For personal use only

ASX RELEASE
3 May 2022

Nova Eye Medical Announces Regulatory Pathway for AlphaRET 2RT® in the USA

Highlights

- **Recent FDA communications establishes USA regulatory pathway**
- **Enrolment of study population to exclude patients with reticular pseudodrusen**
- **2RT® has shown the potential to transform the global treatment of age-related macular degeneration**
- **Pivotal clinical study plan now defined and supported by leading global retinal experts**
- **Partnering discussions underway**

Nova Eye Medical Limited (ASX: EYE) (**Nova Eye Medical** or the **Company**), is pleased to announce that, based on feedback from the United States Food & Drug Administration (FDA), it has defined the clinical study plan and US regulatory approval pathway for the 2RT® retinal rejuvenation laser for intermediate age related macular degeneration (**iAMD**). The clinical study plan and the commercial rights will be pursued by the Company's wholly owned subsidiary AlphaRET Pty Ltd.

2RT® is a proprietary, world first nanosecond laser therapy to treat iAMD. 2RT® works by stimulating the rejuvenation of cells in the retina to initiate a healing response that targets the underlying causes of AMD.

Commenting on the Company's communications with the FDA in relation to the clinical study plan and regulatory pathway for 2RT®, **Nova Eye Medical Managing Director, Mr. Tom Spurling, stated:**

> *"As we pioneer this novel ground-breaking therapy using 2RT® to transform the treatment of intermediate iAMD, we acknowledge that the dialogue with the FDA has been time-consuming. It has also been complex."*
>
> *"We believe that the extent of the dialogue with the FDA demonstrates the potential importance of 2RT® and it is a very positive achievement to have now established a clear path forward."*

For personal use only

2RT® has the potential to transform the treatment of AMD

At present, treatment options for iAMD patients are limited, with nutrient supplements a possible option. For patients with AMD in its late "dry" form there is no treatment and for patients with AMD in its late "wet" form (approximately 10% of AMD patients[1]) invasive ocular injections of anti-VEGF pharmaceuticals are administered over many years, typically every 4-8 weeks. These pharmaceuticals do not cure the disease and are traumatic for many patients. It has been noted that these anti-VEGF pharmaceuticals diminish in their impact after 3-5 years, with patients experiencing a decline in visual outcomes[1]. According to recent reports, health care systems in the most developed economies, including Australia, spend more money on anti-VEGF pharmaceuticals than any other eye therapy as well as treatments for most other diseases[2].

2RT® has the potential to transform the global treatment of AMD by treating patients earlier in the disease state. This represents a revolutionary change from the status quo and thereby provides enormous clinical and commercial potential.

2RT® has been the subject of a 20-year development program by the Company. The 2RT® technology is based on original investigations performed by world-renowned laser expert Prof. John Marshall PhD, FRCPath, FMedDSci (Institute of Ophthalmology, University College London, UK). Prof. Marshall is actively involved in the 2RT® project and is a Board member of AlphaRET

In late 2018, 2RT® was shown to reduce progression of iAMD in a key subgroup of patients by 77%[3] in the seminal "Subthreshold Nanosecond Laser Intervention in Age-Related Macular Degeneration – The LEAD Randomised Controlled Clinical Trial" **(LEAD Study)** published by Robyn H. Guymer AM, MBBS, PhD, et al in the peer reviewed journal *Ophthalmology*, American Academy of Ophthalmology.

The LEAD Study results were confounded by a subgroup of the study population (24%) who had reticular pseudodrusen (RPD) at the time of study enrolment and did not respond well to 2RT® treatment.

For personal use only

FDA feedback further defines pivotal clinical study design including confirmation of exclusion of patients with RPD

AlphaRET's recent communications with the FDA has provided guidance on the clinical study plan and a subsequent regulatory pathway for a clearance to market 2RT® in the USA for the treatment of select patients with iAMD to delay progression to vision threatening, late-stage AMD.

This follows the submission in July 2021 of an Investigational Device Exemption (IDE) application to the FDA to conduct a pivotal study for 2RT® in the treatment of iAMD. Based on the FDA feedback, approval to commence the pivotal clinical study using investigator sites in the USA is contingent upon AlphaRET providing additional clinical data to the FDA, which the Company plans to derive through the course of the study itself which will commence at sites outside the USA.

Most importantly, the FDA has agreed that patients with RPD will be excluded from the pivotal clinical study as they (and the broader retinal community) seek to confirm the findings of the LEAD Study key subgroup analysis.

AlphaRET will commence the confirmatory pivotal clinical study outside of the USA at sites in Australia, Canada and Europe. The recruitment of investigator sites will be undertaken in accordance with the study protocol reviewed by the FDA. The Principal Investigator for the study will be Professor Robyn Guymer AM MBBS, PhD, Deputy Director and Head of Macular Research at the Centre for Eye Research Australia (CERA) and a global expert on AMD. The early data gathered in the study at the investigator sites outside of the USA will then be submitted to the FDA to satisfy the request for certain clinical data. The Company expects that this data will enable the expansion of investigator sites into the USA and the progression of the pivotal clinical study for USA marketing clearance and will not materially impact the overall study schedule.

