AlphaRET

2RT® – Potential Breakthrough Treatment of Macular Degeneration (AMD)

October 2024

AlphaRET a wholly owned subsidiary of Nova Eye Medical Limited

Executive Summary of 2RT® opportunity

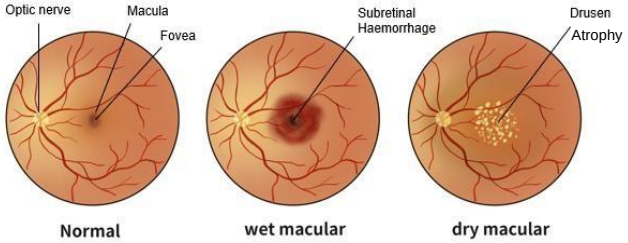
- AMD affects over 200m people globally, 14 million in US and is the leading cause of blindness of the elderly population.
- 2RT® is a laser-based treatment that addresses the root cause of AMD and offers advantages over traditional drug therapy.
- 2RT® treatment efficacy has been shown in an Australian multicentre study to significantly reduce the rate of progression of AMD[1].
- Partner investment capital required to fund the project.

[1]LEAD study post hoc analysis

Introduction to Macular Degeneration (AMD)

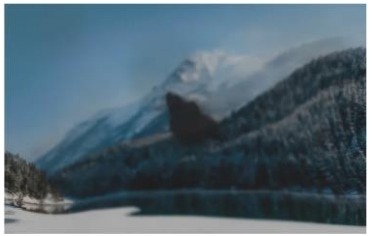
- AMD is a degenerative retinal disease causing progressive vision distortion with loss of central vision loss and eventual blindness.
- AMD is graded into Early, Intermediate and Late stages
- Patient genetics determine disease course with late-stage AMD progressing to either rapidly advancing "Wet" or slow atrophy “Dry’.
- AMD is treated with drugs and their direct cost currently exceeds US$10 Billion globally, $3.5 Billion in USA.

Large unmet need to prevent progression in early-stage AMD before vision loss occurs.



