Incannex announces positive results from phase 2 clinical trial investigating the effect of IHL-42X for treatment of obstructive sleep apnoea

Highlights:

- IHL-42X reduced primary endpoint apnoea hypopnea index relative to baseline at all three doses that were assessed
- Low dose IHL-42X exhibited superior safety and efficacy metrics to mid and high doses
- Low dose IHL-42X reduced AHI by an average of 50.7% compared to baseline with 25% of participants experiencing a reduction in the apnoea hypopnea index of greater that 80%
- Oxygen desaturation index was reduced by 59.7% relative to baseline while taking low dose IHL-42X, improving sleep quality and reducing cardiovascular stress
- In low dose IHL-42X samples, THC concentrations in blood were well below the limits for impaired driving the morning after dose administration
- IHL-42X was well tolerated – low dose IHL-42X was observed to have a lower number of total treatment emergent adverse events than placebo
- Low dose IHL-42X reduced AHI substantially more effectively than is reported for the component active pharmaceutical ingredients, dronabinol and acetazolamide, as unregistered monotherapies.

Melbourne, Australia, June 3, 2022 – Incannex Healthcare Limited (Nasdaq: IXHL) (ASX: IHL), ('Incannex' or the 'Company') a clinical-stage pharmaceutical company developing unique medicinal cannabinoid pharmaceutical products and psychedelic medicine therapies for unmet medical needs, is pleased to announce that it has completed analysis of data from the phase 2 proof-of-concept clinical trial investigating IHL-42X for treatment of obstructive sleep apnoea ('OSA'). IHL-42X reduced apnoea hypopnoea index ('AHI'), improved patient reported sleep quality and was well tolerated.

The clinical trial assessed three doses of IHL-42X at reducing the AHI in patients who suffered from OSA. Data was also collected for other aspects of sleep quality, THC clearance and safety. Trial participants received each of the three doses of IHL-42X and placebo across four seven-day treatment periods, separated by one week washout periods. At the end of each treatment period, they attended the clinic for an overnight sleep study where AHI was determined, along with other measures of sleep quality, quality of life and drug safety.

The study was conducted at the University of Western Australia Centre for Sleep Science and The Alfred Hospital. A total of eleven participants were recruited to the study and ten participants completed treatment periods. The crossover design of the study permitted Incannex to generate high quality data with a reduced participant number compared to a conventional parallel arm study. Each participant serves as their own internal control and inter-participant variation is eliminated. Data

analysis was completed by Novotech, the contract research organisation responsible for management of the study, as well as the Incannex scientific research team, led by Chief Scientific Officer Dr Mark Bleackley. The findings of the clinical trial are presented below.

Effect of IHL-42X on apnoea hypopnoea index (AHI)

AHI is a measure of the number of times per hour a subject's airway is blocked (apnoea) or partially blocked (hypopnoea). It is the main criteria used to diagnose and monitor OSA. AHI data was collected during overnight polysomnography on night seven of the treatment periods.

- All doses of IHL-42X reduced AHI in patients with sleep apnoea compared to baseline (Table 1). This reduction was substantially greater than observed for placebo.
- At the group level the difference relative to baseline with low dose and medium dose was statistically significant ($p<0.05$)
- When comparing directly to baseline within subjects the difference in AHI compared to baseline between all three doses and placebo was statistically significant ($p<0.001$) (Table 2)
- Low dose IHL-42X reduced AHI by >50% relative to baseline in 62.5% of subjects and by >80% in 25% of subjects (Table 2).
- Low dose IHL-42X reduced AHI to the greatest extent at both the group level and when comparing the within subject reduction relative to baseline
- Low dose IHL-42X reduced AHI to a greater extent than predicted based on published data for dronabinol and acetazolamide alone (Table 3).

The reduction in AHI observed during IHL-42X treatment periods means that when treated with Incannex's proprietary drug, subject's breathing was interrupted less frequently during sleep. This supports Incannex's hypothesis that IHL-42X is an effective treatment for OSA. The observation that low dose IHL-42X was the most effective at reducing AHI is encouraging for the development of IHL-42X as a pharmaceutical as a lower dose will reduce risk of side effects and the cost of goods.

