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Differentiated, Late-Stage Pipeline Targeting Large Unmet Ophthalmic Markets Of The Front And Back Of The Eye

- Nyxol with > 330 patients treated across 9 trials (505(b)(2) regulatory pathway)
- APX3330 with > 340 patients treated across 11 trials (NCE development pathway)
- Nyxol and APX3330 achieved promising clinical data and favorable safety profile across multiple Phase 1, 2, and 3 trials

Poised For Commercial Success

- Addressing 4 large markets with unmet needs: RM, Presbyopia, NVD and DR/DME
- Successful trial execution with 2 recent positive Phase 3 & Phase 2 data read-outs for Nyxol in RM and Nyxol + LDP Presbyopia, respectively
- Stable, small-molecule drugs with commercial scalability
- Robust and growing IP portfolio: US and global issued thru 2034 for both assets as well as new 2039 Nyxol patent issued for presbyopia

Multiple Value Creation Opportunities With A Capital-efficient Plan

- $24.5 million cash reported at 12-31-21 sufficient for operations into 2Q 2023
- Lower-cost, fast-enrolling, shorter-duration clinical trials
- Favorable, precedent regulatory environment for ophthalmic drug approval
- Analyst coverage by Cantor, Canaccord, Jones Trading, Alliance Global, and HCW

A Look Ahead Into 2022:

- Nyxol MIRA-3 trial for RM EARLY 2022
- Nyxol Pediatric trial for RM EARLY 2022
- Nyxol LYNX-1 trial for NVD EARLY 2022
- APX3330 ZETA-1 trial for DR/DME 2H22
- NDA Filing for Nyxol for RM LATE 2022

RM = Reversal of Mydriasis
NVD = Night Vision Disturbances
DR/DME = Diabetic Retinopathy/Diabetic Macular Edema

NASDAQ: OCUP

OCUPHIRE PHARMA
Large Unmet Opportunities For The Aging Eye

Nyxol® To Treat Front Of The Eye And APX3330 For The Back Of The Eye Diseases

**Nyxol®**

- **US Market Opportunity**: $9B - $18B
- **128 M Patients**

**APX3330**

- **Diabetic Retinopathy**
  - **US Market Opportunity**: $3B - $7B
  - **10 M Patients**

**Refractive**

- **100 M Patients**
  - **Reversal of Mydriasis**

- **16 M Patients**
  - **Night Vision Disturbances**

**Retina**

- **10 M Patients**
  - **Total**

- **Diabetic Macular Edema**
  - **US Market Opportunity**: $1B - $3B

Source: GlobalData Market Research Report, 2020; Company Estimates for Market Size
Ocuphire Pipeline & Clinical Milestones

Multiple Phase 3 & Phase 2 Clinical Data Readouts Anticipated Over The Next Year

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>Indication</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Regulatory Approval</th>
<th>Anticipated Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.75% Nyxol® Eye Drop</td>
<td>Reversal of Mydriasis (RM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• MIRA-3 Phase 3 data expected in early 2022 (n=330)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• MIRA-4 Pediatric safety study data expected in early 2022 (n=20)</td>
</tr>
<tr>
<td>0.75% Nyxol® + Low-Dose 0.4% Pilocarpine Eye Drops</td>
<td>Presbyopia (P)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• VEGA Phase 3 program initiated in 1H22 (n=300x2)</td>
</tr>
<tr>
<td>0.75% Nyxol® Eye Drop</td>
<td>Dim Light or Night Vision Disturbances (NVD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• LYNX-1 Phase 3 data expected in early 2022 (n=140)</td>
</tr>
<tr>
<td>APX3330 Oral Pill</td>
<td>Diabetic Retinopathy (DR)/Macular Edema (DME)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• ZETA-1Phase 2 data expected in 2H22 (n=90)</td>
</tr>
<tr>
<td>APX2009 (Intravitreal or Local Delivery)</td>
<td>DME or Wet Age-Related Macular Degeneration (wAMD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Seeking partner funding for IND enabling studies and further development</td>
</tr>
</tbody>
</table>

*Note: 0.75% Nyxol (Phentolamine Ophthalmic Solution) is the same as 1% Nyxol (Phentolamine Mesylate Ophthalmic Solution)*
Nyxol MOA & History

Phentolamine Mesylate Reformulated As A Proprietary Topical Eye Drop ➔ Nyxol

Phentolamine Mesylate is Active Ingredient in Nyxol: α1 & α2 Antagonist

<table>
<thead>
<tr>
<th>Blocking α1</th>
<th>Blocking α1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduces Pupil Size</td>
<td>Dilates Blood Vessels</td>
</tr>
</tbody>
</table>

Nyxol blocks α1 receptors on the Iris Dilator Muscle
↓ Decreases Pupil Size (Moderate Miosis)

