8 June 2023

Amendment to ASX announcement - Zelira's diabetic nerve pain drug outperforms Big Pharma drug announcement

AMENDMENT TO ASX ANNOUNCEMENT - ZELIRA'S DIABETIC NERVE PAIN DRUG OUTPERFORMS BIG PHARMA DRUG ANNOUNCEMENT

Zelira Therapeutics Ltd (ASX:ZLD, OTCQB:ZLDAF), a global leader in the development and commercialisation of clinically validated cannabinoid based medicines, refers to its announcement dated 31 May 2023 titled 'Zelira's diabetic nerve pain drug outperforms Big Pharma drug; successful clinical trial against multi-billion-dollar Lyrica®' (**Original Announcement)**.

Zelira has chosen to re-lodge the Original Announcement to make edits that it has become aware of since the release of the Original Announcement removing a quote that was inadvertently attributed to a 3rd party. The quote has now been removed. Importantly, there are no issues with the data or the results of the study as presented in the Original Announcement, or any changes relating to any of the material information disclosed around the study, its processes or outcomes.

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

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Company Secretary

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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 cannabidiol (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**

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ASX ANNOUNCEMENT

31 May 2023

Zelira's diabetic nerve pain drug outperforms Big Pharma drug; successful clinical trial against multi-billion-dollar Lyrica®

DEMONSTRATED SAFETY, TOLERABILITY, AND IMPROVED EFFICACY IN PAIN MANAGEMENT

Key Highlights

- Zelira successfully completed an IRB-approved[1] multi-arm head-to-head study of its proprietary diabetic nerve pain drug ZLT-L-007 against a major Big Pharmaceutical company's multi-billion-dollar annual revenue drug, Lyrica®.
- Topline results demonstrate that ZLT-L-007 outperformed Lyrica®, achieving a significant reduction in NRS pain scores, indicating a decrease in symptom severity.
- ZLT-L-007 was found to be safe and well-tolerated, meeting the primary endpoint for safety with no Serious Adverse Events (SAE).
- These compelling outcomes provide confidence to evaluate the further progression of ZLT-L-007 into formal FDA clinical trials.
- The study also met secondary endpoints, including significant decreases in Visual Analog Scale (VAS) and Short form McGill scores, among others.
- Additional insights from the full study will be reported, as they become available, during FY 2023-2024.

Reference: 1. Under FDA regulations, an IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects.

Zelira Therapeutics Ltd (ASX:ZLD, OTCQB:ZLDAF), a global leader in the research, development, and commercialisation of clinically validated cannabinoid medicines, is pleased to announce that its diabetic nerve pain drug outperformed in a clinical trial against a multi-billion-dollar Big Pharmaceutical company drug Lyrica.®

Zelira's Chairman, Osagie Imasogie, said:

We are delighted to share the outcomes of this strategically designed multi-arm, head-to-head study targeting diabetic nerve pain. The clinical trial included a comprehensive comparison against the widely recognized and highly successful multi-billion dollar revenue-generating drug Lyrica® (Pregabalin).

As a commercially available pain medicine, Lyrica® served as a reliable benchmark to gauge the pain relief efficacy offered by our novel candidate, ZLT-L-007. In addition, Lyrica® has historically achieved peak year annual sales of approximately US$5 billion, clearly indicating the market potential for Zelira's pain relief medication that outperformed the level of pain relief from Lyrica®. In certain instances, provided up to four times the observed pain relief when compared to Lyrica.®

This compelling outcome gives us confidence to evaluate the further progression of ZLT-L-007 into formal FDA clinical trials. Our company remains focused on providing relief to patients and creating new cannabinoid derived drugs to deliver clinically validated safe and efficacious solutions to patients in need, across several therapeutic areas.

Zelira Therapeutics CEO & Managing Director, Dr. Oludare Odumosu said:

We are thrilled with the results from our IRB approved trial in the United States. The findings underscore the exceptional efficacy of our treatments in managing pain, with ZLT-L-007 demonstrating the most substantial reduction in pain severity, particularly at the 60-day and 90-day follow-up periods.

We are particularly proud that this unique, multi-arm comparative study yielded positive results for our primary endpoint of safety in addition to several secondary endpoints. These results align perfectly with our strategy of generating scientifically rigorous and clinically validated data for our patent-protected proprietary cannabinoid-based drugs.

The trial results further affirm the safe and effective use of Zelira's innovative and patent-protected technology, Zyraydi™, which was utilised to create the free-flowing powder formulation used for ZLT-L-007. The Zyraydi™ technology enabled us to deliver ZLT-L-007 in an easy to swallow, relatively small pharmaceutical grade size 2 capsule.