Normal vision

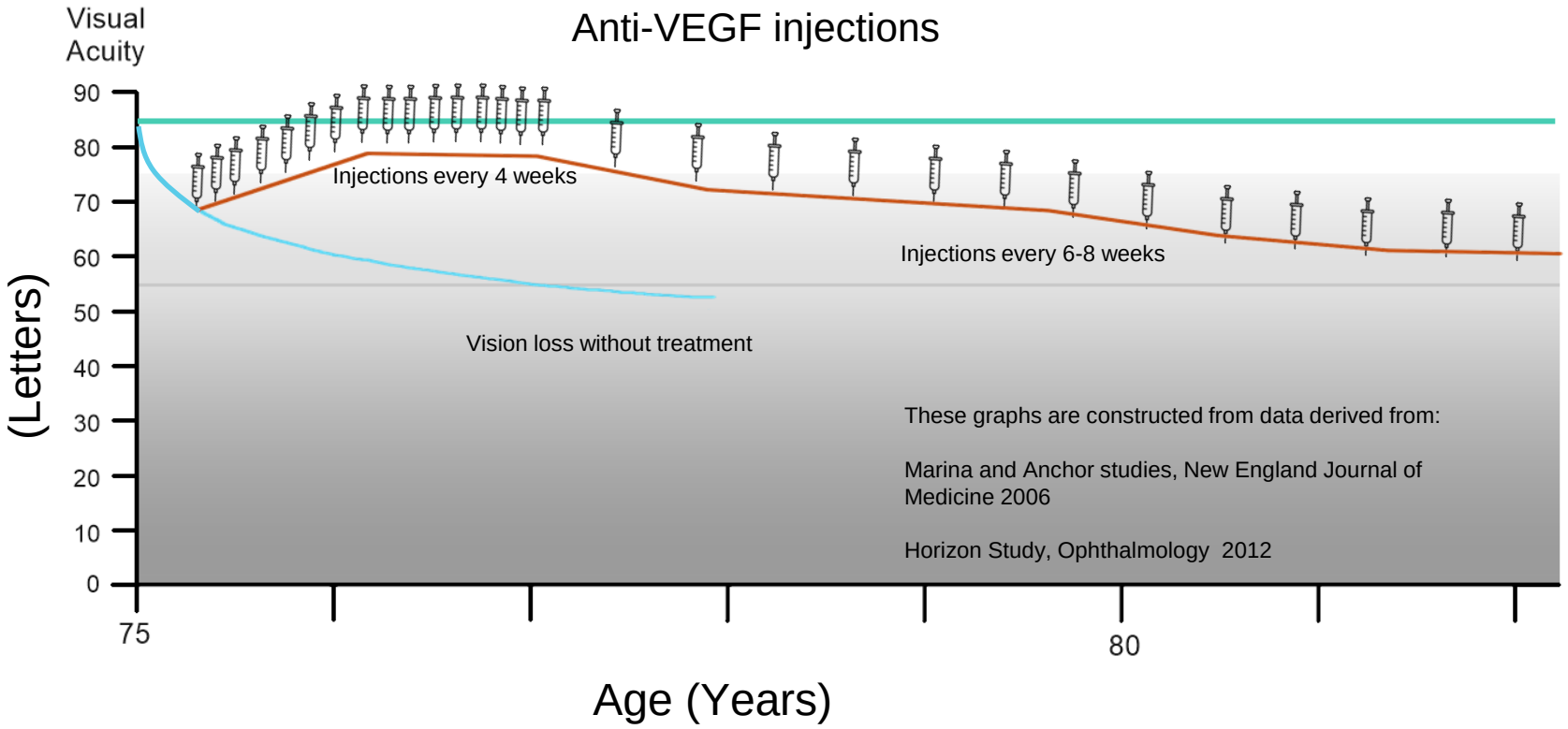
Vision with AMD



Current AMD Treatment Paradigm

- Current treatments for wet AMD supress symptoms.
- Drug treatment starts AFTER VISUAL DECLINE occurs and treatment does regain some vision but within 5 years the patient's vision is severely impaired.
- Drug treatment involves monthly injections in a sterile injecting room for 2 years. This is a high cost to health care systems and a burden on patients and their carers.
- Drugs are injected directly into the eye, which patients dread.
- 2RT® is clinic based bi-annual treatment, well tolerated by patients, has a high safety profile and permitting re-treatment.
- 2RT® targets the intermediate stage of AMD prior to onset of visual decline to push out late stage and prevent onset of blinding symptoms.
- 2RT® is effective in treating Clinically Significant Macular Edema (CSME) and under trials for treating other retinal dystrophies.

Vision Loss Associated with Wet AMD Drug Treatment



2RT® Treatment Overview

- 2RT® is a patented therapy using a nanosecond ultra short pulsed laser (USPL) and unique pixelated laser beam profile that uses intra-cellular cavitation to stimulate rejuvenation of RPE cells.
- Painless “in office clinic” 10 minute bi-annual treatment has demonstrated delay of progression of both Wet and Dry AMD in selected patients[1].
- **No Collateral damage to photoreceptors or neuroretina (unlike any other laser treatment)**

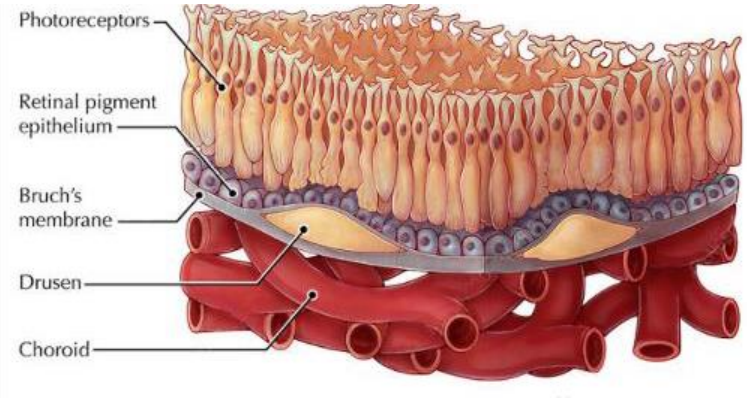
“Based on the LEAD study outcomes, 2RT® is currently a leading candidate treatment in the world for slowing the progression of patients with intermediate AMD to either late stage Wet or Dry AMD.”

Edison Group in its publication “Saving the sight of millions, Blindness: the underrated business case” September 2020 – https://bit.ly/EdisonAMD).

1. University of Melbourne organised “LEAD” 292-person study, led by Professor Robyn Guymer at Centre for Eye Research Australia (CERA). LEAD showed 77% reduction in progression rate of AMD in selected patients.