Phentolamine mesylate is currently approved for 2 indications:

- Regitine® (Pheochromocytoma) – intravenous injection approved in 1952
- OraVerse® (Reversal of oral anesthesia) – intramuscular injection approved in 2008

Phase 1, Phase 2, and Phase 3 Trials: > 330 Subjects Dosed
Exposure in Humans: 28 Days
Patent Coverage: 2034+

505(b)(2) Regulatory Approval Pathway
**Nyxol Product Candidate Profile**

*Novel, Differentiated Alpha 1/2 Blocker Eye Drop For Refractive Indications*

<table>
<thead>
<tr>
<th>Effective</th>
<th>Favorable Safety Profile</th>
<th>Durable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nyxol Improves Vision by Decreasing Pupil Size (about 20-25%)</strong></td>
<td><strong>No Systemic Effects</strong></td>
<td><strong>Effects Last ≥ 24 Hours</strong></td>
</tr>
<tr>
<td>↑ Near &amp; Distance Visual Acuity</td>
<td>No Changes in Blood Pressure</td>
<td>Chronic daily dosing of Nyxol at bedtime reduced pupil size for up to 24 - 36 hours</td>
</tr>
<tr>
<td>↑ Contrast Sensitivity (night)</td>
<td>No Changes in Heart Rate</td>
<td>With nighttime use, patients wake up without eye redness</td>
</tr>
<tr>
<td><strong>Well-Tolerated Topical Effects</strong></td>
<td><strong>IOP Unchanged or Decreased</strong></td>
<td></td>
</tr>
<tr>
<td>Mild, Transient, Reversible Eye Redness</td>
<td><strong>No Headaches</strong></td>
<td></td>
</tr>
<tr>
<td><strong>IOP Unchanged or Decreased</strong></td>
<td>Favorable safety profile vs competitors</td>
<td></td>
</tr>
<tr>
<td><strong>Nyxol: 0.75% Phentolamine Ophthalmic Solution</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preservative Free, EDTA Free, and Stable</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Nyxol Clinical Trials**

Favorable safety profile vs competitors

Effective

Nyxol: 0.75% Phentolamine Ophthalmic Solution
Preservative Free, EDTA Free, and Stable

Effects Last ≥ 24 Hours

Chronic daily dosing of Nyxol at bedtime reduced pupil size for up to 24 - 36 hours

With nighttime use, patients wake up without eye redness
I have to stay indoors. They say it only lasts a few hours, but it lasts all day, and it is very annoying.

RM Patient, Age 51
Reversal Of Mydriasis (RM) Market Opportunity
With No Commercially Available Treatment, Nyxol May Achieve Significant Revenue Potential

The Problem

• At many annual eye exams and specialty visits, pupils are pharmacologically dilated, impairing vision for 6-24 hours

• Dilated eyes:
  – heightened sensitivity to light
  – inability to focus
  – reading, working, and driving are difficult
  – halos and glare

100M+
General and specialty eye exams per year

> 65% of Patients
Report moderate to severe negative impact of dilated exams

80% of Patients
Likely to request a reversal of dilation drop

$10 - $20
Price range for cash pay per patient with room for physician markup

95% of Dilating Drops
Used by Eye Care Providers were used in MIRA Clinical Trials

No Current Commercially Available Treatments

Nyxol's MOA has a minimal side effect profile (unlike cholinergic agonists such as pilocarpine)

$325M - $1B
Estimated US RM Market Opportunity

1. GlobalData Market Research Report
2. GlobalData Market Research Report, 2020 – percentage includes those who answered moderately to highly likely (4-7 on a scale of 1-7).
3. GlobalData Market Research Report, 2020 – percentage includes those who answered moderately to highly likely (6-10 on a scale of 0-10)
MIRA-2/3 Phase 3 Registration Trial Design

Randomized, Double-Masked, Placebo-Controlled, Parallel, One-Day Trial

12 to 16 US sites
185 to 330 target healthy subjects

1:1
2:1

Mydriasis - 1 Hour
Mydriasis

1:1

Mydriatic Agent A, B, or C

Nyxol drop(s)
(2 drops study eye, 1 drop fellow eye)

Follow Up Visit

Primary Endpoint

Treatment (Max Dilation)
0 min

Mydratic Agent A, B, or C

Placebo drop(s)
(2 drops study eye, 1 drop fellow eye)

Placebo

Enrollment MIRA-3 Started in 4Q21

Mydriatic Agents 3:1:1 – 2.5% phenylephrine (alpha-1 agonist), 1% tropicamide (cholinergic blocker), Paremyd® (combination)

Endpoints

Primary: % of subjects (study eye) returning to baseline (within 0.2 mm) photopic pupil diameter (PD) at 90 min

