21 September 2022

Diabetic Nerve Pain Drug Trial Summary Update

Zelira Therapeutics Ltd (ASX:ZLD, OTCQB:ZLDAF), a global leader in the research, development and commercialisation of clinically validated cannabinoid medicines, in addition to the ASX announcement titled 'ZLDs Diabetic Nerve Pain Drug Trial Two-Thirds Enrolled' and dated 15 September 2022, provides the following summary of its Diabetic Nerve Pain Drug Trial.

1. Primary and secondary endpoints
Primary Endpoints:
Secondary Endpoints:

1. Daily Pain Numeric Rating Scale (NRS) at Baseline, Day 30, Day 60, Day 90.
1. Neuropathic Pain Symptom Inventory (NPSI) - Burning (Superficial) Spontaneous Pain at Baseline, Day 30, Day 60 and Day 90.
2. Change in Short Form McGill Pain Questionnaire (SF-MPQ) Score at Day 30, Day 60 and Day 90.
3. Baseline Pain Visual Analogue Scale (VAS).
4. Daily Sleep Interference Scale Score (DSIS) at Baseline, Day 30, Day 60 and Day 90.
5. Clinical Global Impression of Change (CGIC) at Baseline, Day 30, Day 60, and Day 90.
6. Patient Global Impression of Change (PGIC) Score at Baseline, Day 30, Day 60 and Day 90.
7. Baseline Hospital Anxiety and Depression Scale (HADS) Scores.
8. Weight gain captured in the vitals at Day 30, Day 60 and Day 90.
9. Change in daily total activity Counts Per Day per Subject Questionnaire (measured steps and daytime activity) at Day 30, Day 60 and Day 90.
10. Change in the total amount of rescue medication daily per Subject Questionnaire at Day 30, Day 60 and Day 90. Subjects should continue with their standard of care rescue medications previously prescribed by their treating physician.
11. Change in the daily loss of balance captured by the Subject Questionnaire at Day 30, Day 60 and Day 90.
12. Change in the daily capture of sensory issues pins and needles, uncomfortable tingling and burning, oversensitivity, reduced sensation of touch, or sensitivity to pain captured by the Subject Questionnaire at Day 30, Day 60 and Day 90.
13. Change in the daily capture of muscular issues, cramping, muscle weakness or problems with coordination captured per the Subject Questionnaire at Day 30, Day 60 and Day 90.
14. Number of Participants with Treatment-Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Withdrawals Due to Adverse Events (AEs) at Baseline, Day 30, Day 60 and Day 90. An AE was any untoward medical occurrence attributed to study drug in a participant who received study drug. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; life threatening (immediate risk of death); initial or prolonged inpatient hospitalization; persistent or significant disability/incapacity; resulted in congenital anomaly/birth defect.
15. Change in blood pressure as captured in the vitals.

