

ASX RELEASE

Ellex Medical Lasers Limited (ASX:ELX)

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Topic: Ellex Announces Outcome of LEAD 2RT[®] Clinical Trial



Highlights:

- **Ellex releases results of LEAD; a three-year, randomised, multi-centre clinical trial investigating the efficacy of Ellex 2RT[®] Retinal Rejuvenation Therapy in intermediate age-related macular degeneration (iAMD) patients.**
- **The results showed a four-fold reduction in the rate of progression to late stage AMD in 76% of patients who received Ellex 2RT[®] over the 36 months of the study.**
- **Although the primary endpoint of the trial was not met, *post hoc* analyses showed that intervention with Ellex 2RT[®] in patients who did not have coexistent reticular pseudodrusen (RPD) at the commencement of the trial (76% of patients enrolled), resulted in a significant treatment effect (p=0.002) and a clinically meaningful 77% reduction in the rate of progression from iAMD to late AMD versus placebo.**
- **Significant first-mover opportunity to commence a commercial program specifically targeting the 15 million patients per annum in existing markets that may benefit from Ellex 2RT[®] based on LEAD.**
- **The Company has a range of patents in place to protect the underlying intellectual property of Ellex 2RT[®], valid through until 2035.**

Adelaide, Australia, Thursday, 20 September 2018 – Ellex Medical Lasers Limited (ASX:ELX), a world leader in medical technologies for the diagnosis and treatment of eye disease, today announced the results of the Laser Intervention in Early Age-Related Macular Degeneration (**LEAD**) clinical trial. The purpose of the LEAD trial was to investigate the safety and efficacy of nanosecond laser treatment (Ellex 2RT[®]) as a prophylactic intervention for the early stages of AMD to slow progression to late AMD.

The principal trial investigator was Professor Robyn Guymer, AM, MBBS, PhD, FRANZCO, FAAHMS, a world-leading retinal professor and Head of Macular Research and Deputy Director at the Centre for Eye Research Australia (CERA) in Melbourne, Australia. The results of the trial have been subject to independent peer review and have been published today in *Ophthalmology*, the official journal of the American Academy of Ophthalmology.

Summary of Outcome

The LEAD clinical trial is the first time any form of laser intervention has shown a promising clinical response in a large group of well-defined iAMD patients prior to progression to vision impairing late AMD.

Although the entire trial population did not show a statistically significant reduction in the rate of progression to late AMD, the data has yielded promising results and important new information on the ideal patient cohort for treatment with Ellex 2RT®.

Ellex CEO Tom Spurling commented: “The significant reduction in the risk of progression to late AMD in the large subset of patients without coexistent RPD confers a significant first-mover advantage for our proprietary Ellex 2RT® technology in these patients. As indicated by the trial authors, the LEAD clinical results are unique to Ellex 2RT® and cannot be extrapolated to other thermal or non-thermal laser treatments. We estimate the number of iAMD patients without RPD to represent at least approximately 15 million patients annually in Ellex’s existing 2RT® markets.¹ With no currently approved treatment options available for AMD in its early stages in these markets, or indeed anywhere in the world, we believe the LEAD data will be of significant clinical interest to retinal specialists and ophthalmologists seeking an intervention for patients with the early stages of AMD.”

Commenting on the significance of the LEAD trial, Prof. Guymer said: “While this isn’t a cure, and it is not suitable for every patient with AMD in its early stages, the impressive outcomes in reducing progression to late AMD are important as this is the first time that a laser intervention has shown promise in addressing AMD disease progression in more than 20 years of AMD laser research.”

This is the first time a meaningful intervention has indicated a potential for reducing progression of AMD in its early stages in a large randomised controlled trial. The results of the LEAD trial also build on an extensive body of evidence for Ellex 2RT® based on a series of pre-clinical and clinical investigations dating back to 2010.

Prof. Guymer further commented on the newer technologies and techniques used to monitor disease progression in AMD patients: “Based on our findings from the LEAD trial, new multimodal imaging techniques offer the ability to better stratify and monitor progression of AMD patients. This is an important consideration for earlier stage interventions such as Ellex 2RT®, where patient vision is largely unaffected. To that end, traditional outcome measures, including best corrected visual acuity (BCVA), do not adequately capture AMD disease status.”

