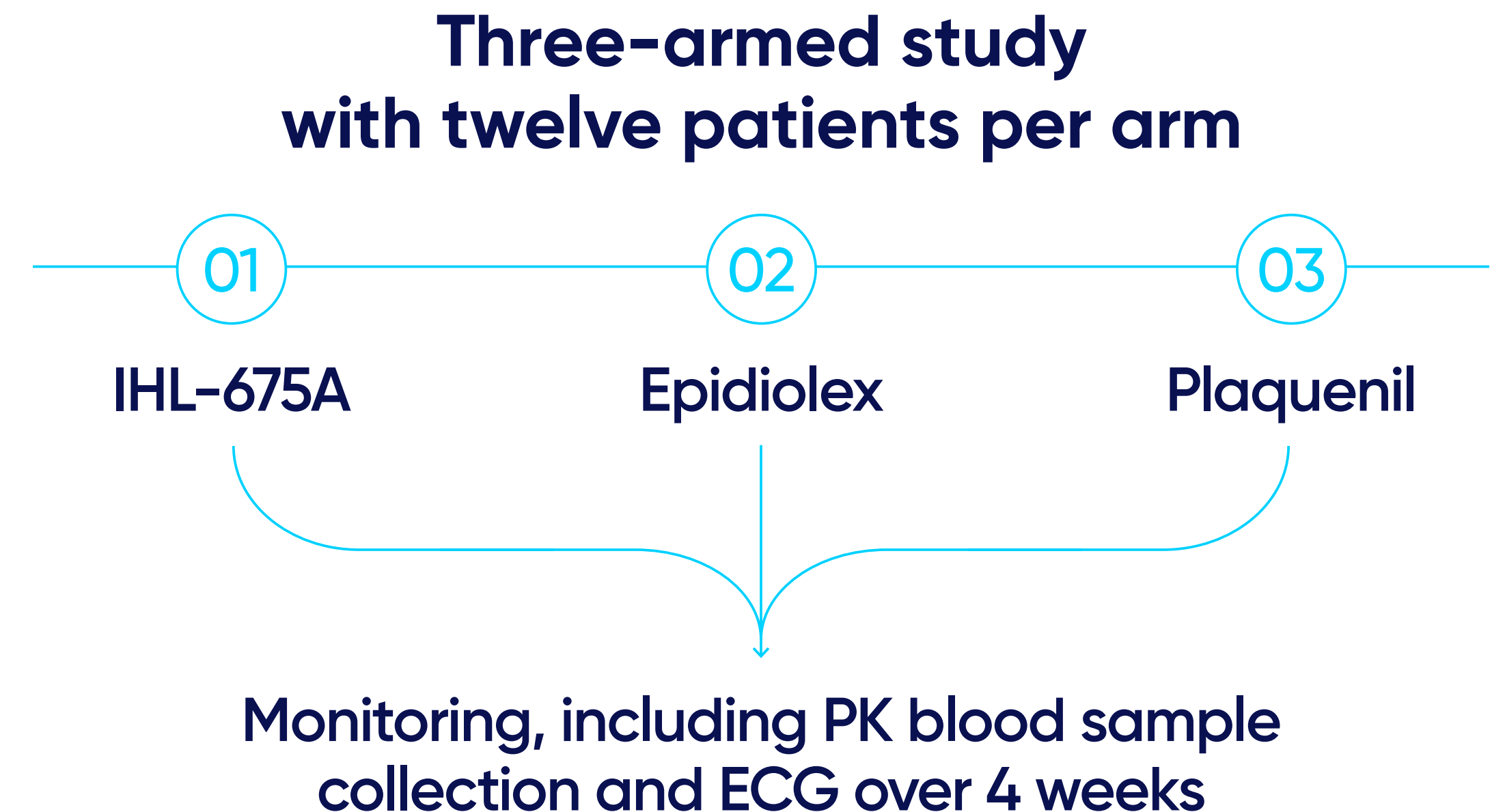
Including; Rheumatoid arthritis,
COPD, Asthma, Bronchitis, Colitis
and Crohn's disease