2. Blinding status	The study drug is packaged and identified as Study Drug A, B for either drugs. The subject and all parties will not know what is being provided. All Study Drug will be in compliance with 21CFR312.6 including the statement "Caution: New Drug - Limited by Federal (or United States) law to investigational use.
3. Product status	Development
4. Treatment method, route, frequency and dose levels	**Group 1**: Subjects will be already taking reference drug at the prescribed dose as recommended by their doctor. **Group 2:** Subjects already taking reference drug at the prescribed dose as recommended by their doctor. Will receive investigative drug -One capsule by mouth twice daily. If no response after two weeks, Principal Investigator can increase the dosing to three times daily. If the Principal Investigator feels that a subject needs an additional dose, an additional capsule can be provided so that the subjects are dosed four times daily. Study drug will be taken by the subjects in the privacy of their own homes. **Group 3:** One capsule by mouth twice daily. If no response after two weeks, Principal Investigator can increase the dosing to three times daily. If the Principal Investigator feels that a subject needs an additional dose, an additional capsule can be provided so that the subjects are dosed four times daily.
5. Description of control group	The trial was designed and approved as a observational multi-arm, head-to-head study. The study was powered to show statistical difference with 60 subjects (20 subjects in each arm). The drug arm of 20 subjects which include subject currently using the pharmaceutical company drug serve as a reference arm for the study. The study was designed to include a third arm to evaluate the synergistic effect/dose de-escalation of the reference drug.
6. Subject selection criteria	**Subject Inclusion criteria:** An individual is eligible for inclusion if all of the following apply: **1.** Males and Females between 18 years to 85 years. **2.** In good general health, as determined by the Investigator. **3.** Willing and able to attend all study visits and utilize ePro. **4.** At the baseline and randomization visits, a score of ≥50 mm on the Visual Analogue Scale, at randomization, subjects must have completed at least 5 daily pain interference diaries, and have an average daily pain score of ≥5 over the past 7 days that is not currently being treated. **5.** Patient who are willing and capable to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures. **6.** Women of childbearing potential are willing to use contraception during study. **Subject Exclusion criteria:** **1.** No current substance (non-prescription) or alcohol dependence. **2.** No Dementia or Alzheimer's disease. **3.** No previous serious adverse event or hypersensitivity to medical cannabis or cannabinoids. **4.** No Psychosis. **5.** No Uncontrolled hypertension, defined as a systolic blood pressure greater than 160 mm Hg or a diastolic blood pressure greater than 100 mm Hg. **6.** No Pregnancy, breastfeeding, or unwillingness to prevent pregnancy during the study drug and cannabis administration portion of the study (using birth control in female participants of child- bearing age). If a subject becomes pregnant while in the study, they should withdraw from the study and the investigator will follow the patient thereafter. **7.** Routine use of opioids greater than 60 mg; if none at all use of opioids. **8.** No Concurrent cannabis or cannabis product use while participating in the study **9.** Subjects with more than 30% decrease on the Pain Visual Analog Scale at randomization as compared to screening; and during the 1week screening period, with more than one pain score <3 in pain scores. **10.** Subject has other kinds of neurological disorder, pain of other reason, or skin condition that could confuse the assessment. **11.** Subject with any other serious or unstable condition which in the opinion of the investigator might compromise participation in the study.

7. Trial locations	USA
8. Name of the principal investigator/partner organisations (if any)	Bryan Doner, DO
9. Trial standard	This study is conducted in accordance with the guidelines of Good Clinical Practice (GCP) and the applicable regulatory requirement(s), including the archiving of essential documents.

This announcement has been approved and authorised for release by the board of Zelira Therapeutics Limited.

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About Zelira www.zeliratx.com

Zelira Therapeutics Ltd (ASX:ZLD, OTCQB:ZLDAF) Zelira is a leading global biopharmaceutical company in the research, development and commercialisation of clinically validated cannabinoid-based medicines. Zelira owns a portfolio of proprietary revenue generating products and a pipeline of candidates undergoing clinical development positioned to enter global markets. The Company is focused on developing and clinically validating branded cannabinoid-based medicines in its prescription [Rx] business for the treatment of a variety of medical conditions including insomnia, autism and chronic non-cancer pain as well as offering over the counter [OTC] products.

Zelira's Rx business generates revenue from two proprietary medications, HOPE® and ZENIVOL®. The Company has two proprietary formulations under the HOPE® brand that are generating revenue in Australia, Washington, D.C., Pennsylvania and Louisiana.

Zelira is also generating revenue in Australia from its proprietary and patented ZENIVOL® – the world's first clinically validated cannabinoid drug for treatment of chronic insomnia. Zelira will also be expanding commercialisation of ZENIVOL® into Germany via its German commercialisation partner Adjupharm GmbH following recent approval from German regulatory authority BfArM.

Zelira's OTC products in the oral and dermatology health care sectors are also generating revenue. Zelira, in partnership with SprinJeneCBD, launched a full line of oral care products, currently generating revenue in the US. The SprinJeneCBD toothpaste product is the first of several scientifically formulated, hemp-derived, oral care products containing cannabinoids, blackseed oil and zinc utilising proprietary and patented technology. Zelira also launched in 2021 the RAF FIVE™ brand, which consists of five OTC acne treatment products using a proprietary formulation incorporating cannnabidiol (CBD).

Zelira has developed Enhanced Distillate Capture and Dissolution Matrix (EDCDM) technology under the brand name Zyraydi, that solves the problem of non-uniformity and separation of cannabinoid from powder bed, opening new ways to develop pharmaceutical grade solid oral dosage forms such as capsules and tablets. Zelira will be assessing opportunities for commercialisation of this technology.

The Company conducts its work in partnership with world-leading researchers and organisations which since inception includes Curtain University in Perth, Australia; the Telethon Kids Institute in Perth, Australia; the University of Western Australia, in Perth, Australia; St Vincent's Hospital in Melbourne, Australia; and the Children's Hospital of Philadelphia (CHOP) in the United States.

For further information, please visit: **zeliratx.com**