Secondary:
- % of subjects returning to baseline at 0min, 30min, 1h, 90 min 2h, 3h, 4h, 6h, 24h (overall, by mydriatic agent, by iris color)
- Mean change in pupil diameter at all timepoints
- Accommodation (Tropicamide/Paremyd)
- Visual Acuity with Glare (new)
- Pupillary Light Reflex (new)
- Safety and tolerability (redness)

Topline Results Expected in Early 2022
MIRA-2 RM Phase 3 Trial Met Primary & Secondary Endpoints

49% Of Patients Returned To ≤ 0.2mm Of Baseline At 90mins Vs. 7% Placebo

Source: MIRA-2 Trial, mITT Population (same as Safety Population), *Data includes all three mydriatics (Phenylephrine, Tropicamide, Paremyd)

### Nyxol Reduced More Subjects to Baseline Pupil Diameter (PD)

<table>
<thead>
<tr>
<th>Time Post-Treatment with Nyxol/Placebo (Hours)</th>
<th>Placebo n=91</th>
<th>Nyxol n=94</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>3%</td>
<td>28%</td>
</tr>
<tr>
<td>1</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>1.5</td>
<td>7%</td>
<td>49%</td>
</tr>
<tr>
<td>2</td>
<td>11%</td>
<td>59%</td>
</tr>
<tr>
<td>3</td>
<td>18%</td>
<td>80%</td>
</tr>
<tr>
<td>4</td>
<td>30%</td>
<td>82%</td>
</tr>
<tr>
<td>6</td>
<td>45%</td>
<td>90%</td>
</tr>
</tbody>
</table>

*p<0.0001

### Nyxol Reduced PD Faster Across All Mydriatic Agents*

<table>
<thead>
<tr>
<th>Time Post-Treatment with Nyxol/Placebo (Hours)</th>
<th>Nyxol (n=94)</th>
<th>Placebo (n=91)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>Max pupil dilation, Treatment</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>1.5</td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>2</td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>3</td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>4</td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>6</td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>

*Data include all three mydriatics (Phenylephrine, Tropicamide, Paremyd)
Summary Of Positive MIRA-2 Phase 3 Results For Nyxol Eye Drops

*Rapid Efficacy With A Favorable Safety Profile In Reversing Mydriasis With Nyxol*

- Met primary endpoint at 90 minutes with high statistical significance with 2 and 1 drop of Nyxol
- Met all key secondary endpoints with high statistical significance
  - Nyxol more rapidly reduced PD across all 3 mydriatic agents - phenylephrine, tropicamide, and Paremyd®
  - More subjects returned to PD baseline with Nyxol in both light and dark irides
  - Nyxol demonstrated a faster return to baseline accommodation
  - Nyxol reduced the dilation time by ~4 hrs

- No serious AEs, no drop-outs from AEs, no systemic AEs were observed in ≥ 5% of subjects
- Mild, transient conjunctival hyperemia reported in the first hour and declined steadily thereafter. Baseline mean of 0.7, the mean hyperemia score increased by approximately 1.0 unit on CCLRU scale
NDA Submission Targeted In Late 2022
Ongoing Activities Sets Ocufhile On Path To A Potential Regulatory Approval In 2023

**Target Label Indication**
The treatment of pharmacologically induced mydriasis produced by adrenergic (e.g. phenylephrine) or parasympatholytic (e.g. tropicamide) agents, or a combination thereof.

**P3 Clinical Trial**
Complete a 2nd Phase 3 trial in RM with ~330 subjects which also meets 24-hour safety population exposure

**Pediatric Safety**
Complete RM trial with 20 subjects ages 3 to 11 per agreed FDA initial pediatric plan

**Manufacturing**
Complete 3 registration batches on 1-year CMC stability

**Regulatory Approval**
Submit NDA by Late 2022

5 single unit dose vials pack

Nyxol®
Pre-Commercial & Go-To-Market Strategy

Activities Underway To Support Capital-Efficient Nyxol RM Commercial Launch

**Market Development**

Engage leading Key Opinion Leaders and Professional Societies to establish OCUP as an emerging company to address unmet needs in the front and back of the eye disorders.

**Patient Journey**

Establish Ocuphire as a patient-centric company and leader in ocular health through education and patient access programs (also using digital and social media marketing).

**Ocuphire Go-To Market**

Evaluating commercial sales and distribution partner(s).

**Physician Targeting**

Conduct HCP segmentation and targeting to drive early adoption and capture post-market data and patient experience.

**Brand Awareness Across Eye Care Professionals**

Initiate branded and unbranded education for ophthalmologists, optometrists and practice professionals.

