RESULTS OF LEAD
CLINICAL TRIAL IN
INTERMEDIATE AMD

INVESTOR PRESENTATION

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- Overview of Intermediate Age-related Macular Degeneration (iAMD)
- Overview of Ellex 2RT® Therapy
- Key Results from LEAD contained in *Ophthalmology* Scientific Publication
- Trial Conclusions
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- Q&A
Overview of LEAD Clinical Trial

The LEAD trial has validated the safety and efficacy of Ellex 2RT® as an intervention for many people with intermediate AMD.

- Double-masked, randomised, sham-controlled trial over 36 months in 292 patients with iAMD across six sites with 1:1 randomisation to Ellex 2RT® or sham treatment received at six monthly intervals
- Primary endpoint – progression to advanced AMD in treated eye of Ellex 2RT® pts versus sham patients
- Secondary endpoints – safety, change in drusen volume and visual function, progression to advanced AMD in non-study eye
- Sub Group – post hoc analysis on patients without coexistent reticular pseudodrusen (RPD) deposits representing 76% of enrolled patients versus 24% with RPD at baseline
- Largest ever randomised study conducted in iAMD patients with a non-thermal, non-invasive pulse laser intervention
- First randomised study in iAMD to utilise modern multimodal imaging (MMI) techniques to detect and define AMD and greater power to detect treatment effects (e.g. OCT, NIR, FAF and CFP)
- Rationally designed following successful pilot study in 50 patients published in 2013

1 Guymer RH, et al. Sub-Threshold Nanosecond Laser Intervention in Age-Related Macular Degeneration: The LEAD Randomized Controlled Clinical Trial. Ophthamol 2018; In press
2 OCT = optical coherence tomography; NIR= near infrared imaging; FAF = fundus autofluorescence; CFP = colour fundus photography
Overview of iAMD

AMD ("Age-Related Macular Degeneration"):  
- leading cause of blindness in the developed world  
- affects one in seven Australians over the age of 50\(^1\)

Unmet need: late stage AMD is treated with 6 weekly injections of drugs directly into a patient’s eye. This can help to preserves vision, but long-term people lose vision due to scarring. Further:  
- onerous on patients and caregivers, and;  
- burden for government health schemes to purchase the drugs

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iAMD AND THE LEAD TRIAL

- One of the goals of the LEAD trial was to examine whether Ellex 2RT\(^\circledast\) could delay iAMD to more advanced forms of the disease, where retinal function declines markedly and vision becomes impaired.
- Treatments for late AMD are limited to regular injections of anti-VEGF drugs to the back of the eye.

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1. Macular Disease Foundation, Access Economics
Indication of retinal health failing, as shown in retinal imaging

Injection in eye

75 years of age

Detection

Disease progression without Ellex 2RT®

Apply Ellex 2RT® nanopulse laser light therapy

Ellex 2RT® to slow disease progression

Good/Normal

Defer injection in eye

Requiring anti-VEGF injection into eye to prevent severe vision loss
Overview of Ellex 2RT®

Ellex 2RT® is Ellex’s proprietary, patented laser therapy that stimulates the eye's natural healing response to treat the early stages of AMD.

- Specially designed rapid nanosecond pulse, non-thermal laser intervention targeting selected retinal pigment epithelium (RPE) cells to promote extracellular repair mechanism and rejuvenation of the retina
- Technology underpinned by a significant patent portfolio until 2035
- CE Mark for Diabetic Macular Edema (DME) in 2012 and early AMD in 2014
- FDA Clearance for Clinically Significant Macular Edema (CSME) in 2013
- Limited installed base to date; clinicians awaiting further clinical evidence from LEAD trial
- First of Ellex’s laser platforms to incorporate per procedure fee software
Consort Diagram

- 79.6% of patients assessed were randomised into trial
- Intent-to-Treat (ITT) analysis on 292 patients
- Protocol deviations/lost to follow up of 14% in sham group versus 19% in 2RT® treatment group
- Per protocol (PP) analysis on 243 patients
Patient Baseline Characteristics

- Patient baseline demographics and baseline ocular characteristics were well balanced between the two ITT arms
- No significant difference in each of the baseline characteristics noted (p>0.05), with exception of Lutein-Vision intake higher in sham treatment arm

1 Lek JJ et al. Subthreshold Nanosecond Laser Intervention in Intermediate Age-Related Macular Degeneration: Study Design and Baseline Characteristics of the Laser in Early Stages of Age-Related Macular Degeneration Study (Report Number 1). Ophthalmology Retina 2017

