
AlphaRET

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# Reducing Progression Rate of Age-Related Macular Degeneration

December 2021

**alpha-ret.com**

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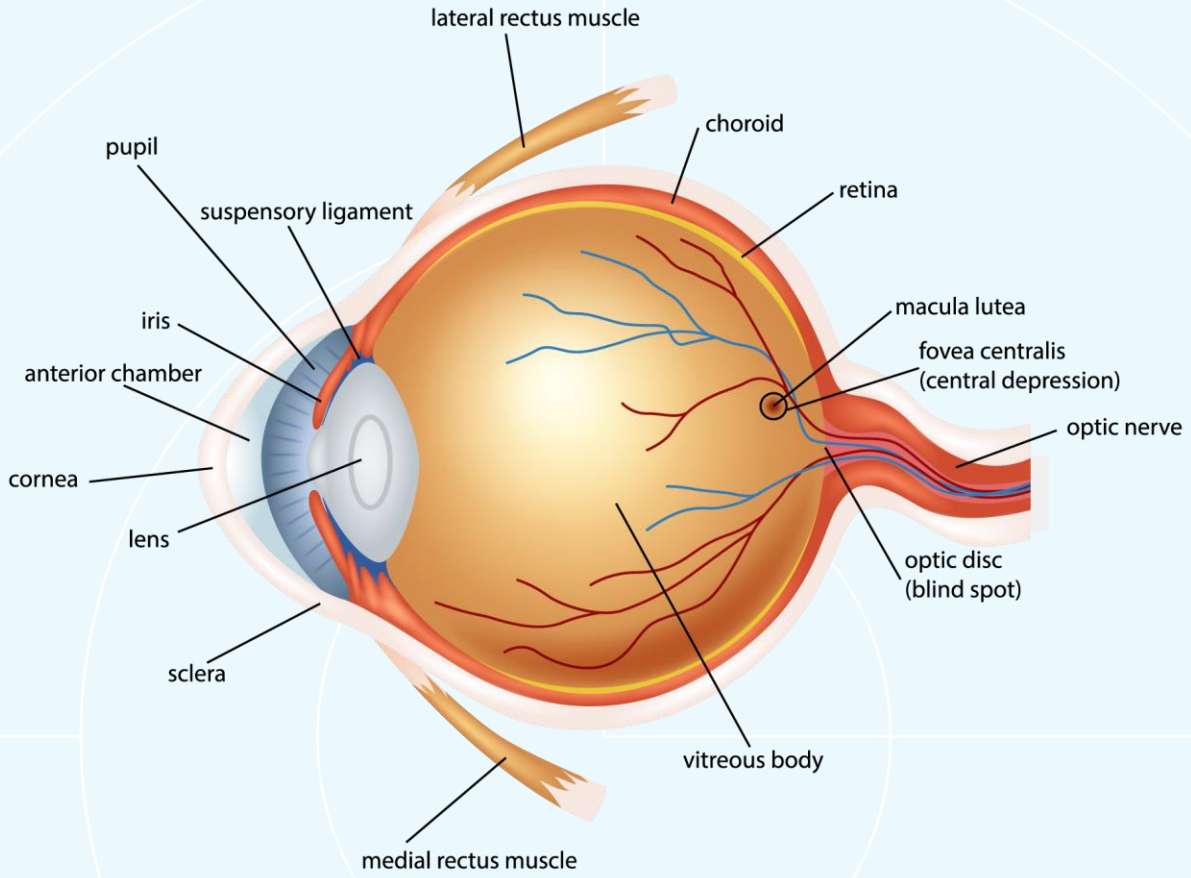


# Age-Related Macular Degeneration

# Reducing Progression Rate of AMD

**AMD is the leading cause of blindness in the developed world for people over 50**[1]

AMD in its **late stage** has two forms: "Wet" (choroidal neovascularization) and "Dry" (geographic atrophy)

Currently drugs provide temporary visual recovery and stabilization for patients with "Wet" AMD. There is no treatment for "Dry" AMD and patients with intermediate AMD take vitamins

Expenditure on such pharmaceuticals is largest spend in the health care systems of developed countries[2]

Global spend on pharmaceuticals **US$5.7billion**[3] and on vitamins for eye health **US$2.4billion**[4]

2RT® to be used 2x per year for treatment of certain patients with intermediate AMD *before* the patient progresses to late stage AMD[4]