Eye Care Practitioners in U.S.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Total Retina Specialists</td>
<td>3,000</td>
</tr>
<tr>
<td>Total Optometrists</td>
<td>46,000</td>
</tr>
<tr>
<td>Total Ophthalmologists</td>
<td>20,000</td>
</tr>
</tbody>
</table>

ASRS; AMA; AAO; Women in Optometry (WO); AOA Excel and Jobson Medical Information
NYXOL® for PRESBYOPIA

“By Age 45, 80% of Americans will struggle with Presbyopia, and by age 50, nearly everyone will.”

NY Times
2021: The Time For Presbyopia Drops

Headlines From Academia And Industry Articles Thru The Year With An Early First Approval

“The correction of presbyopia remains ophthalmology’s ‘Holy Grail’…”

-OIS

Sources: Academic review articles, journals, and publications
Presbyopia Is A Burgeoning Opportunity

Large Market Being Developed, Pupil Modulation Eye Drops May Replace Reading Glasses

The Problem

- Lens loses ability to change shape when viewing objects up close as we age
- Dependence on reading glasses for intermittent and prolonged use
- Growing need for therapies that improve, rather than hinder, quality of life

VUITY™ is the only FDA approved Eye Drop, Launched in Dec 2021

Significant room for improvement for new entrants with better product attributes in a newly developed presbyopia eye drop market

Product Profile: Nyxol® + Low-Dose Pilocarpine (LDP) Combo

Moderate Action On Iris Dilator And Iris Sphincter Muscles For Near Vision Improvement

0.75% Nyxol

- Phentolamine (alpha1/2 antagonist)
- Novel MOA on iris dilator with 24+ hour durability
- Moderate 1+mm pupil reduction
- No daytime redness
- Well-tolerated with no systemic effects
- Stable, preservative-free, single-use vial

0.4% LDP

- Pilocarpine (cholinergic agonist)
- Known MOA on sphincter muscle with potent miotic effects at approved doses (1%, 2%, 4%)
- Low concentration avoids known tolerability issues:
  - headache and browache
  - redness
  - accommodative spasm causing loss of distance vision especially at night

1.5 to 2.5 mm PD reduction moves toward the pin-hole (2 to 2.5 mm, up to 3 mm)

Source: 1) Nyxol® data from 9 completed trials; Pilocarpine Product label and Literature
Presbyopia VEGA-1 Phase 2 Design

Randomized, Double-Masked, Placebo-Controlled, Multi-Center One-Week Trial

Primary:
- % of subjects with \( \geq 3 \) lines of improvement in distance-corrected near visual acuity comparing Nyxol + LDP vs placebo alone at 1 hour

Secondary:
- % of subjects with \( \geq 2 \) and \( \geq 3 \) lines gained at time points from 30 min to 6 hours in photopic lighting comparing Nyxol + LDP vs placebo, Nyxol alone, and LDP alone
- No loss of distance vision
- Pupil diameter at time points
- Safety and tolerability (redness)

Endpoints

VEGA-1

Visit 1 | Evening Dosing (3-4 doses) | Visit 2 (3 – 6 Days Later) | Treatment Arms
--- | --- | --- | ---
Baseline | Nyxol | LDP Drop | Nyxol + LDP
Baseline | Nyxol | No Treatment | Nyxol Alone
Baseline | Placebo | LDP Drop | LDP Alone
Baseline | Placebo | No Treatment | Placebo Alone

4 arms

17 US sites

150 presbyopic patients

0.75% Nyxol

Placebo

Randomization
Screening

Eligibility Criteria

- Males or females \( \geq 40 \) and \( \leq 64 \) years of age
- BCDVA of 0.0 LogMAR (20/20 Snellen equivalent) or better in each eye under photopic conditions
- DCNVA of 0.4 LogMAR (20/50 Snellen equivalent) or worse in photopic conditions in each eye & binocularly

Phase 2 Enrollment Completed Feb to May 2021 – 150 Subjects Reported Topline Results End of 2Q21

Clinical trial NCT#04675151. DCNVA = distance-corrected near visual acuity. BCDVA = best corrected distance visual acuity
VEGA-1 Phase 2 Trial Met Primary & Secondary Endpoints

*Nyxol + LDP Had Strong Response With ≥ 15 Letter Near Gain From 30 Minutes To 6 Hours*

**Table 14.2.1.2 Percent of Subjects with Improvement From Baseline in Photopic DCNVA by Time Point (PP Population).** 15 letters is 3 lines.

Note: PP population differs from mITT by only one subject; results were essentially identical.