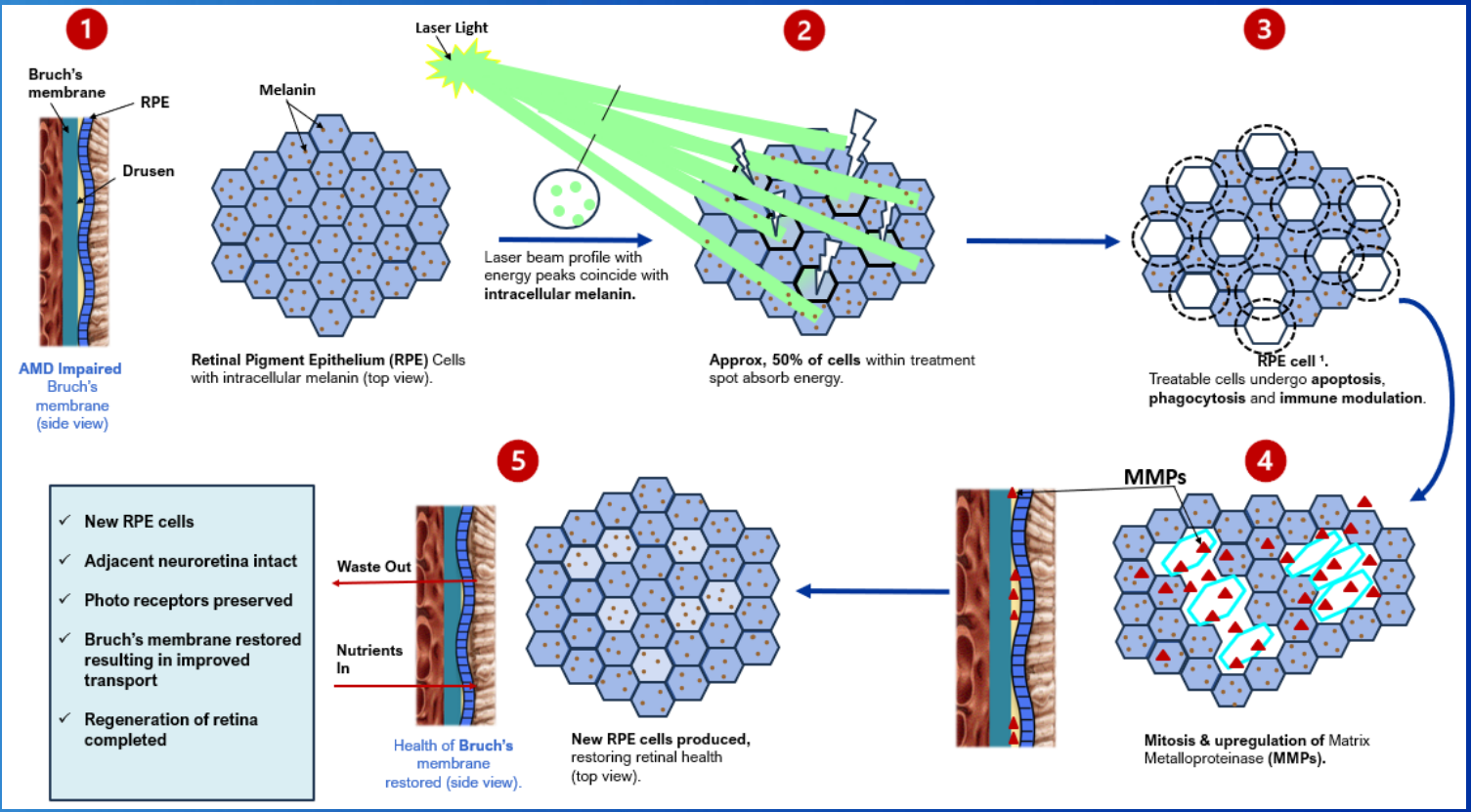
AMD – Failing Hydraulic Conductivity of Bruch's Membrane

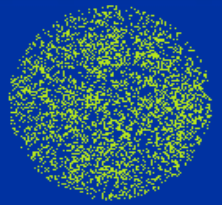
AMD results in the loss of hydraulic conductivity of Bruch's Membrane, with a progressive accumulation of drusen leading to the metabolically insufficiency of the neuro-retina



- Bruch's, is a limiting membrane, supported by the RPE cells to maintain the immune privilege of the eye.
  - Bruch's Membrane separates the retina from the highly vascular and nutrient-rich blood supply, the Choroid.
- With advancing age, lipid waste plaques (Drusen) deposit progressively between the (RPE) and Bruch's membrane.
  - As hydraulic conductivity decreases with age, retinal health diminishes and depending on patient's genetics manifests in neovascular (Wet) or atrophic (Dry) AMD.

Mechanism of Action of 2RT® Laser





- **Laser light spikes absorbed by melanin causes intracellular cavitation.**
- **Activated immune response, stimulates removal of damaged cells and drusen without inflammation or necrosis.**
- **Apoptosis and mitosis results in reduction of drusen load, restoring RPE and Bruch's membrane health, improving nutrient transport.**

Regulatory Approvals for 2RT®

- **Europe and Mutual Recognition Jurisdictions, CE Mark** (including Switzerland, UK, Australia, NZ) - 2RT® is approved for the treatment of early AMD, to improve macular function and appearance in early AMD.

- **Europe and Mutual Recognition Jurisdictions, CE Mark** (including Switzerland, UK, Australia, NZ, Canada) - 2RT ® is approved for treating clinically significant macular edema (CSME).

- **USA - 2RT® has clearance via a 510(k)** for treatment of CSME.

- Granted approvals provide the opportunity for early sales in North America and Europe.

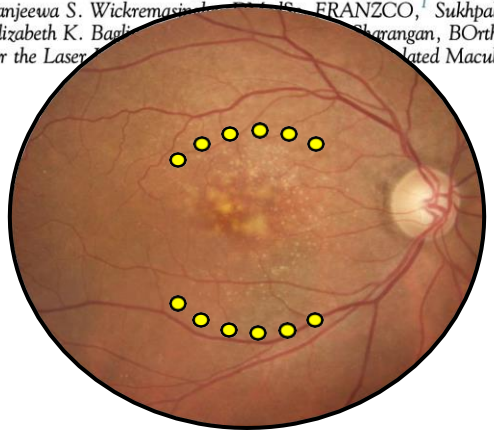
Current installed global base 40 units

AMERICAN ACADEMY OF OPHTHALMOLOGY®

Subthreshold Nanosecond Laser Intervention in Age-Related Macular Degeneration

The LEAD Randomized Controlled Clinical Trial

*Robyn H. Guymer, MBBS, PhD,[1] Zhichao Wu, BAppSc(Optom), PhD,[1] Lauren A.B. Hodgson, MPH,[1] Emily Caruso, BOrth,[1] Kate H. Brassington, MPH,[1] Nicole Tindill, BBus(BIS),[1] Khin Zaw Aung, MBBS,[1] Myra B. McGuinness, MBiostat,[1] Erica L. Fletcher, PhD,[2] Fred K. Chen, MBBS(Hons), PhD,[3] Usha Chakravarthy, MD, PhD,[4] Jennifer J. Arnold, MBBS(Hons),[5] Wilson J. Heriot, MBBS, FRANZCO,[6] Shane R. Durkin, MBBS(Hons), FRANZCO,[7] Jia Jia Lek, PhD,[8] Colin A. Harper, MBBS, FRANZCO,[1] Sanjeewa S. Wickremasinghe, MBBS, FRANZCO,[1] Sukhpal S. Sandhu, MD, FRANZCO,[1] Elizabeth K. Baglin, [illegible] Kugarangan, BOrth,[1] Sabine Braat, MSc,[9] Chi D. Luu, PhD,[1] for the Laser [illegible]lated Macular Degeneration Study Group**