These positive results mark a significant milestone for Zelira, further supporting and validating our Launch, Learn and Develop strategy that has enabled us to generate this level of compelling clinical data validation, before we commence further formal trials to progress ZLT-L-007 towards regulatory approval.

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Zelira partnered with Pennsylvania based Global CRO, Affinity Bio Partners, to manage this clinical trial. Dr. Christina DiArcangelo, CEO of Affinity Bio Partners said:

I am very happy with the outcome of our first-ever head-to-head clinical trial focusing on cannabinoids in the treatment of diabetic neuropathy.

The operational complexities of conducting cannabinoid studies, including adherence to stringent guidelines, Good Clinical Practice (GCP), and regulatory requirements, were effectively and successfully managed.

I wholeheartedly applaud Zelira for their bold commitment to advancing the field of cannabinoid drug development and exploring pharmaceutical compounds that can bring relief to countless patients. Together with our esteemed partners, Spectral Analytics Precision Tele-Monitoring and Affinity Patient Advocacy, we successfully completed this study.

This achievement marks the realisation of a long-cherished vision in the space of global cannabinoid biotechnology, propelling us forward with newfound confidence to design and pursue formal trials in this space. Our objective remains the development of pharmaceutical industry quality, innovative and effective new drug treatments, offering hope and improved quality of life for patients in need.

The topline results for Zelira's diabetic nerve pain trial are outlined below. The study evaluated the efficacy, safety, and tolerability of Zelira's proprietary patent protected ZLT-L-007, against the well-known drug Lyrica® (Pregabalin).

Design

The trial was designed and approved as an observational multi-arm, head-to-head study with 60 subjects, powered to show statistical difference with approximately 20 subjects in each arm.

Group 1: Lyrica® (Pregabalin) only: Subjects (n=22) already taking Lyrica®/Pregabalin reference drug at the prescribed dose as recommended by their doctor.

Group 2: ZLT-L-007 only: Subjects (n=18) take one capsule of Zelira's proprietary investigational drug, ZLT-L-007, by mouth twice daily. If there is no response after two weeks, Principal Investigator could increase the dosing to three times daily. If the Principal Investigator felt that a subject needed an additional dose, an additional capsule could be provided so that the subjects are dosed four times daily.

Group 3: Lyrica® (Pregabalin) + ZLT-L-007: Subjects (n=20) already taking Lyrica®/Pregabalin reference drug at the prescribed dose as recommended by their doctor. Subjects then received the investigative drug, ZLT-L-007, one capsule by mouth twice daily. If there was no response after two weeks, Principal Investigator could increase the dosing to three times daily. If the Principal

Investigator felt that a subject needed an additional dose, an additional capsule of ZLT-L-007 could 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.

The demographic and baseline characteristics of the trial are as follows. The mean age was 59.6 years for the Lyrica® (Pregabalin) only, 56.5 years for the ZLT-L-007 only, 61.3 years for the Lyrica® (Pregabalin) + ZLT-L-007 only, and 59.3 years for the combined group. The median age ranged from 57.0 to 62.0 years, and the minimum and maximum ages varied from 33 to 86 years across the groups. Regarding gender, most participants were female in the Lyrica® (Pregabalin) and Lyrica® (Pregabalin) + ZLT-L-007 only, while it was evenly split between male and female participants in the ZLT-L-007 only. In terms of race, most participants were White, followed by Black and Multiracial individuals. All participants identified as not Hispanic or Latino.

Topline results

1. The study met its primary endpoint for the change in daily pain severity measured by the % change from baseline at, Day 30, Day 60, and Day 90, on the Numerical Rating Scale (NRS).

a. For the NRS Severity parameter, the median values of the percent change from baseline for each treatment group is set forth below. This data provides valuable information on the magnitude of improvement within each treatment group:

Lyrica® / (Pregabalin) only Group:

- 30-day follow-up: Median percent change from baseline: -33.33%
- 60-day follow-up: Median percent change from baseline: -20.00%
- 90-day follow-up: Median percent change from baseline: -35.00%

ZLT-L-007 only Group:

