

Five-Year Post-LEAD Review Shows Improvement in 2RT[®] Treatment Benefits for iAMD

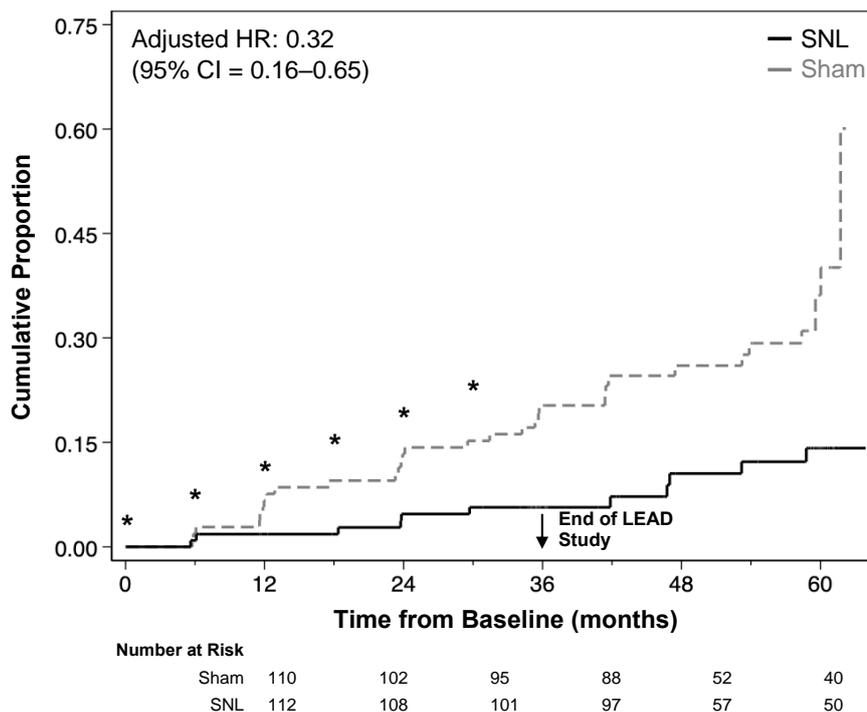
Adelaide, Australia, 5 March 2021 – Nova Eye Medical Limited (ASX: EYE)(Nova Eye Medical or the Company), a medical technology company committed to advanced ophthalmic treatment technologies and devices, today announces the publication of positive five-year patient follow-up data from a sub-study analysis of the LEAD Trial in *Ophthalmology Retina*.¹

A randomised, controlled multi-centre trial conducted in 292 patients during 2012-2018, the LEAD Trial assessed the efficacy of 2RT[®] at three years in patients with intermediate age-related macular degeneration. Importantly, the LEAD Trial was the first time any form of Intervention had been reported to demonstrate a promising clinical response in selected patients with intermediate-stage AMD (iAMD).

In the recently-published five-year post-LEAD review, which enrolled a total of 222 patients (76%) from the LEAD Trial, patients were split equally between the 2RT[®] treatment group (“2RT[®] Group” or “SNL”) and the non-treatment group (“Sham Group”).

Figure 1 plots the results of the LEAD Trial and the five-year post-LEAD review and demonstrates the difference in the rate of disease progression between the 2RT[®] Group (“SNL”) and the Sham Group in patients without coexistent reticular pseudodrusen or RPD².

Figure 1: Rate of Disease Progression, Sham Group versus 2RT[®] Group (without coexistent RPD)



The recent publication in *Ophthalmology Retina* shows that when considering all participants in the LEAD Trial and including additional data from the observational five-year post-LEAD review, there was strong evidence of significant treatment effect modification based on the coexistence of RPD² in the study eye for the 2RT[®] Group. In the 2RT[®] Group, patients without coexistent RPD² reported a significant treatment effect at five years, demonstrating a 68% reduction in the rate of progression, as compared to the Sham Group (adjusted HR = 0.32; 95% CI = 0.16 to 0.65; P = 0.002).