1 "Eyes on the future – A clear look at AMD". Deloitte Access Economics, 2011 , 2. Highlight on Australian Pharmaceutical Benefits scheme year to 30 June 2020 spend on Aflibercept and Ranibizumabs A$577m. Highest on USA Medicare USA Department of Health, August 2018, $2.2bn. 3. Edison Group report Sept. 2020, 4. Reported in PRN Newswire 5 October 2020, supplements for AMD represents the largest share. 5. Based on a *post hoc analysis* LEAD Study

# Intermediate Age-Related Macular Degeneration

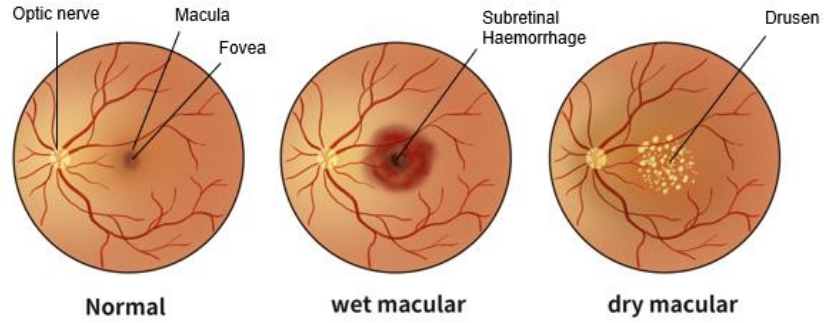
AMD in its early or intermediate stage is based on the number and size of “drusen”.

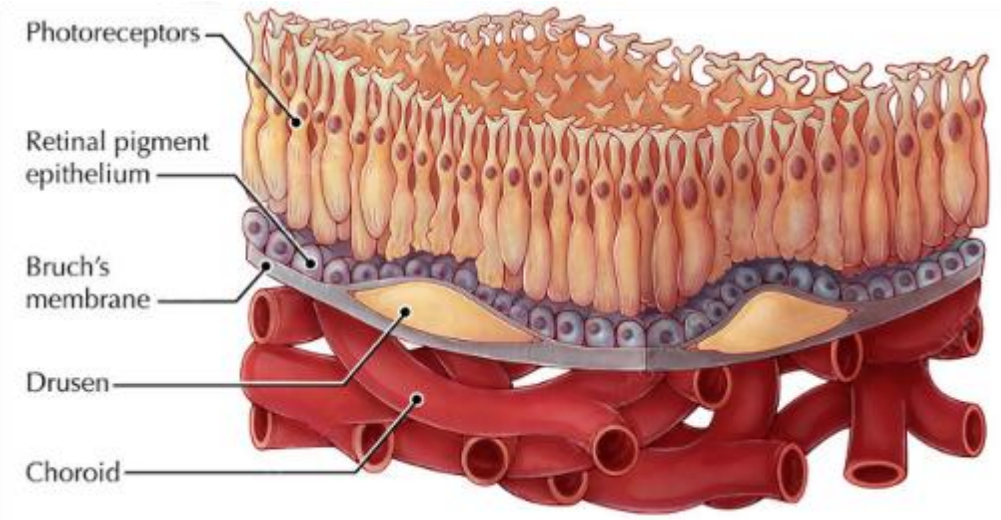
Drusen are deposits that accumulate between the pigmented layer of the retina called the retina pigment endothelium (RPE) and a more outer layer called Bruch’s Membrane (“BM”).

These deposits inhibit the flow of nutrients to the retina. The size and extent of drusen in the macular have been shown to increase the risk of AMD progression.

Intermediate AMD is characterized by large drusen and medium drusen with pigmentary abnormalities. These patients are at significant risk for developing AMD both Wet and Dry.

**Currently there are no treatments for patients with Intermediate AMD. Vitamins and nutritional supplements is the recommended standard of care[1. 2.]**




1. Macular Degeneration Foundation Australia recommendation pamphlet “Nutrition for AMD”.
2. USA National Eye Institute AREDS/AREDS 2 study concluded that supplements reduces the rate of progression from intermediate AMD to advanced AMD by 25%

# 2RT® - Subthreshold Nanosecond Laser

2RT® is a rejuvenative retinal laser therapy that utilizes a nanosecond laser pulse and unique pixelated laser beam profile