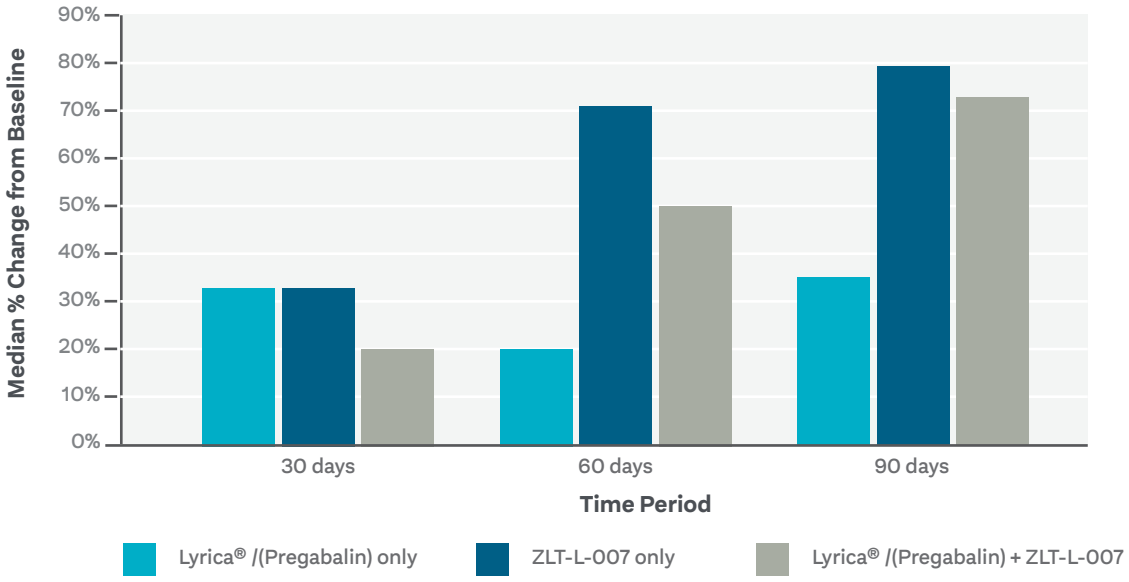
- 30-day follow-up: Median percent change from baseline: -33.33%
- 60-day follow-up: Median percent change from baseline: -71.43%
- 90-day follow-up: Median percent change from baseline: -78.57%

Lyrica® / Pregabalin + ZLT-L-007 Group

- 30-day follow-up: Median percent change from baseline: -20.00%
- 60-day follow-up: Median percent change from baseline: -50.00%
- 90-day follow-up: Median percent change from baseline: -72.50%

b. For the reference Lyrica® (Pregabalin) group, the median percent change from baseline suggests a reduction in symptom severity at all follow-up periods, ranging from -20.00% to -35.00%. For the ZLT-L-007 only group, the median percent change from baseline demonstrates a notable reduction in symptom severity at the 30-day follow-up (-33.33%). However, the median percent change from baseline at the 60-day and 90-day follow-ups (-71.43% and -78.57%, respectively) suggests a larger improvement in symptom severity than Lyrica®/Pregabalin. The median percent change from baseline from the Lyrica® (Pregabalin) + ZLT-L-007 group shows a moderate reduction in symptom severity at the 30-day follow-up (-20.00%). However, the median percent change from baseline at the 60-day and 90-day follow-ups (-50.00% and -72.50%, respectively) indicates a substantial improvement in symptom severity than with Lyrica®/Pregabalin alone.

Numerical Rating Scale Summary - Percentage Change from Baseline by Timepoint



2. The study met another of its primary endpoints for safety measured by Serious Adverse Event (SAE) report with 0 SAE reports for the duration of the study.

3. The study met its secondary endpoint for the change in daily pain severity measured by the % change from baseline, Day 30, Day 60, Day 90 for Visual Analog Scale (VAS). The Lyrica®/ Pregabalin only group demonstrated a decrease in pain severity from baseline at all three timepoints, with median percent changes ranging from -33.33% to -35.00%. This suggests that Lyrica®/Pregabalin alone effectively reduced pain levels in the study participants. The ZLT-L-007 only group exhibited a more substantial decrease in pain severity compared to the Lyrica®/ Pregabalin only group at the 60-day and 90-day follow-ups. The median percent change from baseline ranged from -71.43% to -78.57%, indicating a potentially stronger analgesic effect of ZLT-L-007 in managing pain. The combination of Lyrica®/Pregabalin and ZLT-L-007 in the Lyrica®/ Pregabalin + ZLT-L-007 group showed intermediate results, with median percent changes from baseline ranging from -20.00% to -72.50%. This suggests a potential synergistic effect of the combined treatment, but with less efficacy than ZLT-L-007 alone.*

4. The study also met several secondary endpoints such as measurable change in the Short Form McGill Pain Questionnaire and NPSI.

5. There was no significant change in systolic and diastolic blood pressure measures for the participants in the study measured at the different time points.

Severe

* The median change in baseline for both NRS and VAS results are the same. See chart above.

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