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***n* = 292 participants**
with bilateral large drusen

Sham (*n* = 145)

2RT (*n* = 147)

One study eye, treatment every 6 months

6 monthly follow-up, for 36 month period

5 Sites in Australia, 1 Site in Northern Ireland

Proof-of-concept study of efficacy and safety

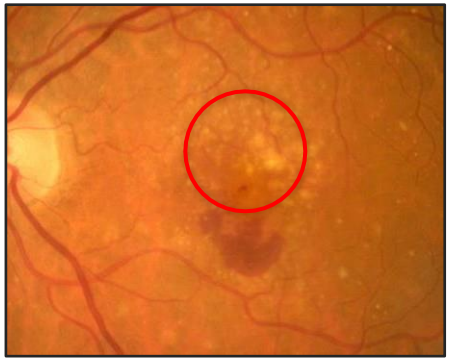
In Vitro Studies → Mouse Model → Human Tissue → Pilot Clinical Study → LEAD Randomised Controlled Trial → IDE Pivotal Study

Pre-Clinical Studies | Clinical Studies

LEAD Primary Endpoint –

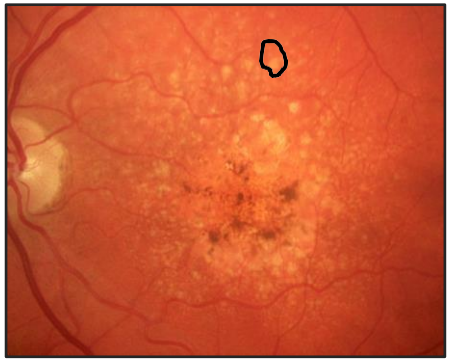
Onset of late stage determined with multi-modal imaging

Neovascular AMD

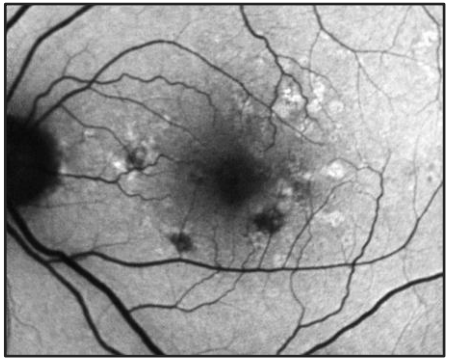


Lesions on Fluorescein Angiography
(or subretinal haemorrhage + fluid)

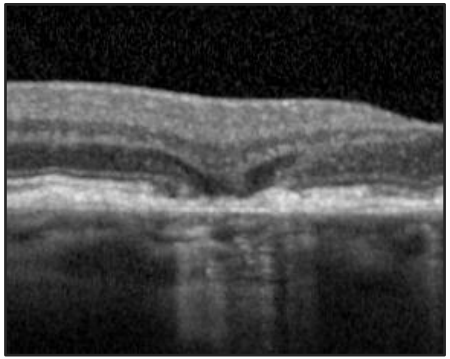
Drusen-Associated Atrophy (any of the following)



Colour Fundus Photography
Geographic Atrophy (GA)



Fundus Autofluorescence (FAF)
FAF-defined Atrophy



Optical Coherence Tomography (OCT)
Nascent Geographic Atrophy (nGA)

Eligibility

≥50 Years Old

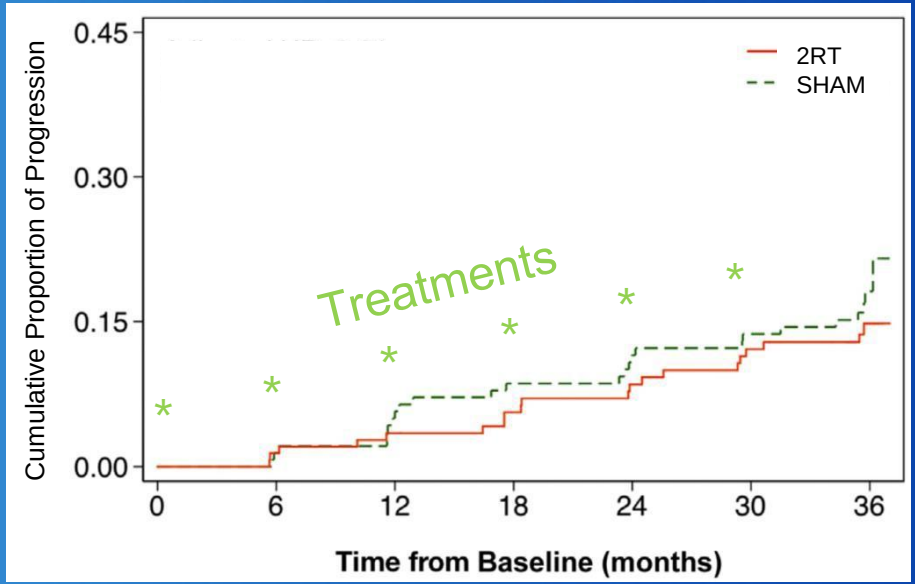
Bilateral Large Drusen
(≥1 druse within 1500µm)