IHL-675A

First assessment in humans

Aim

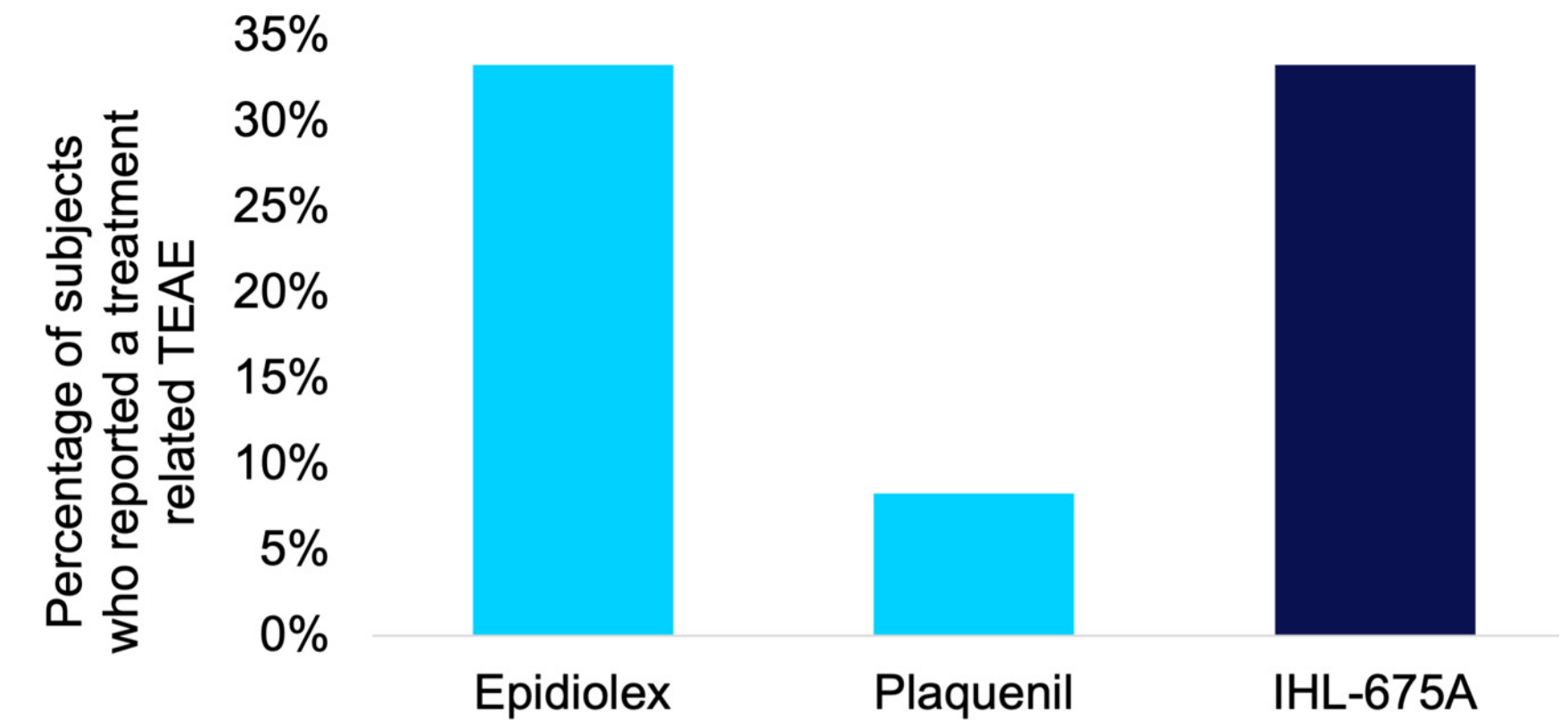
To assess the safety, tolerability and pharmacokinetics of IHL-675A compared to reference listed drugs for CBD and HCQ, marketed as Epidiolex and Plaquenil respectively, in healthy volunteers.