Tom Spurling, Director of Nova Eye Medical, said: “While these data have been calculated by the authors using post-hoc analysis, the improvement in the clinical response in patients without RPD at five years is very exciting, particularly given these patients did not receive further 2RT[®] treatment during the last two-year observation period. Overall, there was a significant reduction in the rate of progression to late-stage AMD in these patients. This is of significant benefit to patients in deferring disease progression and thus maintaining their quality of life. It also supports our previously stated position that 2RT[®] offers the potential to meet a major global unmet need to delay onset of blindness.”

The five-year post-LEAD review also provides critical input to, and has de-risked, the Company’s planned 2RT[®] FDA trial to obtain regulatory clearance in the USA, helping to affirm the patient inclusion and exclusion criteria.

The results of the five-year post-LEAD review can be viewed at: <https://doi.org/10.1016/j.oret.2021.02.015>

The results of the five-year post-LEAD review are further summarised in **Appendix 1**.

AlphaRET Pty Ltd is a wholly owned subsidiary of Nova Eye Medical Limited and was established in October 2020 to progress the development of 2RT

This release dated 5 March 2021 has been authorised for lodgement to ASX by the Board of Directors of Nova Eye Medical Limited and lodged by Simon Gray, Company Secretary.

– ENDS –

1. Guymer et al., 2021. Sub Subthreshold Nanosecond Laser in Age-Related Macular Degeneration: Observational Extension Study to the LEAD Clinical Trial. ACTRN 12612000704897
2. RPD is a key biomarker of retinal pigment epithelium (RPE) dysfunction and has a high association with progression to late-stage AMD.

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ABOUT 2RT

2RT® is a proprietary, patented laser therapy that stimulates a biological healing response in the eye to treat the intermediate stages of age-related macular degeneration (AMD) and Clinically Significant Macular Edema (CSME). Current research suggests that 2RT® stimulates a natural immune response of the retina, which restores natural metabolite flow and restores the retinal pigment epithelium – without damage to the overlying neurosensory retina (specifically, no damage is caused to the photoreceptors) or the underlying Bruch’s membrane. Importantly, 2RT® offers the potential to intervene earlier in the disease process and thereby eliminate or delay the risk of vision-threatening complications associated with AMD.

ABOUT THE LEAD TRIAL

In September 2018, the Laser Intervention in Early AMD (LEAD) Trial, a large randomized, controlled clinical trial, demonstrated the potential for 2RT® to significantly reduce the rate of disease progression in a specific group of intermediate AMD patients. The study, which enrolled 292 patients, examined whether treatment with 2RT® could delay progression of intermediate AMD to late-stage disease. Each participant was randomly assigned to the 2RT® treatment group (“2RT® Group”), or the non-treatment group (“Sham Group”) and received treatment and/or follow-up over three years. Despite not reaching statistical significance, when considering all patients enrolled in the trial, there was a trend to delay progression from early to late stage AMD in those treated with 2RT®. Post hoc analyses showed that in patients who did not have coexistent reticular pseudodrusen (RPD), a fatty deposit that is associated with later stages of AMD (76% of patients enrolled), treatment with 2RT® resulted in a clinically meaningful 77% reduction in the rate of disease progression (adjusted Hazard Ratio (HR)=0.23; 95% Confidence Interval (CI) 0.09-0.59; p=0.002).

ABOUT NOVA EYE MEDICAL

Nova Eye Medical Limited is a medical technology company that develops, manufactures and sells a portfolio of proprietary ophthalmic treatment technologies and devices. Used by eye surgeons in more than 100 countries globally, these technologies include iTrack™ minimally invasive glaucoma surgery (MIGS), a consumable surgical device that restores the eye’s natural outflow pathway to lower pressure inside the eye and to eliminate patient reliance on anti-glaucoma medications for mild-moderate glaucoma. The Molteno3® glaucoma drainage device platform is designed to enhance surgical utility and optimize clinical outcomes for long-term IOP control in cases of severe glaucoma. It also offers the benefit of a simplified and faster surgical procedure. With its sales headquarters based in Fremont, California, Nova Eye Medical is supported by a global network of more than 50 distribution partners. Manufacturing facilities are located in Fremont, California and Dunedin, New Zealand.