Source: VEGA-1 TLR Table 14.2.1.2 Percent of Subjects with Improvement From Baseline in Photopic DCNVA by Time Point (PP Population). 15 letters is 3 lines.
Secondary Endpoints: Improved DCNVA Without BCDVA Loss

Pre-Specified Endpoints Further Demonstrate Nyxol’s Component Efficacy & 10 Letter Effects

VEGA-1 Phase 2 Trial

≥ 15 Letter Gain In Near & < 5 Letter Loss In Distance at 30 Minutes

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=43)</th>
<th>Nyxol+LDP (n=44)</th>
<th>Nyxol (n=30)</th>
<th>LDP (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent of Subjects (%)</td>
<td>14%</td>
<td>61%</td>
<td>33%</td>
<td>26%</td>
</tr>
<tr>
<td>p</td>
<td>0.015</td>
<td>0.03</td>
<td>0.03</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Even with a small sample size, combination arm provided statistically meaningful results vs. LDP and Nyxol alone arms

≥ 10 Letter Improvement in DCNVA at 30 Minutes*

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=43)</th>
<th>Nyxol+LDP (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent of Subjects (%)</td>
<td>51%</td>
<td>77%</td>
</tr>
<tr>
<td>p</td>
<td>0.015</td>
<td></td>
</tr>
</tbody>
</table>

* Trend seen at other assessed timepoints

Source: VEGA-1 TLR Table 14.2.2.2 Percent of Subjects with >= 15 Letters of Improvement in Photopic DCNVA and < 5 Letters of Loss in Photopic Binocular BCDVA by Time Point (PP Population); Table 14.2.1.2 Percent of Subjects With Improvement From Baseline in Photopic DCNVA by Time Point
Secondary Endpoint: Mean Pupil Diameter Over Time
Achieved Pupil Size ~2mm In Nyxol+LDP Consistent With 3-line Improvement In Near Vision

**Source:** VEGA-1 TLR

**Table 14.2.12.1 Observed Values and Change from Baseline in Photopic Pupil Diameter by Time Point (PP Population)**

Pupil Diameter Over Time Graph

- Placebo (n=43)
- Nyxol+LDP (n=43)
- Nyxol (n=30)
- Placebo + LDP (n=31)

**Statistical Significance:**

- **p<0.01**
- ***p<0.0001

**Daily Evening Nyxol Dosing 12 hr minimum interval to Time 0**

Nyxol+LDP arm statistically significant compared to all arms

Source: VEGA-1 TLR Table 14.2.12.1 Observed Values and Change from Baseline in Photopic Pupil Diameter by Time Point (PP Population)
Summary Of Positive VEGA-1 Phase 2 Results

Nyxol + LDP Had Strong Efficacy Response & Well Tolerated Safety Profile

- Met primary endpoint with statistical significance at 1 hour with Nyxol® plus Low-Dose Pilocarpine (LDP)
- Met key secondary endpoints with statistical significance
  - Gained 15 letters (3 lines) in near vision with less than 5 letters of distance vision loss at all timepoints vs. placebo and select timepoints for components
  - Rapid onset of efficacy within 30 mins
  - Durable near vision improvement through at least 6 hours
  - Sustained significant reduction in pupil diameter for at least 18 hours
  - Near vision efficacy seen both monocularly and binocularly
  - Efficacy in both light and dark irides

- No serious AEs, almost all AEs were mild
- No headaches, no brow aches, and no blurry vision AEs were reported
- No material change in distance vision under photopic and mesopic lighting
- No change in IOP
- Mild, transient conjunctival hyperemia (eye redness) observed in <5% of subjects
**Potential ‘Best in Class’ Presbyopia Drop**

*Nyxol+LDP Combination Data Outperforms In Efficacy, Safety, Durability And Onset*

### Nyxol's Potential Differentiated Solution

<table>
<thead>
<tr>
<th>Product Attributes*</th>
<th>Nyxol+LDP</th>
<th>VUITY™</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Efficacy (3 Line Gain in DCNVA - Primary Endpoint Responders)</td>
<td>61%</td>
<td>26-31%</td>
</tr>
<tr>
<td>2a) Safety: Loss of Distance in Mesopic</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2b) Safety: Tolerability</td>
<td>No Headaches</td>
<td>&gt;5% Headaches</td>
</tr>
<tr>
<td>2c) Safety: Conjunctival Hyperemia</td>
<td>&lt;5% redness</td>
<td>&gt;5% redness</td>
</tr>
<tr>
<td>3) Durability (responders at 6 hours)</td>
<td>37%</td>
<td>18%</td>
</tr>
<tr>
<td>4) Fast Onset (responders at 30 mins)</td>
<td>61%</td>
<td>35%</td>
</tr>
</tbody>
</table>

*Differences in cross trial comparisons are not necessarily statistically significant. Nyxol Data: ASCRS (July 2021) Abstract# 76645 (Phase 2) and 74336 (Phase 3). VUITY™ Data: FDA Label and AAO 2021 Presentation.*
Presbyopia Eye Drops Competitive Landscape
Validation of Pupil Modulating Drops Achieving Pin-Hole Effect & Efficacy, Many With Pilocarpine