Results

IHL-675A → Safety/tolerability results

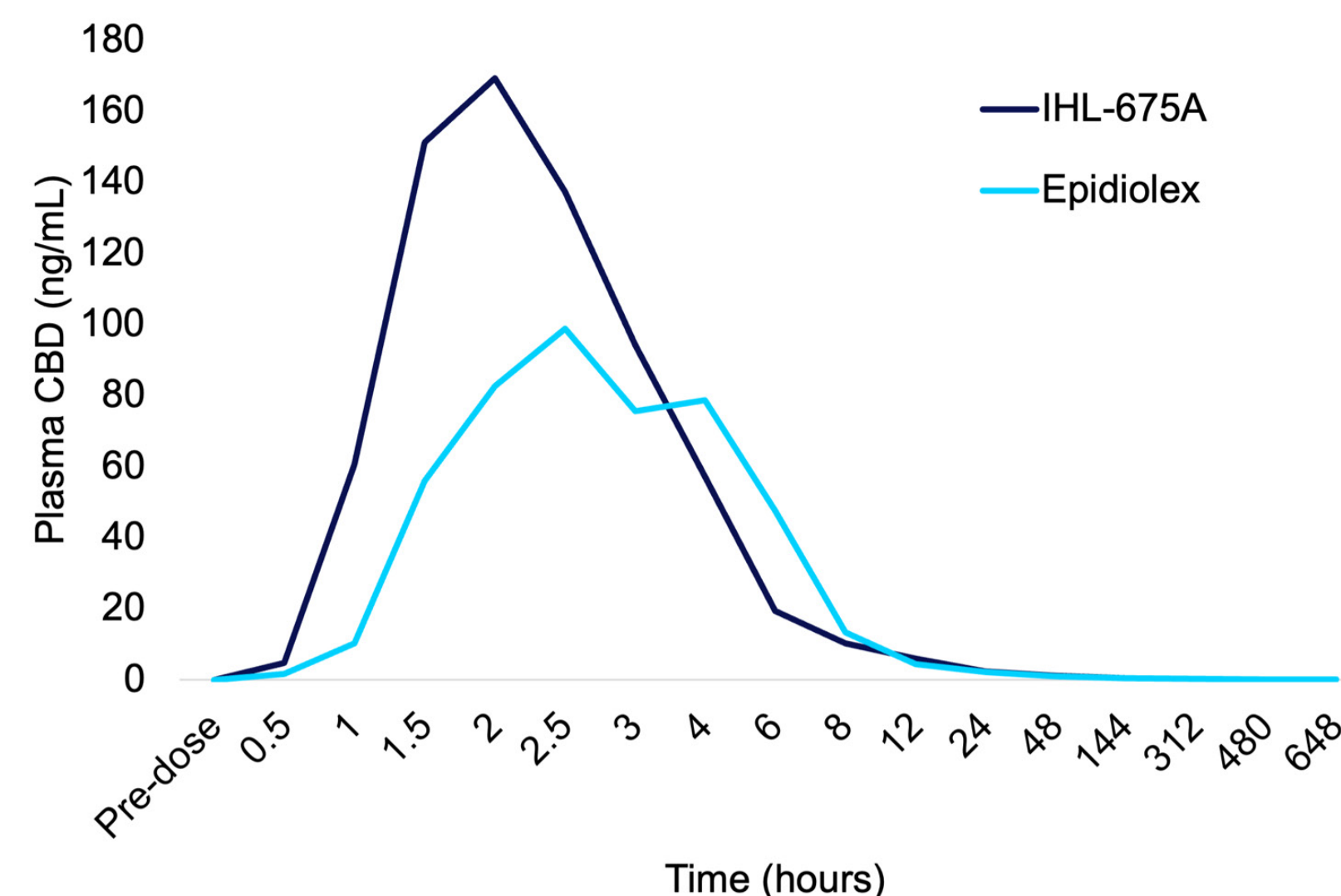
- No adverse events of concern.
- Adverse events were consistent with public reports for Epidiolex and Plaquenil.
- Treatment-related treatment emergent adverse events (TEAEs) included abdominal pain, dizziness, fatigue, frequent bowel movements, headache and somnolence.
- The number of TEAEs for IHL-675A 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.