Furthermore, greater reduction in AHI with low dose IHL-42X compared to dronabinol and acetazolamide at equivalent doses supports Incannex's hypothesis that the two drugs are acting synergistically to reduce AHI and provides confidence that IHL-42X will meet the FDA's combination rule where both APIs must contribute to the therapeutic effect of a fixed dose combination product.

Table 1. Average AHI data for baseline and each treatment period

	Baseline	Placebo	Low	Medium	High
Average AHI	42.84	40.08	21.13	22.22	27.78
Standard deviation	20.33	18.16	15.92	15.52	17.61
% Reduction relative to baseline	N/A	6.44	50.69	48.13	35.16
p value compared to baseline	N/A	0.76	0.029	0.031	0.12

Table 2. Change in AHI from baseline within subject (least square mean)

	Average change in AHI from baseline	p-value relative to placebo (Bonferroni adjusted)	Proportion of subjects with AHI reduction >50% relative to baseline (%)	Proportion of subjects with AHI reduction >80% relative to baseline (%)
Placebo	1.95	N/A	10	0
Low	17.51	<0.001	62.5	25
Medium	14.86	<0.001	33.3	11.1
High	16.18	<0.001	22.2	11.1

Table 3. Comparison of reduction in AHI relative to baseline with low dose IHL-42X and the predicted reduction with component drugs as monotherapies at equivalent doses based on reported data.

	Reduction in AHI compared to baseline (%)
2.5 mg dronabinol (1)	23.4
125 mg acetazolamide (2)	23.4
Low dose IHL-42X	50.7

Effect of IHL-42X on oxygen desaturation index (ODI)

Oxygen desaturation index ('ODI') is the number of episodes of oxygen desaturation per hour of sleep, with oxygen desaturation defined as a decrease in blood oxygen saturation (SpO_2) to lower than 3% below baseline. Reduced oxygen uptake is a key component of the pathology of OSA and contributes to daytime sleepiness and the long-term health consequences associated with OSA. ODI data was collected during overnight polysomnography on night seven of the treatment periods.

- All three doses of IHL-42X reduced ODI compared to baseline to a greater extent than placebo.
- For low and medium dose IHL-42X the difference in reduction in ODI relative to baseline compared to placebo was statistically significant ($p<0.05$)

The greater reduction in ODI during IHL-42X treatment periods compared to placebo means that there is more oxygen in the subject's blood during sleep while taking IHL-42X. This improves sleep quality and reduces risks of oxidative stress, bursts of the stress hormone cortisol, insulin resistance, altered metabolism and cardiovascular disease.

Table 4. Reduction in ODI compared to baseline during each treatment period.

	Reduction in ODI relative to baseline (least squares mean)	Reduction in ODI relative to baseline (%)	p value compared to placebo (Bonferroni adjusted)
Placebo	1.8	18.3	N/A
Low	11.7	59.7	0.021
Medium	12	59.0	0.012
High	8.32	28.5	0.162

Plasma THC levels the morning after IHL-42X dosing

Countries that have set limits for THC above which driving is illegal have set those limits at 1-2 ng/mL (3-6). It is important to understand the clearance of THC after dosing with IHL-42X to determine where there will be an impact on ability to drive in countries where THC limits are in place. Plasma samples were collected 2 hours post dose 1 and the morning after dose 7 for each treatment period. Samples were analysed for concentration of THC using liquid chromatography with tandem mass spectrometry (LC-MS-MS).

The morning after dose 7, THC levels in the low dose IHL-42X samples had an average of 0.20 ng/mL and a maximum of 0.45 ng/mL. Both of which are below the thresholds for impaired driving. With medium and high dose IHL-42X the average THC concentrations the morning after dose 7 were 0.86 and 0.52 respectively.

Effect of IHL-42X on patient reported sleep quality

Each morning of the clinical trial, subjects recorded their sleep quality for the previous night as very poor, poor, fair, good, or very good. To compare patient reported sleep quality, the proportion of subjects who reported good or very good sleep each night was averaged across each treatment period. During the IHL-42X treatment periods subjects more frequently reported that their sleep quality was good or very good than placebo. The highest level of patient reported sleep quality was observed with low and high dose IHL-42X (Table 5).