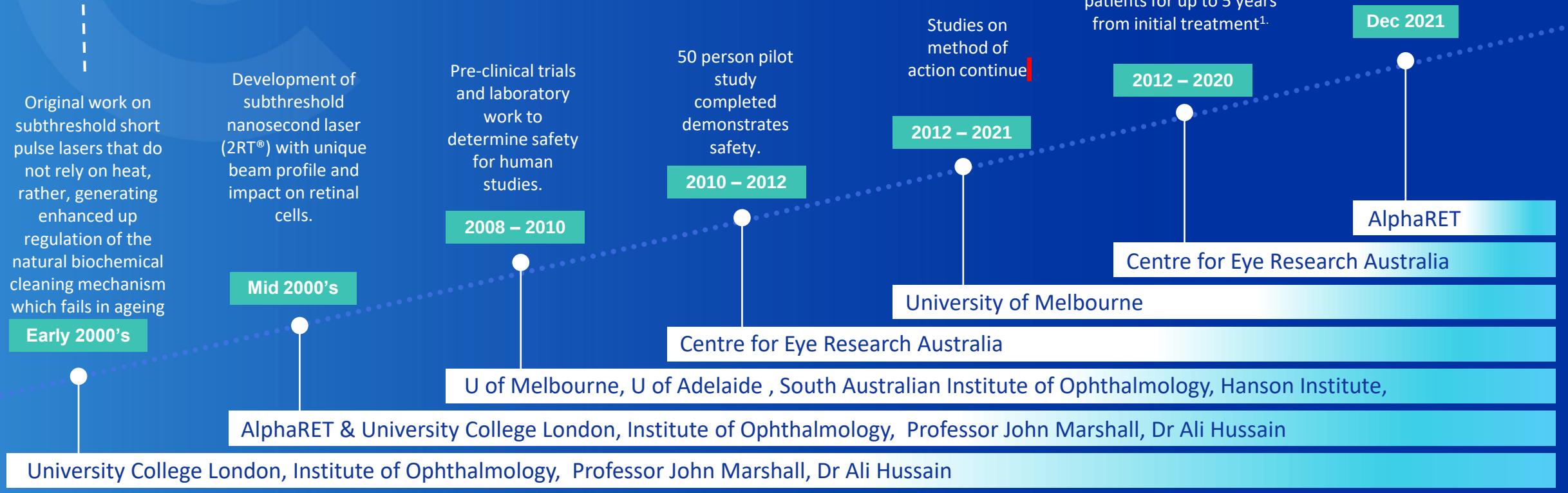
"Based on the LEAD[1] study outcomes, **2RT® is currently a leading candidate treatment in the world** for slowing the progression of patients with intermediate AMD to either late stage Wet or Dry AMD."

*(Identified by Edison Group in its publication "Saving the sight of millions, Blindness: the underrated business case" September 2020 - https://bit.ly/EdisonAMD).*

*1. LEAD study - LEAD (Laser Intervention in Early sage Age related macular Degeneration), 292-person study conducted from 2012-2018 with follow up through to 2020*