Results

Pharmacokinetics: CBD →

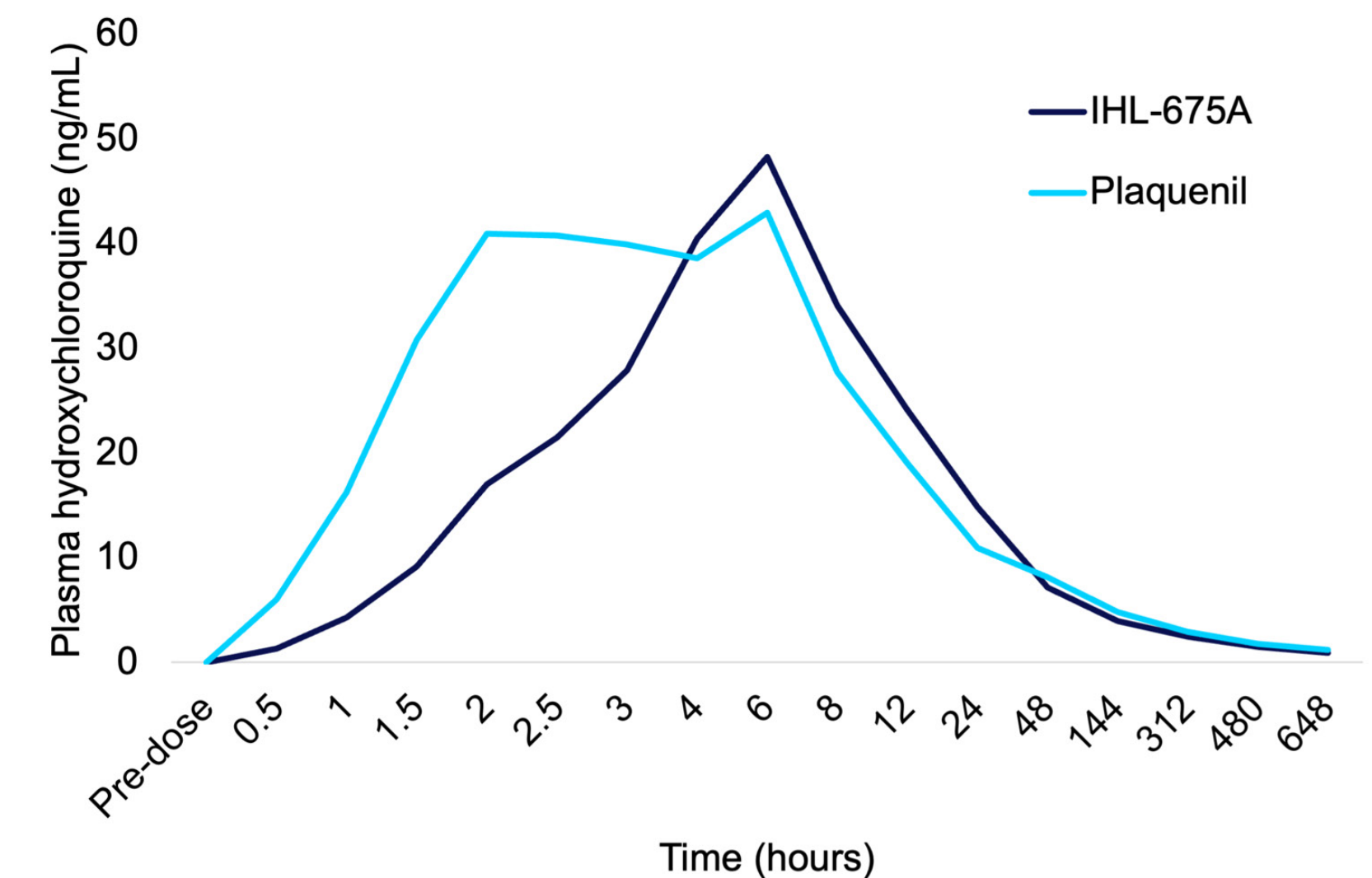
- Compared to Epidiolex, CBD dosed in IHL-675A:
 - Reached a greater maximum concentration (C_{max}), 1.57 times higher
 - Was taken up more rapidly (T_{max}), 26 % faster
 - Was cleared more quickly ($T_{1/2}$), 13 % faster
 - Had a similar level of total exposure (AUC_{inf})
- These differences are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



Results

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.



Results

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.