- **Phase 1**
  - **Orasis** (CSF-1; Low dose pilo)
  - **Visus** (Brimochol®; brimonidine + carbachol)
  - **Novartis** (EV-06)
- **Phase 2**
  - **Lenz** (PRX-100; aceclidine)
  - **VUITY** (1.25% pilo)
  - **Orasis** (CSF-1; Low dose pilo)
  - **Allergan** (VUITY™; 1.25% pilo)
  - **Novartis** (EV-06)
- **Phase 3**
  - **Eyenovia** (MicroLine; 1 or 2% pilo)
  - **Ocuphire** (0.75% Nyxol + 0.4% pilo)

**Other Cholinergic Agonists**

- **Alpha Antagonist & pilocarpine**
  - **Lenz** (PRX-100; aceclidine)
  - **Allergan** (VUITY™; 1.25% pilo)
  - **Visus** (Brimochol®; brimonidine + carbachol)

**Combination drugs**

- **Cholinergic Agonist** (pilocarpine)
  - **Visus** (Brimochol®; brimonidine + carbachol)
  - **Visus** (Brimochol®; brimonidine + carbachol)

**Pupil modulation MOA**

**Soften lens MOA**

*act on sphincter and ciliary muscles in dose-dependent manner

Ocuphire is differentiated by using both the dilator and sphincter muscles moderately to reach a pin-hole pupil size

---

Nyxol Next Steps

- Advance into Phase 3 Presbyopia Registration Trials (1H22)
- Potential NDA Submission (2023)
I’m no longer comfortable driving at night, especially with my son in the car. I have a hard time playing beach volleyball in the evenings due to the bright lights at the courts.

Post-LASIK, Age 42
Market Opportunity In Dim Light Or Night Vision Disturbances

No Approved Treatments With Ripe Opportunity For Growth

The Problem

- Peripheral imperfections scatter light when pupils enlarge in dim light, causing halos, starbursts, and glare that impair vision
- The imperfections may be caused by LASIK surgery, IOL implants, certain types of cataracts (cortical), and natural reasons (especially with age)
- Symptoms cannot be properly corrected by any type of lens (reading glasses, contact lenses) or surgical procedures

No Approved Treatments

Pupil reduction with Nyxol may offer a potential solution to peripheral optical imperfections

Moderate-Severe NVD ~16 M

- Night Myopia 11 M
- Cortical Cataracts 4 M
- Post-Lasik 0.5 M
- Post-IOL Implant 0.3 M

$2B - $4B

Estimated US NVD Market Opportunity

Source: GlobalData Market Research Report, 2020
NVD LYNX-1 Phase 3 Registration Design

Ongoing Randomized, Double-Masked, Placebo-Controlled Two-Week Trial

**LYNX-1**

- 20 US sites
- 140 - 160 patients with NVD

**Endpoints**

**Primary:** % of subjects with \( \geq 3 \) lines of improvement in mesopic low contrast best-corrected distance visual acuity (Day 8)

**Secondary (Days 8 & 15):**
- Pupil diameter
- Visual acuity measures (distance and near)
- Safety and tolerability (redness)

**Phase 3 Initiated in Dec 2020; Completed Enrollment Jan 2022**

**Top Line Expected Early 2022**
Nyxol Demonstrated Clinical Effect In NVD

Key Endpoints Observed In Multiple Phase 2 Trials

NYX-SNV Phase 2 Trial

Improved Low Contrast Distance Visual Acuity*

% of Eyes with Mesopic Low Contrast Visual Acuity Improvement

<table>
<thead>
<tr>
<th>Condition</th>
<th>Placebo (%)</th>
<th>Nyxol (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 line</td>
<td>69%</td>
<td>31%</td>
<td>0.029</td>
</tr>
<tr>
<td>≥ 2 lines</td>
<td>6%</td>
<td>34%</td>
<td>0.04</td>
</tr>
<tr>
<td>≥ 3 lines</td>
<td>19%</td>
<td>0%</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Source NYX-SNV

ORION-1 Phase 2 Trial

Durable > 24-hour Pupil Modulation Effect

Pupil Diameter Change from Baseline in Mesopic Conditions (Study Eye)

Baseline Pupil Diameter: Placebo 4.6mm, Nyxol 4.7mm

<table>
<thead>
<tr>
<th>Day 8</th>
<th>Day 15</th>
<th>Day 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.99 -20%</td>
<td>-1.00 -21%</td>
<td>-0.88 -19%</td>
</tr>
</tbody>
</table>

Source: NYXG-201

*NYX-SNV trial was small and not designed for a statistical 3-line improvement in low-contrast visual acuity; the ~20% effect was used for powering and sizing of Phase 3 trial
APX3330 TABLETS

- **DR**: Diabetic Retinopathy
- **DME**: Diabetic Macular Edema
**Diabetic Retinopathy & Macular Edema**

*Oral Alternatives To Injectable Therapies Are Needed For Earlier Stages Of Disease*

### The Problem

- **Diabetic retinopathy (DR) and diabetic macular edema (DME)** are a leading cause of vision loss worldwide.