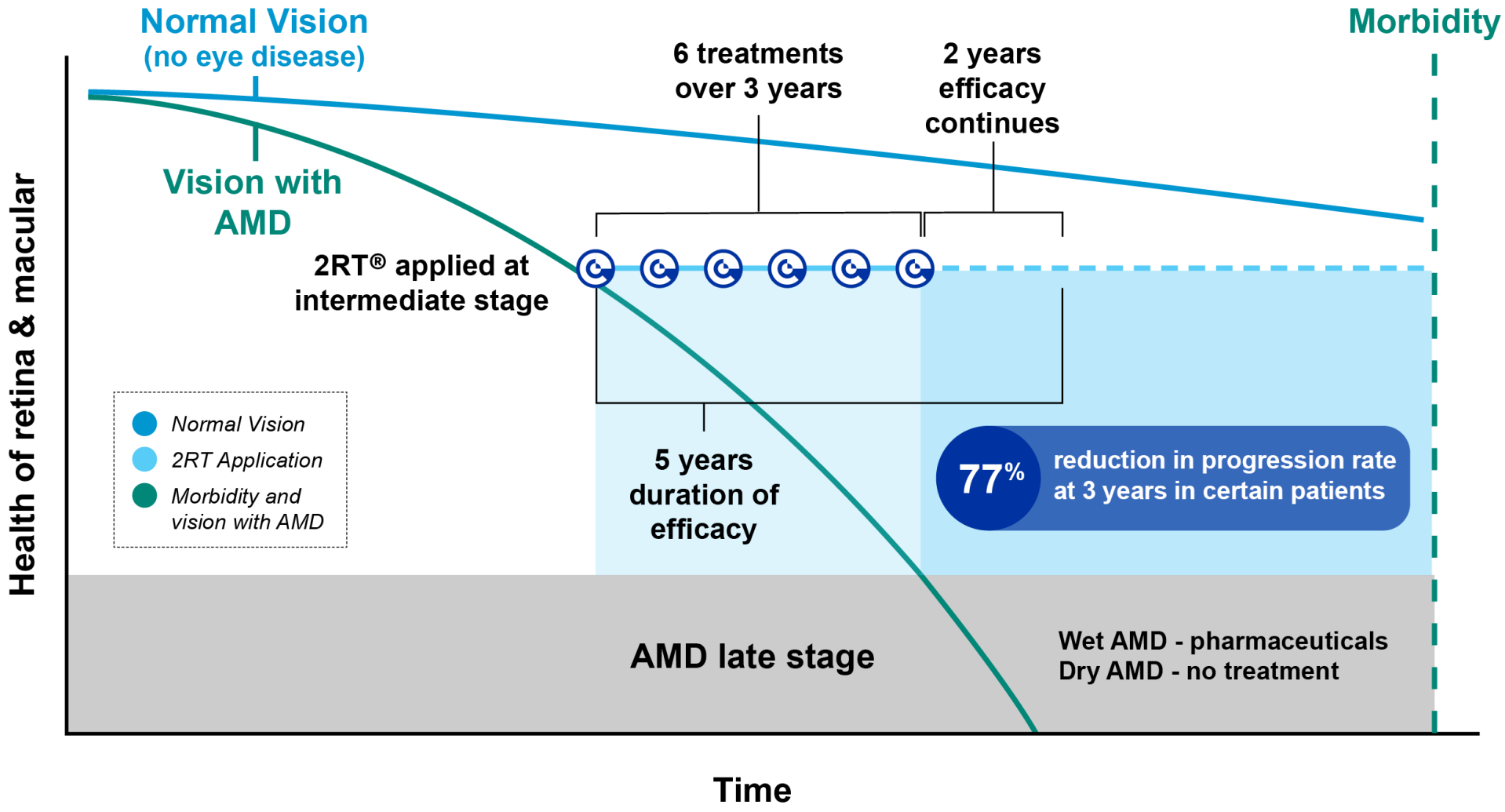
# 2RT® - 20 Year Development History

Lasers were first used in ophthalmology in the mid 1960s[2]. They relied on heating and destroying tissue for therapeutic effect. In the 1990's it was found that thermal lasers hastened AMD progression and use was stopped.




1. Based on *a 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
2. "Evolution of Concepts and Technologies in Ophthalmic Laser Therapy" Daniel Palanker

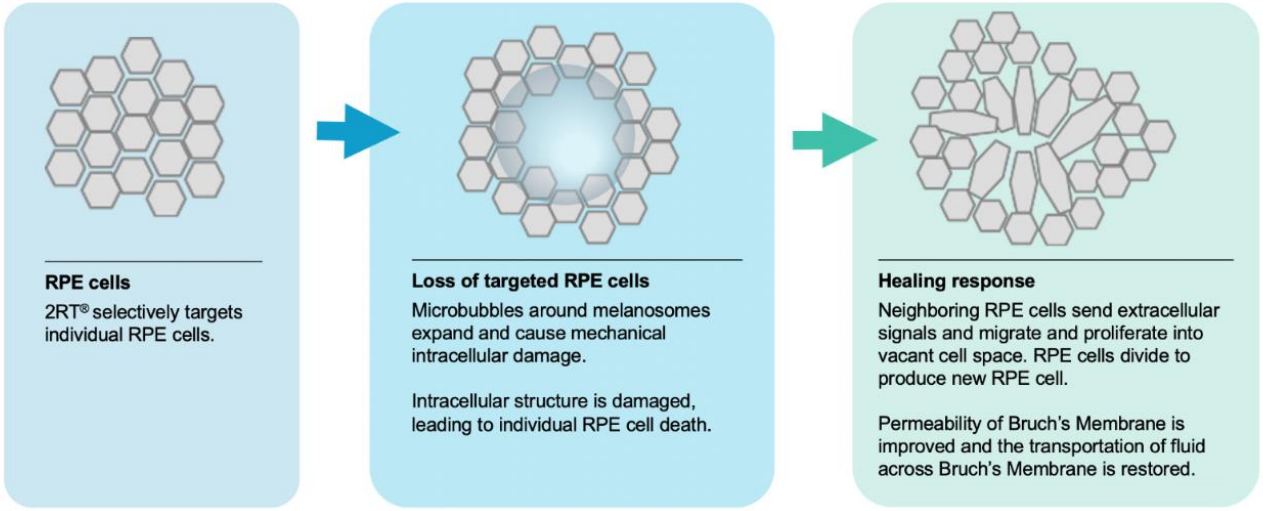
# 2RT® for intervention in AMD progression in certain patients



