Photobiomodulation for Dry Age-Related Macular Degeneration

Clark E. Tedford, Ph.D. – CEO
A leading cause of vision loss in Americans >60 years of age.

Age-Related Macular Degeneration (AMD)

What is needed?

Low cost, regenerative treatment deliverable to millions, globally
Business Overview – Improve Vision in the Elderly

• Medical Device Company Targeting Dry - Age Related Macular Degeneration
• Multiple wavelength, LED Instrument Station
• Non-invasive Photobiomodulation (PBM)
• Positive Human Clinical Data with up to 1 year follow-up
• Proprietary Issued Patent and Pending Patent Application(s)
LT-300: Ophthalmalmologic LED Device

- Light emitting diodes (LED) provide low level, non-coherent light
- Class II Device (510K)
- Noninvasive procedure
- Targets Retina and macula

Commercial Design Prototype Illustration - System is Limited by Federal Law to Investigational Use Only
Age-related Macular Degeneration
Dry Age Related Macular Degeneration

Normal vision
Dry Age Related Macular Degeneration

Blurred vision
Dry Age Related Macular Degeneration

Loss of contrast
Dry Age Related Macular Degeneration

Loss of central vision
Dry Age Related Macular Degeneration and it gets worse
Macular Degeneration (AMD)

Affects ~10 million people in the United States. This number is expected to double to ~22 million by 2020.

Direct health care costs of AMD in the USA and Canada are ~$98 billion.

Two types:
- Wet type, affecting 10%;
- Dry type, affecting 90%.

Wet type: Intra-ocular anti-VEGF drugs.

Dry type: No proven treatments.
Does PBM Treatment Lend Itself to the Disease?

Does PBM Mechanism of Action Fit the Disease?
The human eye is uniquely accessible to phototherapy...
PhotoBioMedicine – Ophthalmic Applications
Does PBM treatment lend itself to the Disease?

YES!
Cytochrome C Oxidase is Key Photoacceptor

LLLT Photons Target Cu$_A$ at 810 nm and Fe$_{a3}$Cu$_B$ at 650 nm

- Improves Blood Flow
- Enhances O$_2$ binding
- Increases CCO Activity
- Improves ATP Formation
- Reduces Oxidative Stress (NO, ROS)
- Resets Cellular Metabolic Function
LLLT Therapy

Improves Mitochondrial Function

Activates transcription factors NFκB

CELL SURVIVAL

Creates stable microenvironment

Alters protein synthesis

Alters gene transcription

Confidential - Do Not Distribute
LLLT stimulates Longer-Term Benefits

Activation of Multiple Downstream Pathways/Effectors

• Mitochondrial Enzyme Activity - ↑ MTT reduction (Hamblin, Lo)

• Apoptosis - ↑ Bcl-2, HSPs (Oron), PI3k/Akt, ↓ Bax, Caspase

• Cytoprotection - ↑ BDNF, BMP, TSP-1 (Lapchak)

• Protein Processing - α- & β- secretase, Aβ peptide (Kindy)

• Inflammation - ↓ IL1β, TNFα, TGFβ, β-secretase, (Kindy)
Mitochondrial Dysfunction and Oxidative Stress Play a Key Role in Aging and Degenerative Diseases

- Mitochondrial Disease - LHON
- Degenerative Eye Diseases - Macular Degeneration, Diabetic Retinopathy, Retinitis Pigmentosa, Glaucoma
- Neurodegenerative Diseases - Parkinson’s Disease, Alzheimer’s Disease, Huntington’s Disease, Multiple Sclerosis
- Cardiovascular Disease and Stroke
- Metabolic Diseases - Diabetes
AMD Ophthalmology Therapy Implications

PBM offers non-pharmaceutical, non-surgical way to:

• Suppress VEGF
• Suppress inflammation
• Stimulate retinal cell regeneration/revitalization
• Protect/revitalize optic nerve and retinal cells against toxicity

Mouse retina
Does PBM Mechanism of Action fit the Disease?

YES!
Is There Animal Model Data to Support the PBM Approach in Ocular Disease?
PBM Animal Studies

- Eells, et al., University of Wisconsin, have demonstrated:
  - Protective effect and enhanced recovery in a Rat Retina model – methanol toxicity
  - LED Tx x3 in first 50 hrs after methanol exposure
  - Significant recovery of rod, M cone and UV cone mediated retinal function (ERG data P < 0.001)
670 nm Treatment
At 5 hr, 25 hr, 50 hr
28 mW/cm² - 2 min
4 joules/cm²
Histopath showed retinal edema, swelling of photoreceptor inner segments & changes in photoreceptor nuclei, but LED treated were indistinguishable from untreated control!