<table>
<thead>
<tr>
<th>Demographics</th>
<th>SNL treatment (n=147)</th>
<th>Sham treatment (n=145)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.3 (7.0)</td>
<td>69.8 (8.1)</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>103 (70.1%)</td>
<td>112 (77.2%)</td>
</tr>
<tr>
<td>Ethnicity (Anglo-Saxon)</td>
<td>134 (91.2%)</td>
<td>128 (88.3%)</td>
</tr>
<tr>
<td>Smoking history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>77 (52.4%)</td>
<td>77 (53.1%)</td>
</tr>
<tr>
<td>Past or current</td>
<td>70 (47.6%)</td>
<td>68 (46.9%)</td>
</tr>
<tr>
<td>Macu-Vision® intake (yes)</td>
<td>50 (34.0%)</td>
<td>45 (31.0%)</td>
</tr>
<tr>
<td>Lutein-Vision® intake (yes)</td>
<td>9 (6.1%)</td>
<td>24 (16.6%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study eye ocular characteristics</th>
<th>SNL treatment (n=147)</th>
<th>Sham treatment (n=145)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCVA (number of letters)</td>
<td>83 [80, 87]</td>
<td>84 [79, 88]</td>
</tr>
<tr>
<td>Pigmentary abnormalities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Definitely present</td>
<td>46 (31.3%)</td>
<td>51 (35.2%)</td>
</tr>
<tr>
<td>Absent or questionable</td>
<td>101 (68.7%)</td>
<td>94 (64.8%)</td>
</tr>
<tr>
<td>Reticular pseudodrusen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Definitely present</td>
<td>35 (23.8%)</td>
<td>35 (24.1%)</td>
</tr>
<tr>
<td>Absent or questionable</td>
<td>112 (76.2%)</td>
<td>110 (75.9%)</td>
</tr>
</tbody>
</table>

Data are frequency (%), mean (standard deviation) or median [25th to 75th percentile]. SNL = sub-threshold nanosecond laser. BCVA = best-corrected visual acuity. * = active ingredients of Macu-Vision® include Vitamin C, Vitamin E, zinc oxide, cupric oxide. # = active ingredients of Lutein-Vision® include Lutein, Selenomethionine, Zeaxanthin, omega-3 triglycerides-fish oil.

Table 1: Demographics and baseline ocular characteristics
Safety

- Ellex 2RT® was well tolerated with no statistically significant difference in Serious Adverse Events (SAEs) reported.
- Ocular Adverse Events (AEs) with Ellex 2RT® were retinal haemorrhages that resolved in all cases without any untoward sequelae.
- All other adverse events recorded were statistically no different between the Ellex 2RT® treatment group and sham group.
- 3.4% of patients reported after-images >1 day after treatment.
- No difference between the groups in events unrelated to the progression to late AMD.

### Table 2: Number and proportion of patients with adverse events

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>SNL treatment (n=147)</th>
<th>Sham treatment (n=145)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitely related ocular adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants reporting one or more adverse events</td>
<td>15 (10.2%)</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>After-images*</td>
<td>5 (3.4%)</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>Retinal haemorrhage</td>
<td>10 (6.8%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Possibly related ocular adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants reporting one or more adverse events</td>
<td>25 (17.0%)</td>
<td>24 (16.6%)</td>
</tr>
<tr>
<td>Epiretinal membrane</td>
<td>1 (0.7%)</td>
<td>4 (2.8%)</td>
</tr>
<tr>
<td>Symptomatic PVD or floaters</td>
<td>8 (5.4%)</td>
<td>5 (3.4%)</td>
</tr>
<tr>
<td>Ocular discomfort following treatment</td>
<td>7 (4.8%)</td>
<td>11 (7.6%)</td>
</tr>
<tr>
<td>Cataract requiring surgery</td>
<td>3 (2.0%)</td>
<td>2 (1.4%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (2.0%)</td>
<td>5 (3.4%)</td>
</tr>
<tr>
<td>Other adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unrelated ocular adverse events</td>
<td>81 (55.1%)</td>
<td>70 (48.3%)</td>
</tr>
<tr>
<td>Non-ocular adverse events</td>
<td>103 (70.1%)</td>
<td>109 (75.2%)</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants reporting one or more serious adverse events</td>
<td>56 (38.1%)</td>
<td>50 (34.5%)</td>
</tr>
<tr>
<td>Cardiovascular or cerebrovascular disorders</td>
<td>14 (9.5%)</td>
<td>13 (9.0%)</td>
</tr>
<tr>
<td>Death (unknown cause)</td>
<td>0 (0.0%)</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>Infections</td>
<td>8 (5.4%)</td>
<td>2 (1.4%)</td>
</tr>
<tr>
<td>Injury and procedural complications</td>
<td>10 (6.8%)</td>
<td>9 (6.2%)</td>
</tr>
<tr>
<td>Neoplasms (benign and malignant)</td>
<td>7 (4.8%)</td>
<td>8 (5.5%)</td>
</tr>
<tr>
<td>Nervous system disorder</td>
<td>3 (2.0%)</td>
<td>3 (2.1%)</td>
</tr>
<tr>
<td>Respiratory disorder</td>
<td>5 (3.4%)</td>
<td>3 (2.1%)</td>
</tr>
<tr>
<td>Surgery and medical procedures</td>
<td>7 (4.8%)</td>
<td>5 (3.4%)</td>
</tr>
<tr>
<td>Other (medical)</td>
<td>23 (15.6%)</td>
<td>22 (15.2%)</td>
</tr>
</tbody>
</table>

Data are number of participants (%). PVD = posterior vitreous detachment. * = visible for more than one day, as reported at the one-week phone call after the initial treatment.