Visual Acuity
20/40 or better OU

LEAD Results Comparison - Primary Uutcome to 5 years

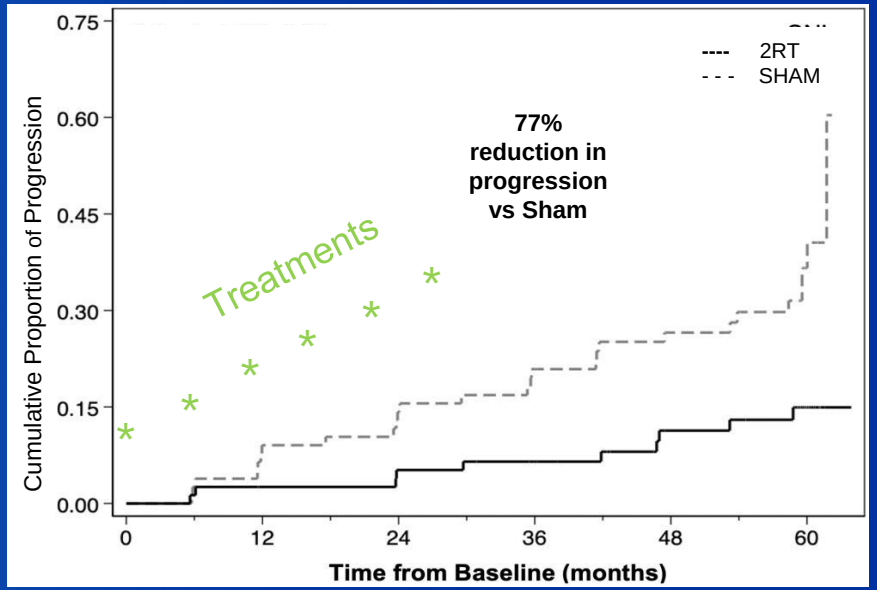
LEAD Primary outcome

- At the time of protocol development, the pathological impact of Reticular Pseudodrusen (RPD) was not understood.
- RPD presence confounded study results



Post Hoc - RPD patients excluded (24% of study population)

- Significant reduction in progression compared with Sham
- Strong evidence of treatment effect modification based on coexistence of RPD



LEAD Study Informs Confirmatory Pivotal Study Design

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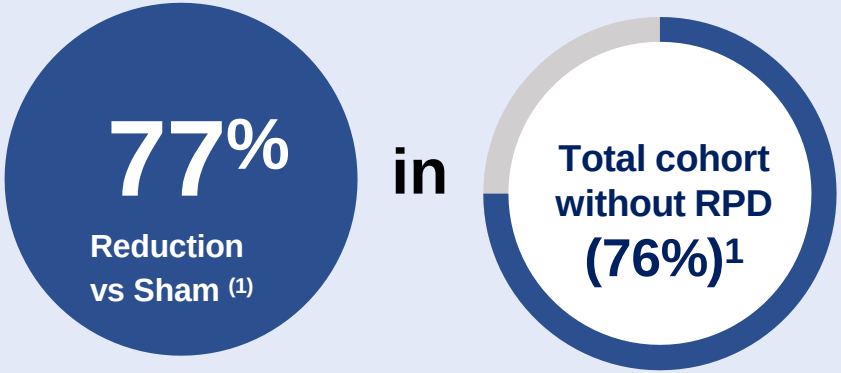
Trial:

LEAD[1] study conducted by the Centre for Eye Research Australia (Melbourne), a 292 patient cohort treated with 2RT from 2012-2018 with follow up through to 2020.

Results:

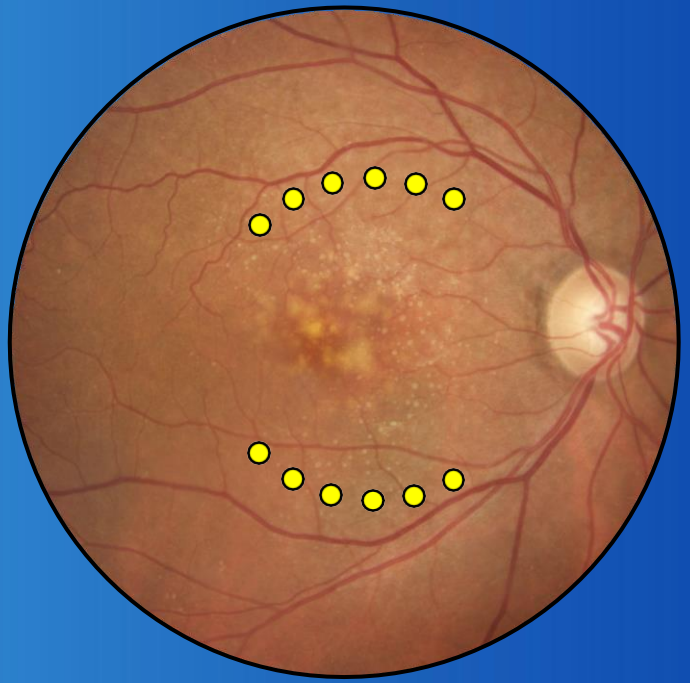
Post-hoc analysis demonstrated 76%[1] of patients treated had a 77%[1] reduction in progression to late-stage AMD over
36 months of treatment, and sustained effect for **24 months following treatment cessation[2].**