Eells, et al., Wisconsin, 2004
LLLT Reduces Inflammation and Improves Healing in Preclinical Retinal Laser Damage Models - *Eells*

*Eells, et al., Wisconsin, 2008*
LLLT Reduces Outer Retinal Inflammation in CFH⁻/⁻ Mice

Figure A and B. Retinal sections stained with C3 (red). C3 accumulates on Bruch’s membrane and outer segments. Figure C and D Following 670 nm treatment, C3 was significantly reduced on Bruch’s membrane and photoreceptor outer segments (p = 0.0001 for each). E. These data were confirmed with qPCR analysis. Abbreviations, Bruch’s membrane (BM), photoreceptor (PR), complement component (C3). Scale bars = 40 mm.

Begum, et al., 2013
Is There Clinical Data to Support Use of PBM in Dry Age-related Macular Degeneration?
TORPA (Toronto-Oak Ridge Study for Dry AMD)

Prospective Study
- University of Toronto, Dr. Devenyi – Chief, Retinal Surgical Center

Inclusion Criteria:
- > 50 years of age.
- Clinically diagnosed Dry ARMD in study eye.
- BCVA between 20/20 and 20/200.

Exclusion Criteria:
- Visually-significant cataract.
- Visually-significant capsular clouding post-cataract/IOL
- Any visually-significant disease process.
ETDRS Visual Acuity logMAR Test – Validated Clinical Outcomes

- 22 eyes
- 3 x per week for 6 weeks
- ETDRS Visual Acuity statistically significant at 1 year post-treatment
- Contrast Sensitivity also showed statistically significant improvements
One Year Benefit in ETDRS Visual Acuity logMAR

- \( F(4,68) = 18.86, p < 0.0001 \)
Comparison of TORPA benefits versus Rheopheresis Placebo Arm in Dry AMD patients

Lines of EDTRS VA Change from Baseline

Baseline

Post-baseline Interval

12 Month

1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0

PBM
PLACEBO

1.1
-1.9
Is There Animal Model Data to Support Use of PBM in Dry Age-related Macular Degeneration?  
YES!

Is There Clinical Data to Support Use of PBM in Dry Age-related Macular Degeneration?  
YES!
Competition
### Medical Device Competition

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<thead>
<tr>
<th></th>
<th><strong>ACUITY / SCYFIX</strong></th>
<th><strong>ELLEX</strong></th>
<th><strong>LUMITHERA</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>MECHANISM</strong></td>
<td>Electro - microstimulation, Not elucidated</td>
<td>Microbubble damage to RPE cells</td>
<td>Restorative, multifactorial, PBM is well documented</td>
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<tr>
<td><strong>EASE OF USE</strong></td>
<td>Non invasive – 2x daily</td>
<td>Laser to retina – episodic treatments</td>
<td>Non invasive – episodic treatments</td>
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<td><strong>TREATMENT TIME</strong></td>
<td>20 mins x 2</td>
<td>Office procedure</td>
<td>5 min per eye</td>
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<tr>
<td><strong>SIDE EFFECTS</strong></td>
<td>Unknown</td>
<td>Cellular damage at laser site</td>
<td>None recorded</td>
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<td><strong>EFFICACY</strong></td>
<td>Approx. 60% response</td>
<td>Drusen area decrease. VA?</td>
<td>&gt; 90% response. VA &amp; CS improvement and Drusen reduction</td>
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LumiThera’s approach is a multi-factorial treatment designed to target underlying disease mechanisms

- Photobiomodulation is regenerative and restorative
- Noninvasive and cost-effective
- Pharmaceutical agents are single-target approaches
- Drugs are in early development – Phase I/II
- Devices – unknown mechanisms or disruptive
PBM in dry AMD Summary

• Huge unmet medical need  Yes!
• Safe and effective non-invasive solution  Yes!
• Multiple ocular platforms for expansion  Yes!
• Experienced, dedicated PBM team  Yes!
• Several exit points with favorable ROI  Yes!
• IP and pilot clinical human data established  Yes!
• Significantly improve lives  Yes!
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