- Diabetes damages small blood vessels within the eye causing leakage, oxygen starvation, and abnormal vessel growth.

- **DR patients are not routinely treated with approved injectable anti-VEGF drugs**
  - DR progresses resulting in vision loss.

- **Current treatment for DME are not satisfactory**
  - 25% non-responders
  - 50% partial responders to anti-VEGF drugs.

### Large, Unmet Need in Diabetic Eye Diseases (US)

<table>
<thead>
<tr>
<th></th>
<th>DR</th>
<th>DME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>~7.7M Patients</td>
<td>~750K Patients</td>
</tr>
</tbody>
</table>

### Limited Retinal Treatment Options for Diabetic Patients

**Estimated US DME Market Opportunity**: $1B - $3B

**Estimated US DR Market Opportunity**: $3B - $7B

APX3330: Drug Development History And Patents

Significant Preclinical & Clinical Data Supporting Human Safety, MOA, and PK

11 Phase 1 & Phase 2 Trials

>340 Subjects Dosed

Exposure in Humans 365 Days

Patent Coverage 2034+

APX3330 New Chemical Entity

Preclinical Efficacy & Toxicology Package

APX3330 IND

6 Phase 1 Trials

5 Phase 2 Trials

Phase 2b Trials

Phase 3 Registration

NDA Filing

Studied in inflammation/hepatitis & cancer patients
(Studied by Eisai & Apexian, respectively)

Focus on Ophthalmology

DR

DME
APX3330 History And Ref-1 Inhibition Mechanism

Ref-1 Involved In Multiple Key Pathways That Contribute To Diabetic Retinopathy and DME

- Ref-1 (reduction-oxidation effector factor-1) is a novel target discovered by Dr. Mark R. Kelley at Indiana University School of Medicine
- APX3330 is a small molecule oral drug candidate and a first-in-class inhibitor of Ref-1
- APX3330 previously developed by Eisai for multiple hepatic inflammatory indications and later by Apexian for advanced solid tumors
  - Similar oncology origin as approved anti-VEGFs
- MOA uniquely decreases both abnormal angiogenesis and inflammation by blocking pathways downstream of Ref-1
APX3330 Down-Regulates VEGF Protein And Anti-Inflammatory Cytokines

*In Vivo And In Vitro Evidence Of APX Dual Pathway Mechanism Of Action*

**APX3330 Reduces VEGF Protein in the Brain of Preclinical Models**

- Treatment of APX3330 (10mg/kg, oral gavage) in rats with type 1 diabetes and induced stroke shows a significant decrease of VEGF signaling.
- Increased VEGF is a hallmark of uncontrolled neovascularization and inflammation in diabetic retinopathies; current approved treatments successfully decrease VEGF levels in the eye.

**APX3330 Reduces Pro-inflammatory Cytokines in Murine Cell Lines Involved in Macular Degeneration**

- In vitro APX3330 suppresses pro-inflammatory cytokines in LPS stimulated murine macrophage cell lines known to be involved in macular degeneration:
  - TNF-α is a potent cytokine that enhances secretion of VEGF-A and VEGF-B by human choroidal fibroblast cells. [*J Cell Physiol, 2011*]
  - Genetic ablation of IL-6 led to significant suppression of AMD (murine CNV model). [*Am J Pathol, 2007*]
Preclinical Data: Oral APX3330 Blocks Neovascularization

Lesion Volume Decrease With Oral APX3330 In Murine Laser CNV Model Similar To EYLEA® Data

- Silva et al. Oral APX3330 treatment reduces L-CNV lesions in preclinical mouse model and confirms Phase 2 DR/DME clinical dose with sufficient distribution to human retina using PBPK modeling. Presented at the ARVO 2021 Annual Meeting
- Published data on EYLEA
Phase 1/2 Clinical Trials: PK Data Supporting The ZETA-1 Trial

Apexian preclinical data

Eisai preclinical data

Silva et al. Oral APX3330 treatment reduces L-CNV lesions in preclinical mouse model and confirms Phase 2 DR/DME clinical dose with sufficient distribution to human retina using PBPK modeling. Presented at the ARVO 2021 Annual Meeting

APX3330 Is Bioavailable And Reaches The Retina Via Oral Administration

Does oral administration of APX3330 reach the retina in sufficient concentration?

