7 April 2020

Zelira Therapeutics Meets Primary and Secondary Endpoints for Phase (1b/2a) Medicinal Cannabis Trial for Insomnia

- **Zelira's proprietary cannabis formulation (ZTL-101), produced statistically significant and dose responsive improvements in Insomnia Severity Index (ISI) scores compared to placebo.**
- **Across all participants ISI scores decreased by 26% while those on the highest dose achieved a 36% reduction in ISI.**
- **Treatment significantly improved objective and subjective measures of Total Sleep Time, Wake Time During the Night, Time to Sleep, Quality of Sleep and Feeling Rested after Sleep.**
- **Treatment also significantly improved subjective measures of stress, fatigue and social functioning.**
- **ZLT-101 therapy was well tolerated, with no serious adverse events.**
- **On-track to launch world's first clinically validated medicinal cannabis product for insomnia in 2020.**
- **Expands Zelira's product portfolio alongside the HOPE™ product range.**

Zelira Therapeutics Ltd (**ASX: ZLD, OTCQB: ZLDAF**), a global leader in the development of clinically validated cannabis medicines, is pleased to announce it has received the final clinical report for its Phase 1a/2b medicinal cannabis trial for insomnia. The trial was undertaken at the world-class University of Western Australia (UWA) Centre for Sleep Science and was led by principal investigator Professor Peter Eastwood.

The trial used a randomised, double-blind, cross-over design to assess the efficacy of Zelira's proprietary cannabis formulation (ZTL-101) to treat patients diagnosed with chronic insomnia symptoms. Twenty-three patients were treated for 14 nights with ZTL-101 and 14 nights with placebo, separated by a one-week washout period. After dosing commenced, each participant was able to take a single (0.5ml of 11.5mg total cannabinoids) or double (1 ml of 23mg total cannabinoids) their dose of the medication, delivered sublingually, according to their symptoms.

Primary Endpoints Achieved:

ZTL-101 is safe

- No serious adverse events reported
- Non-serious adverse events were mild and transient, with over 95% resolved by the next morning
- Maximal dose was well tolerated

ZTL-101 is efficacious (Figure 1)

- Across all participants ISI scores decreased by 26% while those on the highest dose achieved a 36% reduction in symptoms as measured by the Insomnia Severity Index (ISI)
- ZTL-101 treatment was dose responsive
- Patients on highest dose reclassified from 'moderate' to 'sub-clinical' insomnia according to ISI classification
- Statistically significant reduction in ISI scores achieved at all doses vs placebo

Secondary Endpoints Achieved

ZTL-101 improved Objective and Subjective Measures of Insomnia (Tables 1-2)

Statistically significant and dose responsive:

- Improvement in time spent asleep (33-65 min)
- Reduction in wake time during the night (10 min)
- Improvement in sleep quality
- Improvement in feeling rested on waking

ZTL-101 improved Quality of Life (Table 3)

Statistically significant:

- Independent reduction in stress levels and fatigue
- Improvement in functioning

Professor Peter Eastwood, Principal Investigator for the study, and Director at the Centre for Sleep Science at the University of Western Australia said "*This study represents the most rigorous clinical trial ever undertaken to assess the therapeutic potential of medicinal cannabis to treat the symptoms of chronic insomnia. The fact that ZLT-101 treatment achieved statistically significant, dose responsive improvements across a broad range of key insomnia indices is impressive, particularly given the relatively short two-week dosing window."*

"The significant improvement in subjective sleep quality and feelings of waking up rested as reported by participants was particularly notable. Positive patient experiences with minimal side-effects are critical to the success of any insomnia drug and highlights the potential for ZTL-101 to address a key area of unmet need. It is likely that further improvements in efficacy could be achieved by dosing over a longer period and potentially at higher doses."

"Taken together, these results are comparable to other approved insomnia therapies at a similar stage of development and suggests that ZLT-101 can be developed as a novel treatment for chronic insomnia. This is a very exciting outcome."