Commenting on the pivotal clinical study, **Principal Investigator Professor Robyn Guymer, AM MBBS, PhD, said:**

> *"I am pleased the be a part of this follow up study. 2RT® addresses the disease in its earlier stages. No other device or pharmaceutical in the world does this. Like all chronic disease, early detection and treatment is vital to prevent complications and the ensuing burden on health care systems, and patients and their families. The LEAD study was very encouraging but was not conclusive. I look forward to starting this work, providing additional information to the FDA and then a successful study outcome."*

For personal use only

Dr. Philip Rosenfeld, Professor of Ophthalmology at the Bascom Palmer Eye Institute of the University of Miami Miller School of Medicine in Miami, pioneered the use of Avastin (anti-VEGF pharmaceutical) for the treatment of wet AMD and an advisor to AlphaRET commented as follows:

> *"The LEAD Study completed by Professor Guymer was a well-controlled clinical trial that showed the immense potential of 2RT®. However, a second study is required. If the second study is successful, AlphaRET will have the data needed to harness that potential and significantly change the landscape in AMD therapy in the USA and around the world. It is not unusual that the FDA is taking such a cautious approach and requesting additional data prior to establishing investigator sites in the USA. In fact, I am pleased that we now have a clear understanding of what is needed by the FDA to move 2RT® forward in the USA."*

Opportunity summary and partnering discussions

The annual revenue opportunity following the completion of a successful pivotal clinical study and subsequent commercialisation program is estimated at US$600 million. AlphaRET will move forward to add value with work on the study establishment and investigator site selection and in parallel continue to engage with potential partners and funding sources to support the clinical study. The recent clarification of the clinical study design and protocol that excludes patients with RPD, and subsequent US FDA regulatory pathway is facilitating these partnering discussions.

This release dated 3 May 2022 has been authorised for lodgement to ASX by the Board of Directors of Nova Eye Medical Limited and lodged by Simon Gray, Company Secretary.

Footnotes

1. Keenan TD, Vitale S, Agrón E, et al. Visual Acuity Outcomes after Anti-Vascular Endothelial Growth Factor Treatment for Neovascular Age-Related Macular Degeneration: Age-Related Eye Disease Study 2 Report Number 19. Ophthalmol Retina. 2020;4(1):3-12. doi:10.1016/j.oret.2019.06.001
2. Australian Pharmaceutical Benefits Scheme year to 30 June 2021 spend on Aflibercept and Ranibizumabs A$635m. Highest on USA Medicare USA Department of Health, August 2018, $2.2bn
3. A *post hoc* analysis of the data in the "Subthreshold Nanosecond Laser Intervention in Age-Related Macular Degeneration - The LEAD Randomized Controlled Clinical Trial"

– ENDS –

For personal use only

Company
Tom Spurling
Managing Director
+61 417 818 658
tspurling@nova-eye.com

Company
Kate Hunt
Head of Marketing
+61 404 080 679
khunt@nova-eye.com

Investors
Mark Flynn
Investor Relations
+61 416 068 733
mflynn@nova-eye.com

ABOUT ALPHARET PTY LTD AND NOVA EYE MEDICAL LIMITED

Nova Eye Medical Limited is a medical technology company that develops, manufactures and sells a portfolio of proprietary ophthalmic treatment technologies and devices. AlphaRET, its wholly owned subsidiary, is focussed on commercialisation of the 2RT® retinal rejuvenation laser.

In addition, Nova Eye Medical manufactures and sells glaucoma treatment technologies used by eye surgeons in more than 100 countries globally. The technologies include iTrack™, a consumable surgical device for the treatment of glaucoma. The Company also manufactures and sells the proprietary Molteno3® glaucoma drainage device for the treatment of severe or complex glaucoma. 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 THE PIVOTAL CLINICAL STUDY

Two protocols have been defined for the pivotal clinical study: a fast-track protocol, 24 months, for patients with iAMD at a higher risk of progression (“Protocol A”) and a more extensive protocol for general iAMD patients (“Protocol B”). Both protocols will be conducted concurrently. Protocol A will provide an earlier study outcome than Protocol B, however. The concurrent execution of both Protocol A and Protocol B will enable the Company to harvest data across the broader range of indications possible and provides greater scope for a successful study outcome.

- Protocol A will recruit approximately 250 patients into either a treatment arm or a control arm. Each patient in the treatment arm will undergo four (4) 2RT® treatments at 6monthly intervals, followed by six months of follow-up, equating to a total study period of 24 months. This protocol is based on a signal in the LEAD Study that suggested that

For personal use only

2RT® therapy slowed progression in patients with iAMD with anatomical changes that indicate a much higher risk of progression.