Table 2: Number and proportion of patients with adverse events
Primary Endpoint Results

**INTENT TO TREAT (ITT)**

- No significant difference in progression to late AMD under ITT analysis ($p=0.122$) or the PP analysis ($p=0.092$)
- At 36 months, 13.6% progressed to late AMD in the 2RT® treatment group versus 17.2% in the sham eye (ITT)
- At 36 months, 15.1% progressed to late AMD in the 2RT® treatment group versus 20.2% in sham eye (PP)
- Non-significant trend in favour of the 2RT® treatment group

**PER PROTOCOL (PP)**

* Adjusted Hazard Ratio (HR) - 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
Treatment Effect on Late AMD

- Estimated effect on Forest plot of 2RT® examining the two phenotypes of late AMD (neovascular AMD and drusen-associated atrophy)
- Pronounced treatment effect on drusen-associated atrophy favouring 2RT® (HR=0.53)
Patients without RPD at Baseline - Analysis

- A clinically meaningful 77% reduction in the risk of progression (HR=0.23) in patients who received 2RT® versus sham
- 2RT® showed a significant treatment effect in this patient population (p=0.002)
- RPD is a key biomarker of retinal pigment epithelium (RPE) dysfunction and has a high association with progression to late-stage AMD
- The 76% of patients without baseline RPD enrolled in LEAD approximates incidence rates in prospective studies, thereby representing a large, clinically important group with no treatments currently approved
Patients with RPD at Baseline - Analysis

- Increased rate of progression to late-stage AMD in the 2RT® treatment group compared to the sham treatment group, although the treatment effect was not significant (p=0.112 for ITT and p=0.258 for PP analysis).

- Ellex 2RT’s mechanism of action requires the selective loss and subsequent healing of the RPE, there may be a stage of AMD disease whereby RPE integrity is so greatly compromised as to render treatment with Ellex 2RT® is unsuitable.

- Such data is clinically valuable in selecting patients who are likely to respond to Ellex 2RT®.
LEAD Trial Conclusions

• Though the primary endpoint across the entire study cohort was not met, Ellex 2RT® displayed an exceptional safety profile.

• Patients with no reticular pseudodrusen (RPD) deposits at baseline had a 77% reduction in the risk of progression to late stage AMD at any stage during the trial, which was conducted over three years.

• This result is highly clinically meaningful and showed a remarkable treatment effect.

• RPD negative sub group represents approximately 75% of all iAMD patients with bilateral large drusen and no geographic atrophy.

• LEAD was the first ever trial to show significant efficacy in an iAMD population.

• Important new clinical information to guide retinal specialists in patient selection towards those without evidence of RPD.

• Results are applicable only to Ellex 2RT® – authors discourage extrapolation of results to other thermal or non-thermal lasers.
Market Dynamics and Commercial Opportunity

- Publication in *Ophthalmology*, the most important peer-reviewed ophthalmology journal globally, underscores the significance of the clinical results\(^1\)

- Where Ellex 2RT® is approved for AMD, these markets represent an addressable market of 15 million patients per annum for screening and then treating those early stage patients without detectable RPD\(^2\)

- Addressable market similar in size (patients) to late stage ‘wet’ AMD

- Ellex’s commercialisation plan will be developed based on physician feedback, peer-to-peer educational programs focused on disease diagnosis, patient selection and treatment protocols

- Future regulatory clearances in the US, Japan and China will increase the pool of treatable patients to 25 million per annum\(^3\)

- No currently approved treatments for iAMD – only dietary and lifestyle modifications (a standard that resulted from analysis of the AREDS1 and AREDS2 studies\(^4,5\))

- Therapeutic approvals have been limited to late stage ‘wet’ AMD, which represents the minority of AMD patients

- Ellex intends to explore regulatory requirements for the US market

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1 Guymer RH, et al. Sub-Threshold Nanosecond Laser Intervention in Age-Related Macular Degeneration: The LEAD Randomized Controlled Clinical Trial. *Ophthalmol* 2018; in press

2 Marketscope Report August 2017 Ophthalmic Laser Report Table 2 "Global Forecast for AMD in all its Forms", adjusted for Ellex estimates on RPD patients

3 On in the USA, South China and in Japan


THANK YOU
Q/A SESSION