Dr Richard Hopkins, Managing Director ex-US markets said "*We are delighted as these results have exceeded our expectations. The trial has yielded a comprehensive data-pack that supports our plans to launch the world's first clinically validated insomnia product into global markets in 2020. In addition to insomnia, we'll also be targeting indications such as chronic pain, mental and neurological disorders where insomnia is recognised as a key risk factor for disease."*

"We would like to acknowledge the dedicated team at the UWA Centre for Sleep Science and express our gratitude to the patients and supporting investigators/organisations who participated in the study."

An estimated 70 million Americans have insomnia where the market for prescription and over-the-counter medications is forecast to be worth over US$4 billion in annual revenue by 2022. Zelira is leading the development of clinically validated full spectrum cannabis medicines to access global markets for insomnia medications.

Osagie Imasogie, Chairman of Zelira, commented *"The positive outcome to this trial represents an important milestone for Zelira and its commitment to address the unmet need for clinically validated cannabis medicines and offer more treatment options to physicians and patients."*

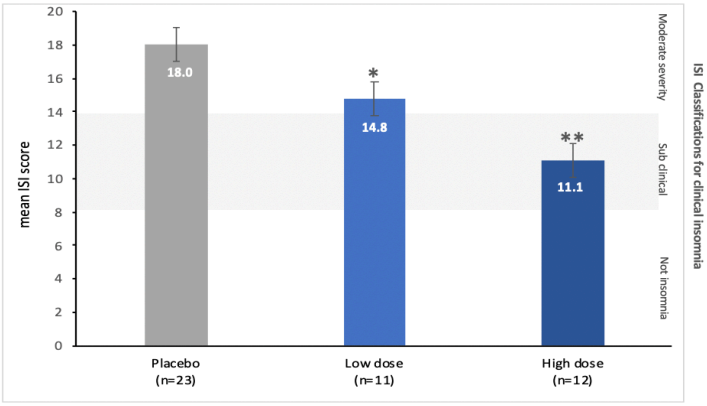
"These positive results add ZLT-101 to the portfolio of Zelira products being commercialised, including the recently launced HOPE™ range, in the US and globally, as a result of rigorous scientific work by the Zelira team. Zelira will continue to deploy its unique Launch, Learn and Develop strategy to launch more scientifically validated products, targeting various conditions, into the market in 2020. Zelira's clinically validated products, such as ZLT-101, continue to play a disruptive role in the traditional pharmaceutical industry."

Next Steps:

Zelira will seek to deploy its Launch, Learn and Develop strategy to supply its clinically validated insomnia formula in countries and states where medicinal cannabis has been legalised including Australia, the USA, Germany and the United Kingdom. The company remains on-track to launch in the Australian market by early Q3, 2020.

The company is also evaluating undertaking further clinical development of ZTL-101 in order to achieve its goal of product registration in Australia.

Figure 1: ZTL-101 treatment significantly improves Insomnia Severity Index scores.



- ISI scores significantly improved following ZTL-101 treatment vs placebo at all doses.
- High dose of ZTL-101 achieved a **36%** reduction in ISI scores.
- High dose of ZTL-101 saw people downgraded from 'Moderate Severity' to 'Sub Clinical' Clinical Insomnia.

Statistical significance calculated using adjusted means for low dose subgroup (ZTL-101 vs placebo-18.7 ISI) and high dose subgroup (ZTL-101 vs placebo- 17.4 ISI). *p<0.05, **p<0.005.

Table 1: Impact of ZTL-101 treatment on objectives sleep scores measured using Actigraphy.