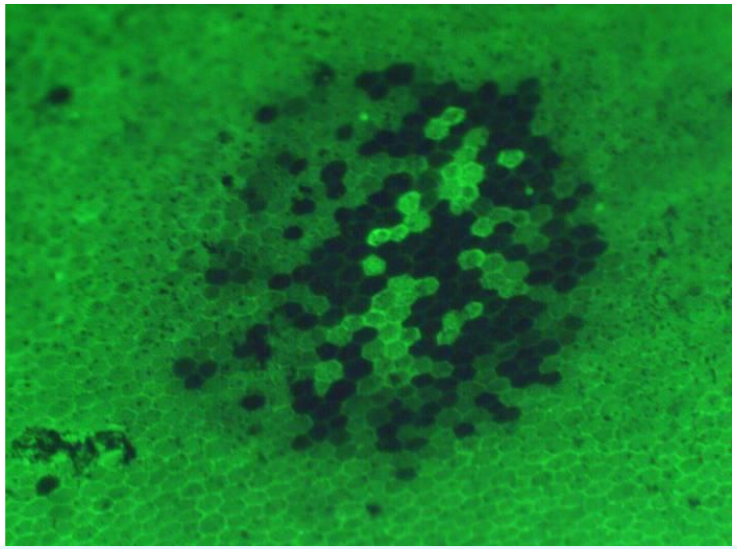

Intervention concept schematic based on *a post hoc* analysis reported within "Subthreshold Nanosecond Laser Intervention in Age-Related Macular Degeneration - The LEAD Randomized Controlled Clinical Trial" Robyn H. Guymer, MBBS, PhD, et al and published in peer reviewed journal *Ophthalmology* of the American Academy of Ophthalmology

# 2RT® has a unique method of action

2RT® stimulates a process of cell division and production of new cell growth and the associated release of membrane cleaning enzymes, which improves permeability of Bruch's membrane in the inner retina and thereby restores the transport of fluid across Bruch's membrane.



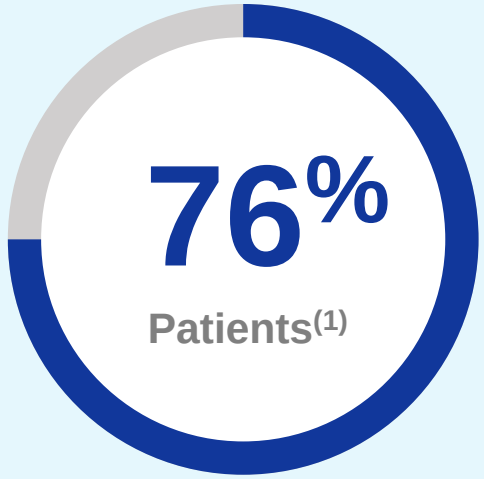

Professor Erica L. Fletcher MScOptom, PhD,Department of Anatomy and Neuroscience, The University of Melbourne,Australia.



2RT® pixelated beam profile selectively ablates multiple individual RPE cells within the 400 micron beam diameter.

# Randomised Control Study Completed Demonstrates Efficacy & Safety in Certain Patients

**LEAD (Laser Intervention in Early sage Age related macular Degeneration), 292-person study conducted from 2012-2018 with follow up through to 2020 -** showed 76%(1) of patients in the study had a 77%(1) reduction in progression to late stage AMD over thirty six months of treatment, an effect that endured for 24 months after treatment ceased.


The LEAD study did not meet its primary end points, but it has been lauded as a well-conducted study which has provided strong evidence of safety, the potential efficacy of 2RT and an understanding of the natural history of AMD. LEAD provides a sound foundation for a follow up study.