- While the LEAD study demonstrated significant success, it did not meet its primary end points because 24% of the patients had reticular pseudodrusen (RPD)[1] obscuring the promising results.
- **Additional studies required will exclude RPD patients to validate post hoc analysis**

1. Based on a post hoc analysis reported within " Subthreshold Nanosecond Laser Intervention in Age-Related Macular Degeneration – The LEAD Randomised Controlled Clinical Trial" Robyn H. Guymer, MBBS, PhD, et al and published in peer reviewed journal Ophthalmology of the American Academy of Ophthalmology 2. 5 year paper**

LEAD 5 - Year Summary

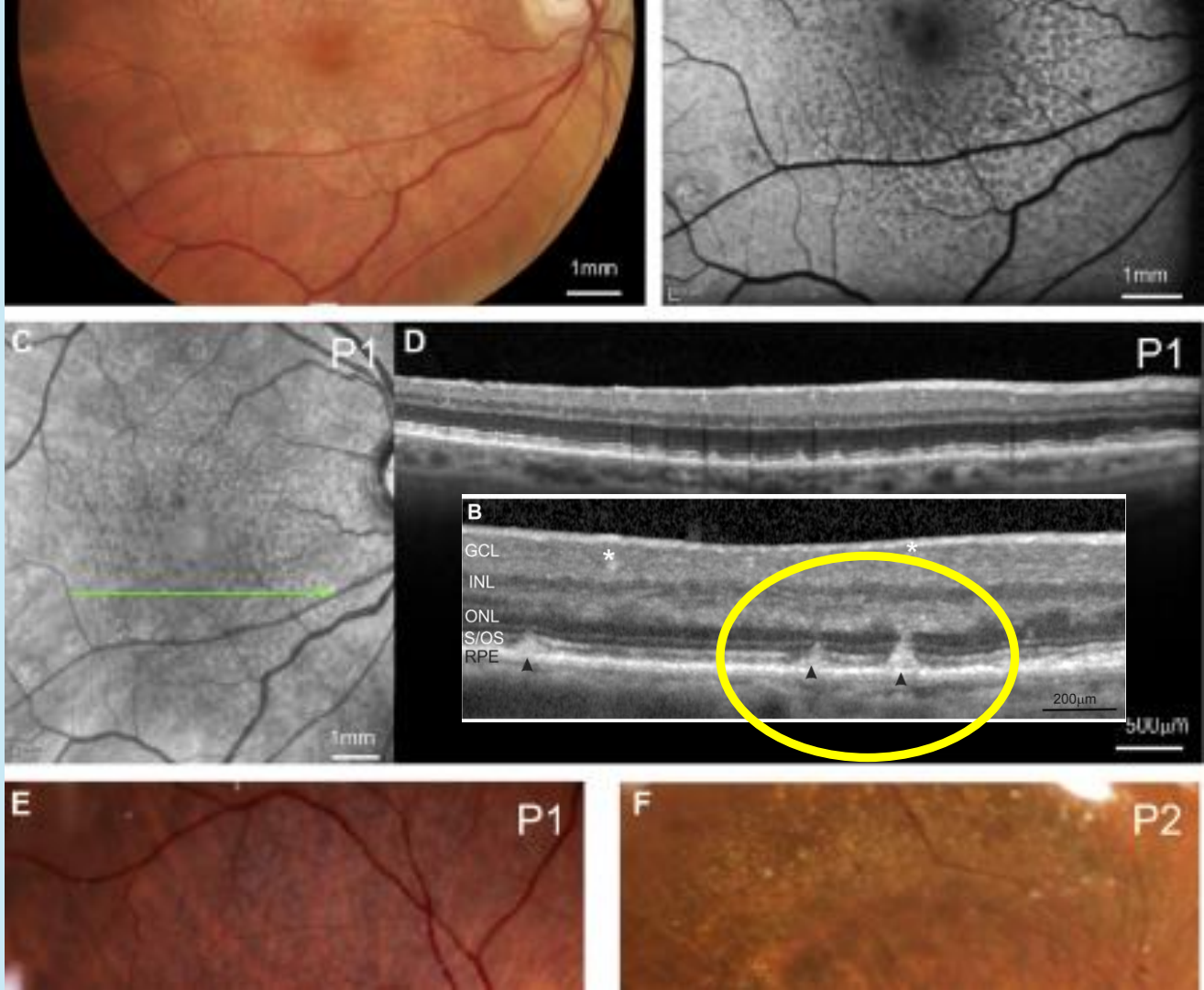


- Delay of Late AMD compared with untreated cohort.
- Conversion to Wet AMD significantly reduced.
- Sustained beneficial 2RT treatment effect for those without coexistent RPD out to 5 years.