For additional information about Nova Eye Medical and its technologies, please visit: www.nova-eye.com

ABOUT ALPHARET

Established in October 2020, AlphaRET Pty Ltd (AlphaRET) is a wholly owned subsidiary of Nova Eye Medical Limited. AlphaRET is focussed on executing the commercialisation efforts for 2RT® and clearly delineates the 2RT® project from the Company’s core glaucoma business. In the immediate term AlphaRET will prioritize the USA regulatory pathway for 2RT®, which includes the filing of an Investigational Device Exemption (IDE) with the US Food and Drug Administration (FDA) for a major clinical study. The aim of the study will be to obtain regulatory clearance from the FDA to treat early-stage AMD patients with 2RT®.

Appendix 1 – Graphical Summary of the Five-Year Post-LEAD Review

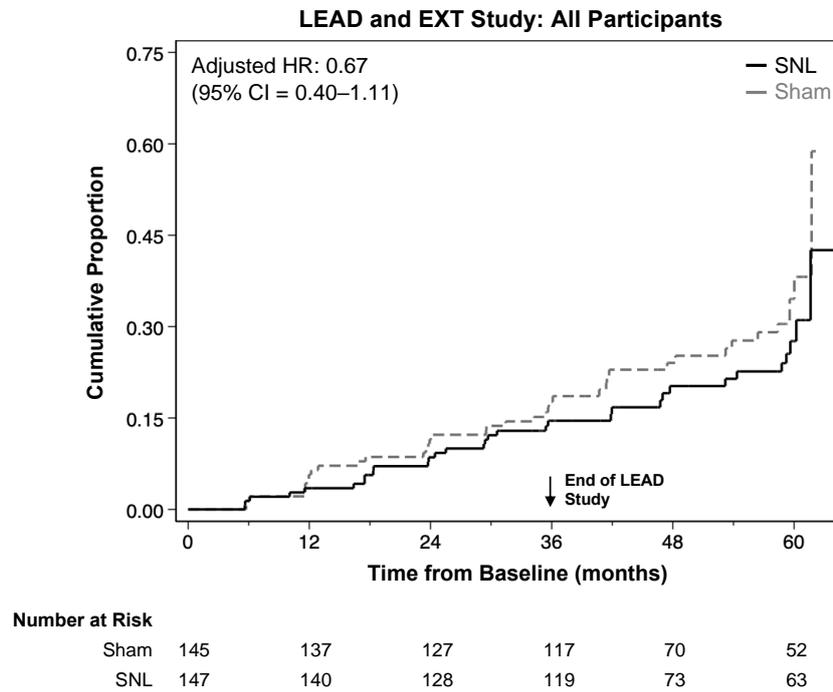
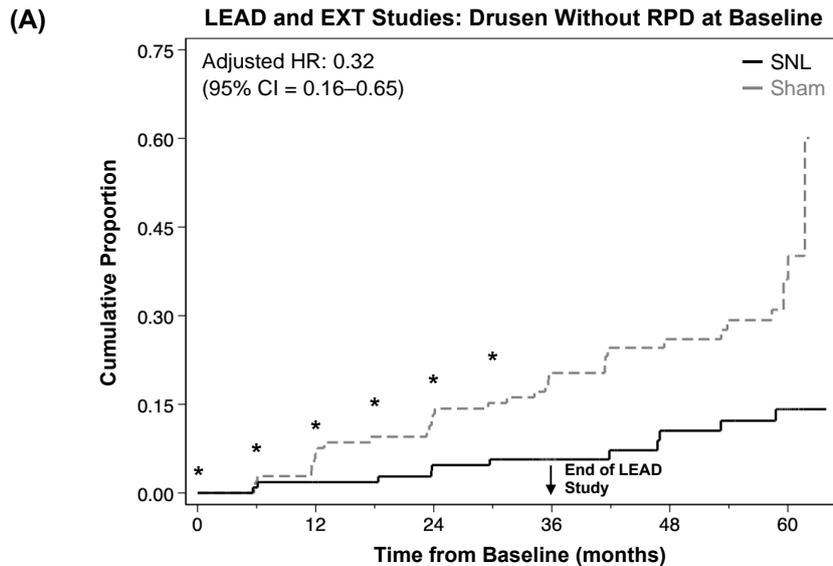
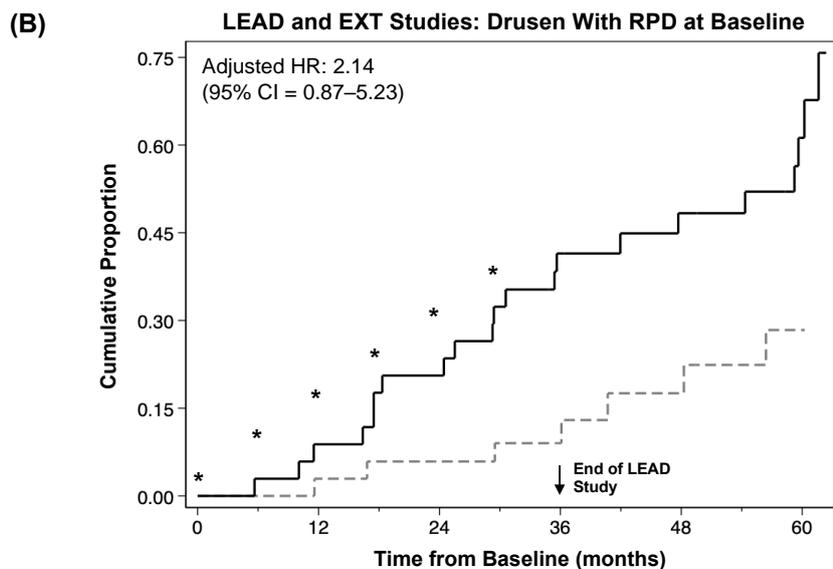