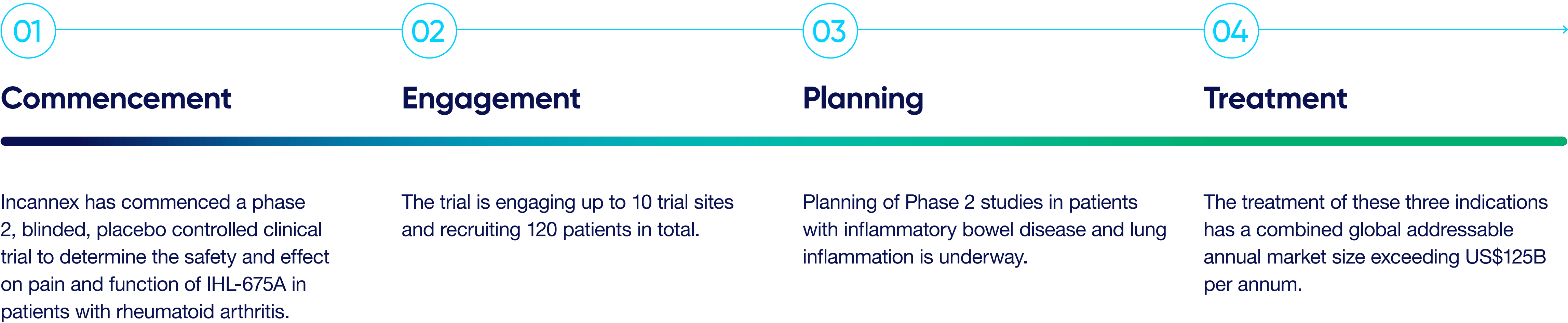
Trends in PK profiles indicate that the uptake of CBD may be more rapid for IHL-675A than Epidiolex and the uptake of HCQ may be slower for IHL-675A than Plaquenil.

05.

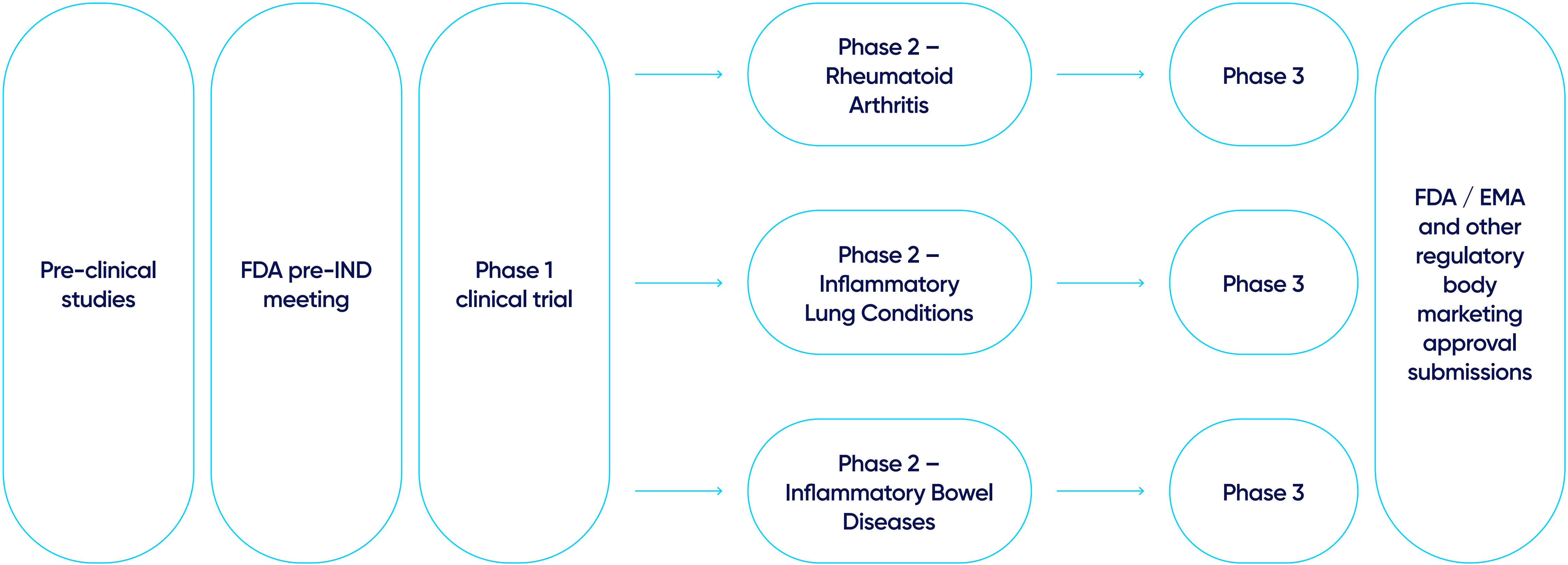
This could be advantageous for IHL-675A. CBD provides immediate relief for inflammation and pain whereas HCQ is a slower acting molecule and provides extended relief.

Next Steps

Phase 2 Clinical Trials



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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