ZLT-101 vs Placebo	Total Sleep Time (min)	Sleep Efficiency (%)	Wake After Sleep Onset (min)	Sleep Onset Latency (min)
Low dose (n=11)	↑28*	↑2.61*	↓9.52	↓0.25
High dose (n=12)	↑42**	↑3.57**	↓12.31*	↓1.19*
Average	**↑33****	**↑2.89****	**↓10.17***	**↓0.41**

ZTL-101 significantly:

- Increased the time people spent asleep (TST more than 30 mins and SE by 3%)
- Decreased the amount of time people spend awake during the night (WASO by less than 10 mins)
- Responses improved with increasing dose

Definitions:
Total Sleep Time (TST): Total amount of sleep time recorded. **Sleep Efficiency (SE):** Sum of time spent asleep divided by the total time in bed. **Wake After Sleep Onset (WASO):** Amount of time spent awake after sleep onset. **Sleep Onset Latency (SOL):** Duration of time from 'lights out' until patient falls asleep.

Statistical significance calculated using adjusted means for ZTL-101 vs Placebo * p ≤ 0.05, ** p≤ 0.001

Table 2: Impact of ZTL-101 treatment on subjective sleep scores measured using patient sleep diaries.

ZLT-101 vs Placebo	Total Sleep Time (min)	Quality of Sleep (score)	Rested on Waking (score)	Sleep Onset Latency (min)
Low dose (n=11)	↑60*	↑0.53*	↑0.26	↓10.2
High dose (n=12)	↑77**	↑0.98**	↑0.75**	↓10.5
Average	**↑65****	**↑0.74****	**↑0.51***	**↓8.5***

ZTL-101 significantly:

- Increased the time people thought they spent asleep
- Improved the quality of sleep people felt they had
- Improved how rested they felt on waking
- Responses improved with increasing dose

Statistical significance calculated using adjusted means for ZTL-101 vs Placebo * p ≤ 0.05, ** p≤ 0.001

Table 3: Impact of ZTL-101 treatment on subjective measures of quality of life.

	Multidimensional Fatigue Inventory			Work and Social Adjustment Scale	
ZLT-101 vs Placebo	General Fatigue[1]	Mental Fatigue[1]	Total Fatigue[1]	Home Management[2]	Total WSAS[2]
Low dose (n=11)	↓1.68*	↓2.0*	↓4.54	↓0.41	↓1.8
High dose (n=12)	↓1.38	↓1.0	↓3.63	↓0.63*	↓2.13
Average	**↓1.57****	**↓1.37***	**↑3.71****	**↓0.6***	**↓2.2***

ZTL-101 significantly:

- Reduced people's total fatigue – particularly mental fatigue and stress[3] (data not shown)
- Improved the ability of people to function – particularly the ability to manage the home

Questionnaires: 1. Multidimensional Fatigue Inventory, 2. Work and Social Adjustment Scale (WSAS), 3. DASS – Stress. Statistical significance calculated using adjusted means. * p ≤ 0.05, ** p≤ 0.001

This announcement has been authorised by the Board.

About Zelira Therapeutics (www.zeliratx.com)

Zelira Therapeutics Ltd is a leading global therapeutic medicinal cannabis company with access to the world's largest and fastest growing cannabis markets. Zelira owns a portfolio of proprietary revenue generating products and a pipeline of candidates undergoing clinical development that are positioned to enter global markets from 2020. The company is focused on developing branded cannabis products for the treatment of a variety of medical conditions.

The Company is undertaking product development programs targeting specific conditions (e.g. HOPE™) and human clinical trial programs focused on insomnia, autism and opioid reduction with activities in Australia and the USA.

The Company conducts this work in partnership with world-leading researchers and organizations including Complutense University in Madrid, Spain; Curtin University in Perth, Western Australia; the Telethon Kids Institute in Perth; the University of Western Australia, in Perth; St. Vincent's Hospital in Melbourne, Australia; and the Children's Hospital of Philadelphia (CHOP) in the United States.

The Company has developed two proprietary formulations (HOPE™) already launched and generating revenues in Pennsylvania, has laboratory capabilities to develop formulations in Pennsylvania and Louisiana with ability to conduct clinical trials and is establishing a national footprint across the US for the licensing of its products.

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