Background of the LEAD Trial

The LEAD trial (Australian New Zealand Clinical Trials Registry ACTRN12612000704897 and clinicaltrials.gov NCT01790802) was a double-masked, randomised, sham-controlled trial conducted over six sites: five in Australia and one in Northern Ireland.

There were 292 participants in the trial, which completed recruitment in April 2015. Participants recruited into the trial were 50 years or older, with a diagnosis of AMD, and having at least one

large druse in both eyes and no evidence of atrophy as measured by multi-modal imaging (MMI). These phenotypic characteristics met the definition of iAMD.

Participants were randomly assigned 1:1 to the Ellex 2RT[®] treatment group or a sham treatment group. Participants received treatment as a standardised series of 12 laser spots applied to the macular region of the treated eye. Each participant was reviewed at six-monthly intervals over a total period of 36 months. Repeat treatment was conducted at each 6-month review for participants who remained eligible for retreatment.

The 36-month review period was completed for the last randomised patient in early May 2018.

Detailed LEAD Trial Results

The primary endpoint of the trial was progression to late AMD in the treated eye of 2RT[®] patients, as defined by multi-modal imaging, versus sham patients based on a 1:1 randomisation of participants. After 36 months of follow-up, on an Intent to Treat (ITT) analysis, 13.6% of participants in the Ellex 2RT[®] treatment group and 17.2% of participants in the sham treatment group (unadjusted Hazard Ratio [HR]=0.78, 95% Confidence Interval [CI] 0.43–1.41; p=0.412 and adjustedⁱⁱ HR=0.61, 95% CI 0.33–1.14; p=0.122) developed late AMD. Although not statistically significant, there was a trend favouring the Ellex 2RT[®] treatment group.

For the per protocol (PP) population, which represented those patients who completed the trial without significant clinical protocol violations, 86% of the ITT patients in the sham treatment group and 81% in the ITT Ellex 2RT[®] treatment group completed the trial as planned. The PP analysis reflected the ITT results, with a statistical trend favouring 2RT[®], given the unadjusted HR=0.75, 95% CI 0.41–1.39; p=0.362 and adjusted HR=0.56, 95% CI 0.29–1.10; p=0.092.

The baseline characteristics of the Ellex 2RT[®] treatment group and the sham treatment group were well-balanced in terms of demographic and clinical characteristics.

In a *post hoc* analysis, which analysed the difference in treatment effect, the LEAD trial demonstrated that compared to a sham (placebo) treatment, intervention with Ellex 2RT[®] in patients who did not have coexistent RPD (76% of patients) at the commencement of the trial resulted in a 77% reduction in the rate of progression from intermediate AMD to late AMD at three-year follow-up.

The presence of RPD is a key biomarker of retinal pigment epithelium (RPE) dysfunction and has a high association with progression to late-stage AMD. Unlike regular drusen deposits, which are located between the RPE and Bruch's membrane, RPD are located above the RPE and are often associated with late AMD. The 24% rate of prevalence of RPD at baseline in the LEAD trial was based upon a definition that required at least five RPD to be present in the eye.

The *post hoc* analysis showed that in 222 (76.0%) participants without coexistent RPD in the treated eye at baseline, the rate of progression to late AMD was reduced by 77% in the Ellex 2RT[®] treatment group compared to the sham treatment group (adjusted HR=0.23, 95% CI 0.09–0.59; p=0.002). In participants with baseline RPD, representing 24% of the ITT population, the effect modification analysis indicated that there was an increased rate of progression to late AMD

in the Ellex 2RT[®] treatment group compared to the sham treatment group (adjusted HR=2.56, 95% CI 0.80–8.18; p=0.112). The trial investigators postulate that there may be a stage of the AMD disease whereby RPE integrity is so greatly compromised that treatment with Ellex 2RT[®] is unsuitable.

There were no device-related serious adverse events in this trial. Comparing the two treatment groups, treatment-related ocular adverse events occurred in 10% of the Ellex 2RT[®] treatment group compared to 0.7% in the sham treatment group. In addition, 6.8% of the treatment group had retinal haemorrhage compared to none in the sham group and five (3.4%) participants and one (0.7%) participant reported persistent after-images (visible for more than one day) at one-week following the initial treatment in the Ellex 2RT[®] treatment group and sham treatment group respectively. These adverse events were resolved without sequelae.