Table 5. Patient reported sleep quality during each treatment period

	Proportion of subjects reporting good or very good sleep quality
Placebo	26.50%
Low	49.49%
Medium	38.47%
High	50.13%

Sleep metrics captured by actigraphy

For the duration of the clinical trial, subjects wore an Actiwatch, a watch-like device that uses actigraphy to capture data on activity and sleep. IHL-42X at all doses improved sleep efficiency (what percentage of time in bed a subject is asleep), the number of awakenings per night, and the total minutes the subject was awake during the night (WASO) compared to placebo (Table 6). These improvements were greatest for low and high dose IHL-42X. This means that while taking IHL-42X subjects were asleep for a greater proportion of time they were in bed and woke up less often.

Table 6. Sleep metrics captured by actigraphy

		Placebo	Low	Medium	High
Sleep efficiency	**average**	76.83	84.81	81.34	84.17
	p value compared to placebo	N/A	0.0048	0.058	0.0078
Awakenings per night	**average**	49.31	35.8	41.44	37.33
	p value compared to placebo	N/A	0.0053	0.055	0.012
WASO (min)	**average**	62.59	37.55	47.22	38.55
	p value compared to placebo	NA	0.00011	0.0031	0.0010

Safety considerations

Adverse events were recorded from the time the subjects enrolled in the trial until their end of study visit. After recording of treatment emergent adverse events (TEAE) the study team, including investigators and medical monitors, reviewed the TEAEs to determine whether they were likely related to the investigational product. The TEAEs were consistent with what has been reported for dronabinol and acetazolamide alone. For each treatment period the proportion of subjects reporting one or more TEAEs (Table 7) as well as the total number of TEAEs (Table 8) were extracted from the clinical study report. Low dose IHL-42X had a similar proportion of subjects reporting TEAEs and a lower number of total TEAEs than placebo. This indicated that low dose IHL-42X is well tolerated.

Table 7. Proportion subjects of TEAEs reported for each treatment period

	Placebo	Low	Medium	High
Total TEAE (%)	81.8	33.3	55.6	66.7
Related TEAE (%)	27.3	22.2	44.4	55.6

Table 8. Total number of TEAEs reported during each treatment period

	Placebo	Low	Medium	High
Total TEAE	15	6	22	16
Related TEAE	7	4	16	12

References:

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This announcement has been approved for release to ASX by the Incannex board of directors.

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About Incannex Healthcare Limited

Incannex is a clinical stage pharmaceutical development company that is developing unique medicinal cannabis pharmaceutical products and psychedelic medicine therapies for the treatment of anxiety disorders, obstructive sleep apnoea (OSA), traumatic brain injury (TBI)/concussion, lung inflammation (ARDS, COPD, asthma, bronchitis), rheumatoid arthritis and inflammatory bowel disease. U.S. FDA approval and registration, subject to ongoing clinical success, is being pursued for each drug 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.

Incannex has a strong patent filing strategy in place as it develops its products and therapies in conjunction with its medical and scientific advisory board and partners. Incannex is listed on the Australian Stock Exchange (ASX) with stock code “IHL” and also has American Depository Shares listed on NASDAQ under code “IXHL”.

Website: www.incannex.com.au
Investors: investors@incannex.com.au

Forward-looking statements

This press release contains "forward-looking statements" within the meaning of the "safe harbor" provisions of the U.S. Private Securities Litigation Reform Act of 1995. These forward-looking statements are made as of the date they were first issued and were based on current expectations and estimates, as well as the beliefs and assumptions of management. The forward-looking statements included in this press release represent Incannex's views as of the date of this press release. Incannex anticipates that subsequent events and developments may cause its views to change. Incannex undertakes no intention or obligation to update or revise any forward-looking statements, whether as of a result of new information, future events or otherwise. These forward-looking statements should not be relied upon as representing Incannex's views as of any date after the date of this press release.

Contact Information

Incannex Healthcare Limited
Mr Joel Latham
Managing Director and Chief Executive Officer
+61 409 840 786
joel@incannex.com.au

US IR Contact
Rx Communications Group
Michael Miller
+1-917-633-6086
mmiller@rxir.com