- Protocol B will recruit approximately 550 patients into either a treatment arm or a control arm. Each patient in the treatment arm will be treated with 2RT® every six months over a 30 month period (6 treatments) and followed to 36 months for the primary end points. This protocol will solidify the findings from the post hoc analysis of the LEAD Study.

Current clinical work in Australia on the higher risk patient group

AlphaRET, in conjunction with CERA has already commenced a small, separate study to understand more about the response to 2RT® of the patients with anatomical changes that indicate a much higher risk of progression to late-stage AMD targeted in Protocol A. This study, project name "Protocol A Australia", has so far recruited 10 out of 60 patients. Recruitment has been impacted by COVID 19 related staff absence and clinic restrictions. Completion of Protocol A Australia is expected in late 2023. This work has an estimated total cost of $400,000.

Program milestones

Program milestones are set out below:

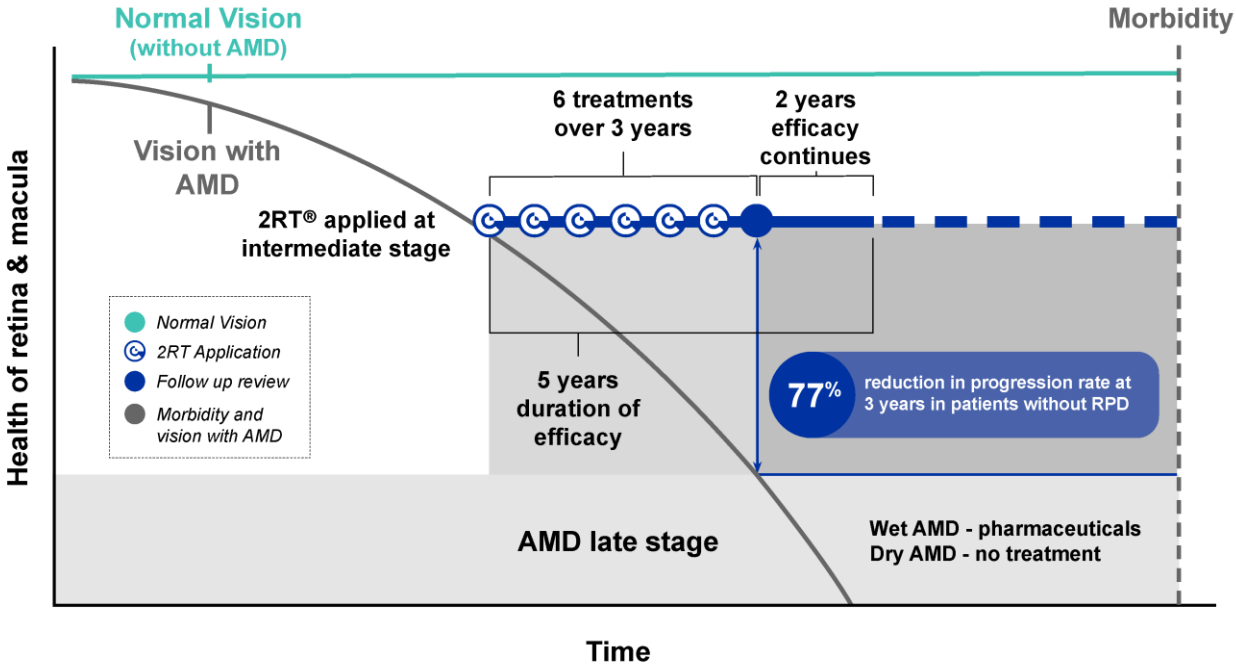
i. Engage contract research organisation and investigator site selection Australia, Canada and Europe
ii. Partnering arrangements finalised
iii. Recruitment and study commencement in Australia, Europe and Canada
iv. Additional clinical data provided to FDA and approved
v. Expansion of study sites into USA
vi. Feedback from "Protocol A Australia" received to provide indication of outcome for "Protocol A" study
vii. Protocol A study complete
viii. Protocol B study complete
ix. Commercialisation activities outside the USA and submissions to FDA to support commercialisation activities inside the USA.

Milestones i) through vi) are currently planned to be completed by late 2023 to early CY 2024 and to some extent depend on partnering outcomes. Subsequent milestones will be progressively met through to 2026

For personal use only

Schematic describing 2RT® intervention

The schematic shows when 2RT is applied in the disease progression and the reduction in progression identified in the LEAD Study *post hoc* analysis of the patients without reticular pseudodrusen at baseline.



1. Based on post hoc analysis reported within "Subthreshold Nanosecond Laser Intervention in Age-Related Macular Degeneration - The LEAD Randomized Controlled Clinical Trial" Robyn H. Guymer, MBBS, PhD, et al and published in peer reviewed journal Ophthalmology of the American Academy of Ophthalmology. The post hoc analysis found that the 77% reduction in the rate of progression occurred in patients who did not have reticular pseudodrusen (RPD) at enrolment. 24% of the study population had RPD at enrolment