Excluding Reticular Pseudodrusen (RPD)

- Scattered drusenoid deposits located in sub-retinal space
- Detrimental effect on RPE health
- Patients with RPD are at high risk for progression to late AMD
- RPD presents as “haystack” appearance on OCT (yellow circle)
- RPD presents as ribbon or net-like pattern with *en face* imaging
- Multi-modal imaging allows the identification of RPD
- Multi-modal imaging now ubiquitous in ophthalmic healthcare facilities

- **Multimodal screening with Ai promises efficient means of patient selection and exclusion of RPD patients.**



Vision Loss with Wet AMD

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Vision Loss Delayed with 2RT

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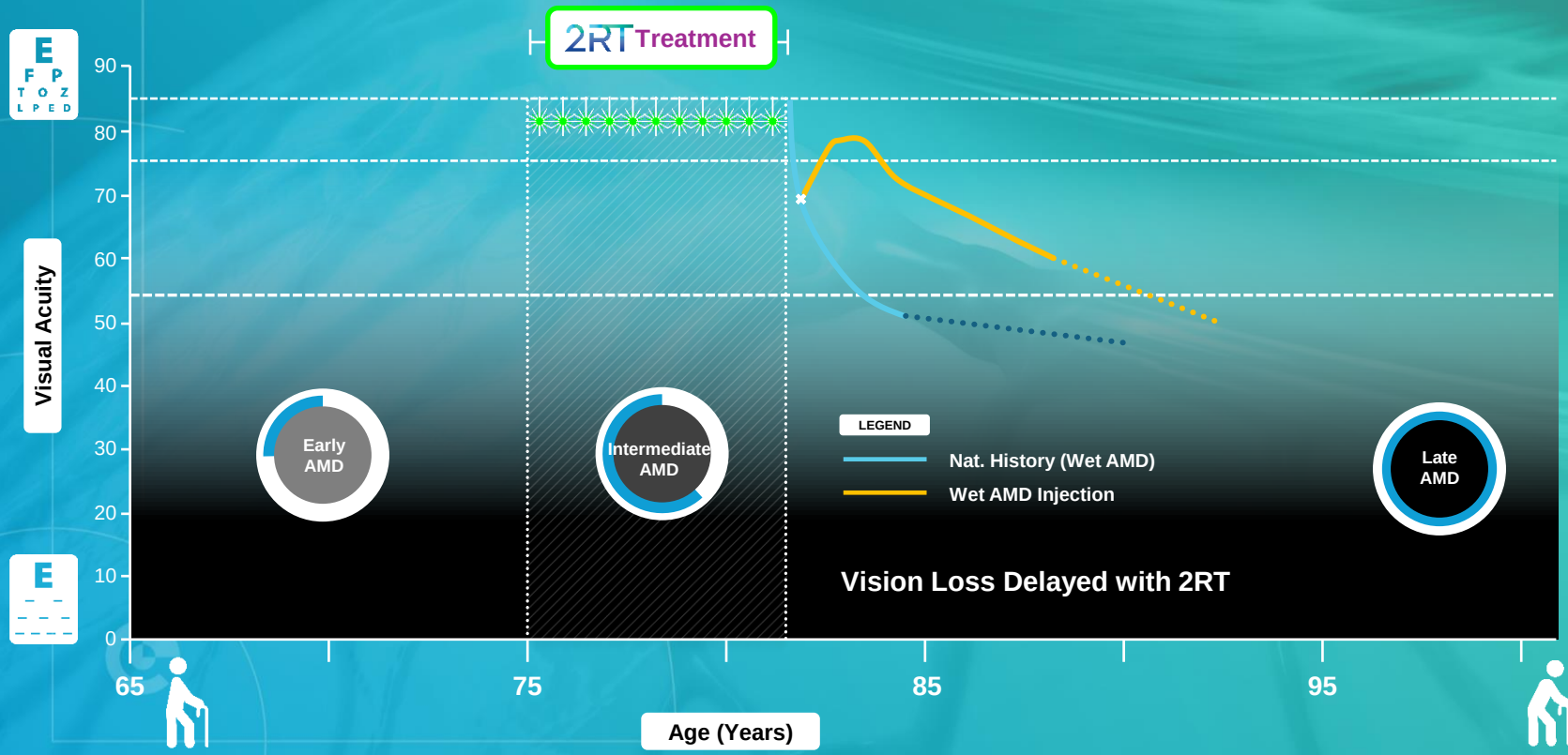