The investigators noted the fact that 24% of patients in the study had critical phenotype of retinal drusen, known as reticular pseudodrusen (RPD), and that these patients were negatively impacted by the laser treatment. This neutralised the outcome for the total study population(1).

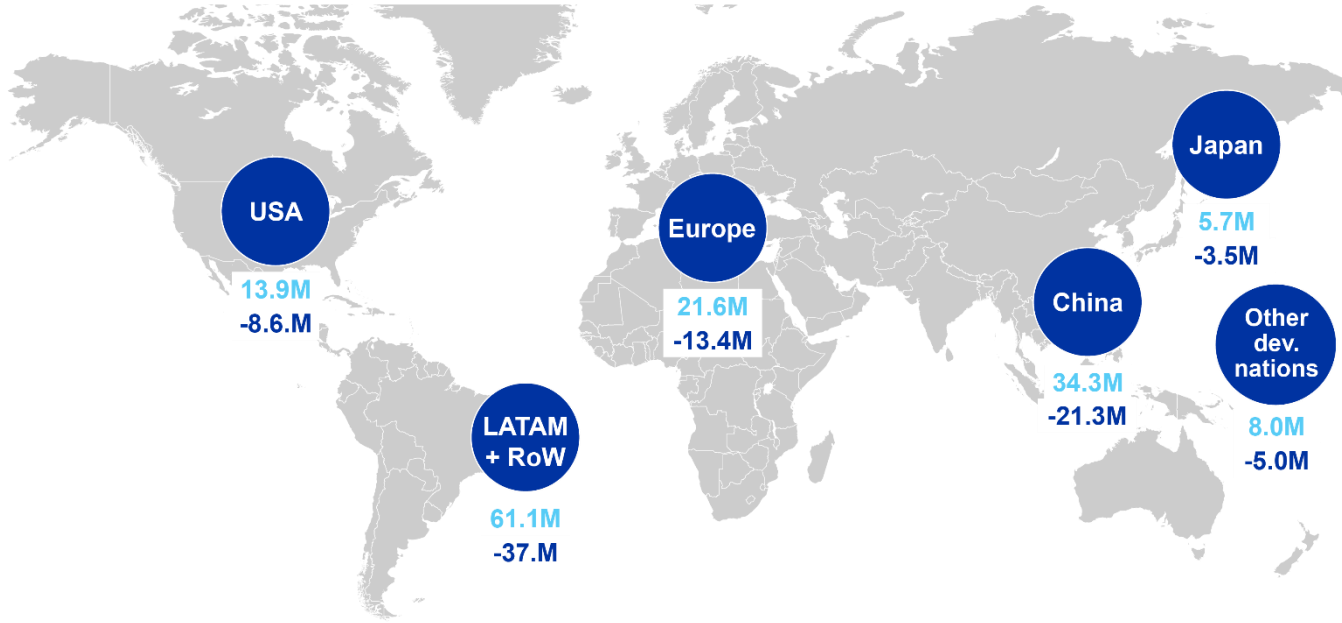
(1) Based on *a post hoc* analysis reported within " Subthreshold Nanosecond Laser Intervention in Age-Related Macular Degeneration - The LEAD Randomized Controlled Clinical Trial" Robyn H. Guymer, MBBS, PhD, et al and published in peer reviewed journal *Ophthalmology* of the American Academy of Ophthalmology

# 2RT® Roadmap Pivotal Study

- PRE-CLINCAL WORK
- PILOT CLINICAL TRIAL
- CE MARK (iAMD) APPROVED FOR SALE IN AUST, NZ & EUROPE
- EFFICACY & SAFETY DEMONSTRATION CLINICAL STUDY (“LEAD”)
- PROTOCOL PREPARATION FOR PIVOTAL USA STUDY TO CONFIRM LEAD
- USA FDA INVESTIGATIONAL DEVICE EXEMPTION APPROVAL
- PIVOTAL USA STUDY

# Global Unmet Need

## 2RT® MARKET ASSESSMENT




**Estimated 144.6 million people with Early/Intermediate AMD[1]**

**Patients who do not meet 2RT® treatment criteria[2]**

| Estimated population with Intermediate AMD treatable with 2RT® (market per year) | |
|---|---|
| USA | **5.3 million** |
| Europe | **8.2 million** |
| Other developed nations | **3.0 million** |
| Japan | **2.2 million** |
| China | **13.0 million** |
| LATAM and ROW | **23.2 million** |

**Estimated 54.9 million people with Intermediate AMD treatable with 2RT®**

1. Marketscope 2018 Ophthalmic Laser Report.
2. Company estimate based on outcome of *post hoc* from LEAD study.

# Estimated Revenue Opportunity for 2RT®

Subject to the completion of a pivotal study or similar to confirm results of the LEAD study (77% reduction in rate of progression to late-stage AMD in select patients with iAMD) the opportunity is very large.