The results have been published online in *Ophthalmology*.

Commercial Implications for Ellex

- **Proprietary laser intervention for early stage AMD:** The Ellex 2RT[®] laser is a unique, proprietary ophthalmic laser technology that has been developed by Ellex to induce macular RPE cell rejuvenation. The characteristics of Ellex 2RT[®] cannot be extrapolated to other thermal and non-thermal laser treatments. The Company has a range of patents in place to protect the underlying intellectual property of Ellex 2RT[®], valid through until 2035.
- **Ellex 2RT[®] as therapy for the early stages of AMD:** Analysis of the 76% of patients without coexistent RPD showed that Ellex 2RT[®] was able to reduce the rate of progression to late AMD by 77% in this large subset of iAMD patients. This provides Ellex with the clinical evidence that, subject to the appropriate selection of patients in relation to the absence of RPD and the early signs of atrophy, the use of Ellex 2RT[®] as an intervention for an early stage of AMD to delay the onset of late stage AMD is now a real possibility.
- **First mover advantage in the intervention of the early stages of AMD:** Ellex is not aware of any other specific intervention that has been the subject of a large, randomised, controlled clinical trial, which has demonstrated strong evidence of treatment effect with a clinically meaningful delay in the progression from iAMD to late AMD in a large group of well-defined iAMD patients. Ellex's total immediate, addressable market, based on existing approvals in Australia, Europe and Asia, represents approximately 15 million patients. This addressable market is expected to expand, pending successful regulatory clearances in the targeted markets of the USA, China and Japan, by at least approximately 25 million patients.ⁱⁱⁱ
- **Expanded market access:** In recent years Ellex has undertaken a limited commercial rollout of Ellex 2RT[®] in approved markets in parallel with ongoing clinical investigations. With the publication of the LEAD trial data, Ellex will now look to accelerate the market

expansion of Ellex 2RT® in all approved markets through a number of expanded sales and marketing initiatives.

- **Recurring revenue business model:** Ellex has successfully trialed a pay-per-procedure business model through its 2RT® Early Adopter Program. This provides Ellex with a recurring revenue stream that hitherto had not been available to its pre-existing ophthalmic laser product range.
- **Manufacturing capacity and sales infrastructure to support global growth potential:** Subject to detailed production and supply chain planning, the recently-established Ellex manufacturing site in Mawson Lakes, South Australia, has the capacity and infrastructure in place to support production of Ellex 2RT® that will be distributed through the Company's existing global sales and distribution channel.
- **Commercialisation plan:** Ellex's commercialisation plan for Ellex 2RT® will be based on a foundation of physician-based, peer-to-peer educational programs focused on disease diagnosis, patient selection and treatment protocols, and will leverage the expertise of early adopters.

- ENDS -

ABOUT Ellex 2RT®

Ellex 2RT® is a non-thermal laser therapy that stimulates a natural, biological healing response in the eye and has demonstrated potential as an intervention which can positively influence early stage age-related macular degeneration.

ABOUT ELLEX

Ellex designs, develops, manufactures and sells innovative products that help eye surgeons around the world to effectively and efficiently treat eye disease. Ellex is a world leader in this field. Headquartered in Adelaide, Australia, Ellex has ophthalmic lasers and devices that treat glaucoma, retinal disease primarily caused by diabetes, secondary cataract and vitreous opacities, as well as age-related macular degeneration. Manufacturing is carried out in Adelaide, Australia and Fremont, California. Sales and service directly to eye surgeons is conducted via subsidiary offices in Minneapolis, Lyon, Berlin and Tokyo. A network of more than 50 distribution partners around the world services other markets. **For additional information about Ellex and its products, please visit www.ellex.com.**

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ⁱ Marketscope Report August 2017 Ophthalmic Laser Report Table 2 "Global Forecast for AMD in all its Forms".

ⁱⁱ The potential confounders of baseline age (as a continuous measure), sex, intake of Lutein-Vision® or Macu-Vision® at baseline (yes vs. no for each), presence of RPD and pigmentary abnormalities (definitely present vs. absent/questionable) were additionally included as covariates in a fully adjusted model as specified *a priori*.

ⁱⁱⁱ Marketscope Report August 2017 Ophthalmic Laser Report Table 2 "Global Forecast for AMD in all its Forms".