Figure 1: Kaplan-Meier failure plot of the progression to late age-related macular degeneration (AMD) presented separately for participants randomized to the subthreshold nanosecond laser (SNL; black line) and sham treatment (grey line) groups in the 36-month Laser Intervention in the Early Stages of AMD (LEAD) randomized controlled trial, including data from both the LEAD study and observational extension study (EXT). Asterisks indicate the visits during the LEAD trial where SNL or sham treatment was performed. The difference in rate of progression is presented as a hazard ratio (HR; with 95% confidence intervals [CI]) from a model that adjusted for baseline covariates.



Number at Risk

Sham	110	102	95	88	52	40
SNL	112	108	101	97	57	50



Number at Risk

Sham	35	35	32	29	18	12
SNL	35	32	27	22	16	13

Figure 2: Kaplan-Meier failure plot of the progression to late age-related macular degeneration (AMD) in the study eye for participants randomized to the subthreshold nanosecond laser (SNL; black line) and sham treatment (grey line) groups in the 36-month Laser Intervention in the Early Stages of AMD (LEAD) randomized controlled trial, including data from both the LEAD study and observational extension study (EXT) and presented separately for: **(A)** those who did not have coexistent reticular pseudodrusen (RPD) at baseline ($n = 222$), and **(B)** those who did ($n = 70$). Asterisks indicate the visits during the LEAD trial where SNL or sham treatment was performed. The difference in rate of progression is presented as a hazard ratio (HR; with 95% confidence intervals [CI]) from a model that adjusted for baseline covariates