Business model comprising of capital equipment sale and procedure fee has corollary with laser vision correction technology, which was launched in the US in the early 2000s by start-up companies.

*[1]Marketscope 2018 Ophthalmic Laser Report. [2] Guymer et al "Subthreshold Nano Second Laser Intervention in Age Related Macular Degeneration – The LEAD Randomised Controlled Clinical Trial". [3] AlphaRET estimate. [4] AlphaRET estimate based on [1]Marketscore 2018 Ophthalmic Laser Report " for USA, Europe and Other Developed Nations by Company.*

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# Randomised Control Study Completed Demonstrates Efficacy & Safety in Certain Patients - detail

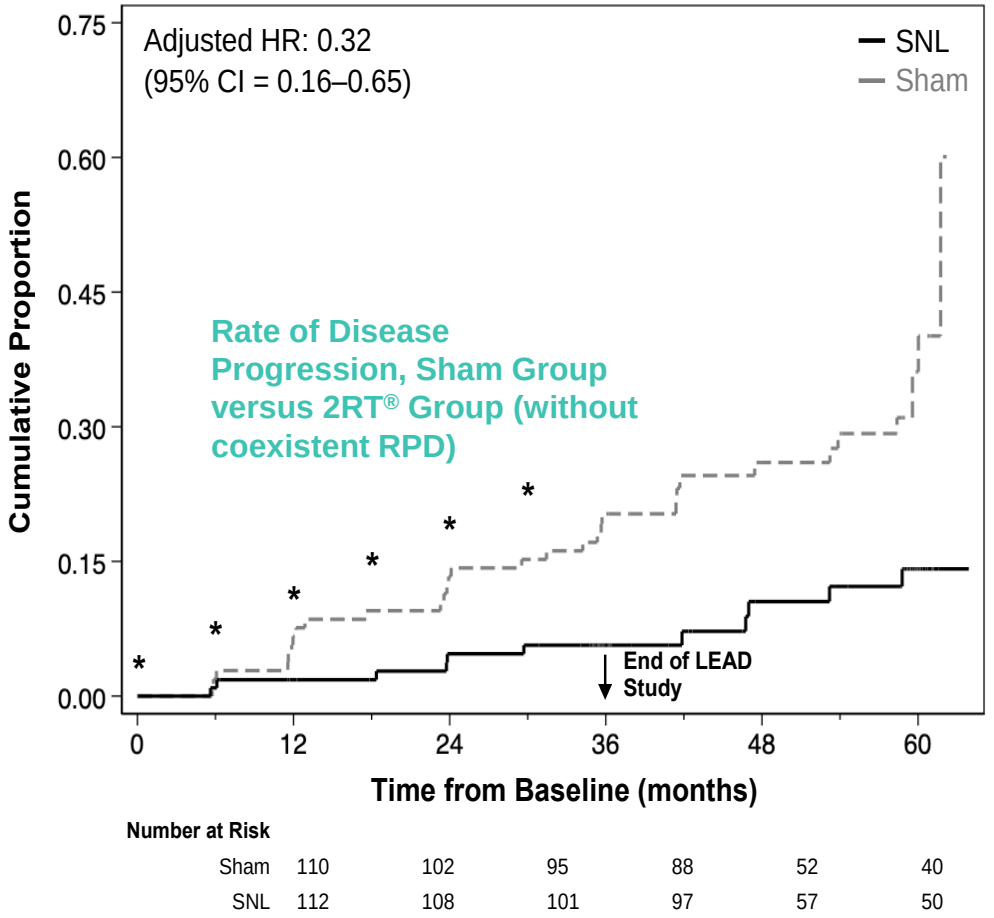
Publication of positive five-year patient follow-up data from a sub-study analysis of the LEAD Trial in Ophthalmology Retina.1

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 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 (right) 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 RPD[2].




(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.