Vision Loss Further Delayed with 2RT

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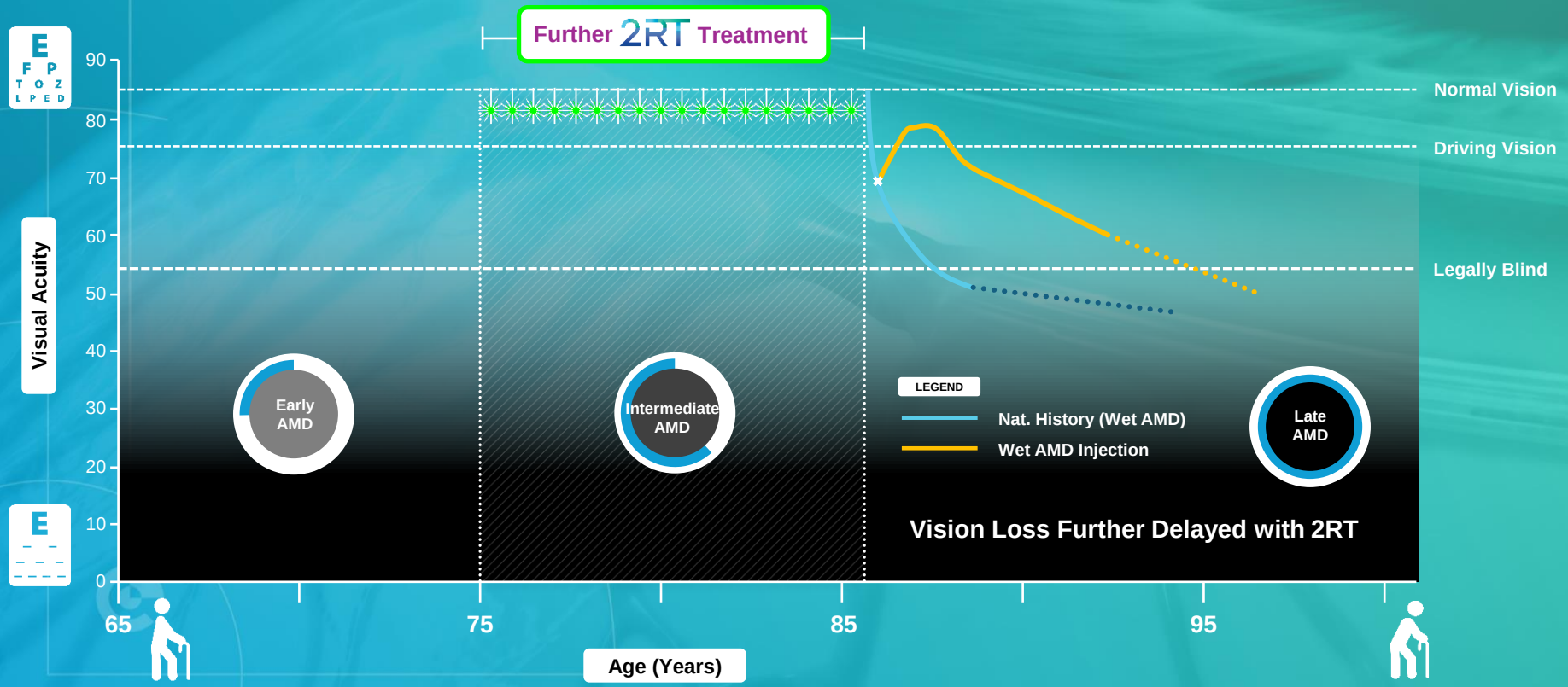
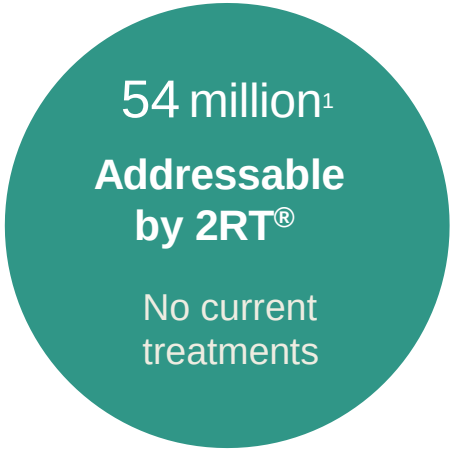


Addressable Population

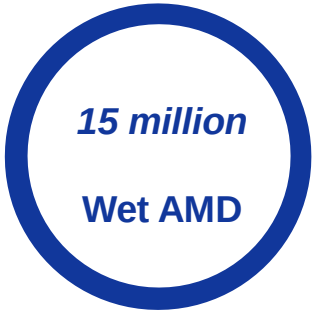
A major opportunity with widespread implications

Intermediate stage – 2RT®

Nutraceuticals are currently recommended but are ineffective [2]

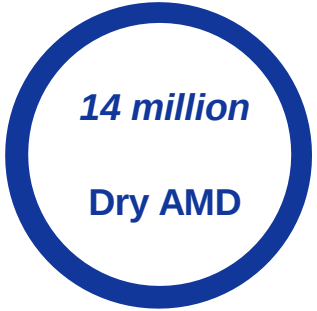


Late stage - drugs



- Australian PBS A$0.7 billion (3)
- US Medicare US$3.5 billion (4)

Highest spends on any drug in US and Australia. Treating symptoms only. Requires retreatment.



- Iveric Bio, acquired by Astellas in April 2023 for US$5.9 billion
- Apellis, US$3.4 billion (NASDAQ: APLS), FDA approval with labelling conditions received 17 Feb 2023. Injections every 6 to 8 weeks
- Approval in Europe not achieved

DISEASE PROGRESSION

1. AlphaRET estimate based on LEAD study and MarketScope 2018 Ophthalmic Lasers Report
2. Macular Degeneration Foundation Australia recommendation pamphlet “Nutrition for AMD”.USA National Eye Institute AREDS/AREDS 2 study concluded that supplements reduces the rate of progression from intermediate AMD to advanced AMD by 17% in one cohort 3. Australian June 2023 PBS data. 4. Expenditure on Eylea, Avastin and Lucentis USA Medicare Report August 2018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