**Mouse**

- 25 mg/kg APX3330 oral gavage measured in mouse retina\(^1\)

**Rat**

- 10 mg/kg APX3330 oral gavage measured in rat eye\(^2\)

**Human**

- 300 mg BID (600 mg/day total)

  Established PBPK model predicts APX3330 reaches sufficient human retinal concentrations\(^3\)

Phase 1 PK Clinical Data

**Human Drug Exposure Multiple Times Higher than Mouse Efficacious Levels**

Human Pharmacokinetics of APX3330 at 120 mg/day

- **Human 120 mg/day**
  - 40 µg/ml
- **Mice 25 mg/kg**
  - 2 µg/ml

Source: Eisai/Apexian Human PK data

---

1. Apexian preclinical data
2. Eisai preclinical data
### APX3330 Product Candidate Profile For Multiple Retinal Indications

**First-In-Class Ref-1 Inhibitor With Favorable Human Safety Data**

<table>
<thead>
<tr>
<th>Expected Efficacy Data</th>
<th>Favorable Safety Profile</th>
</tr>
</thead>
</table>
| **Improving Eye Health in Diabetics**  
  ↓ Inflammation  
  ↓ Abnormal Angiogenesis | **Few Systemic Adverse Effects**  
  • < 5% Mild Gastrointestinal (diarrhea)  
  • < 5% Mild Skin Rash (reversible)  
  • Lack of Significant Acute Neurologic, Cardiovascular, Liver, or Pulmonary toxicity |
| **Enhance Compliance & Exposure**  
  Oral pill may reduce the burden of frequent anti-VEGF injections | **No Ocular Effects**  
  • No observed ocular AEs |

**APX3330: Well-tolerated Oral Dose up to 600mg/day**

Twice Daily Dosing

![Eye Icon](image)
DR/DME ZETA-1 Phase 2b Design

**Ongoing, Randomized, Double-Masked, Placebo-Controlled 24-Week Trial (Similar To Eylea Pivotal DR P3)**

**ZETA-1**

- 24 US sites
- ~100 participants with moderate-to-severe NPDR or mild PDR
- Noncentral DME is permitted

**Eligibility Screening**

**Randomization**

**Endpoints**

**Primary:** % of subjects with a ≥ 2 step improvement on the DRSS (Diabetic Retinopathy Severity Scale) score at week 24

**Secondary:**
- Central subfield thickness (CST)
- BCDVA (ETDRS)
- DRSS change at week 12
- Rescue subjects
- Safety and tolerability

**Exploratory:**
- Labs / PK

**Phase 2b Start Initiated in April 2021**

**Top Line Expected in 2H22**

NPDR = non-proliferative diabetic retinopathy (which includes non centrally involved diabetic macular edema)

PDR = proliferative diabetic retinopathy (which includes non centrally involved diabetic macular edema)
Innovative Approach For Retinal Diseases With APX Platform

APX3330 May Treat Patients Across The Spectrum Of Retinal Diseases

Potential Differentiated Solution

• **Potential First Oral Rx for Retina Diseases**
  - First-line earlier intervention for the diabetic eye
  - Add-on therapy to current anti-VEGF treatments

• **Proven Novel Mechanism**
  - May decrease both inflammation and angiogenesis

• **Convenient Daily Regimen**

• **Favorable Oral Safety Profile**
  - As seen in 11 completed Phase 1 and Phase 2 clinical trials

• **Improve Patient Compliance**
  - Potentially alleviate the frequent burden of injections
Team/Boards, Milestones, And Financial Data
Ocuphire Management Team

Decades Of Biotech And Drug Development Experience

Mina Sooch, MBA
President & CEO
and Founder

Drey Coleman
VP, Clinical
Operations

Barbara Withers, PhD
VP, Clinical and Regulatory Strategy

Charlie Hoffmann, MBA
VP Corporate Development and Operations

Amy Rabourn, CPA
VP, Finance

Mitch Brigell, PhD
Head, Clinical Development and Strategy

Ronil Patel, MS
Senior Director BD and Market Strategy

Daniela Oniciu, PhD
Global Head, R&D, Chemistry and Product Development

Chris Ernst
Global Head, QA and Manufacturing

Daniela Oniciu, PhD
Global Head, R&D, Chemistry and Product Development
Ocuphire's World-Class Medical Advisory Board
Fortunate For The Insights Of Leading KOLs & Drug Candidate Co-Founders

Jay Pepose, MD, PhD
UCLA

Marguerite McDonald, MD
Columbia University

Ed Holland, MD
Loyola University Chicago

Jack Holladay, MD
University of Texas

Thomas Samuelson, MD
University of Minnesota

Y. Ralph Chu, MD
Northwestern University

James Katz, MD
University of Illinois

Mark Kelley, PhD
Indiana University
Co-Founder Apexian/APX3330

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Vanderbilt University

Mitch Jackson, MD
Chicago Medical School

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Vanderbilt University

Ed Holland, MD
Loyola University Chicago

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Indiana University

Douglas Devries, OD
University of Nevada

Jack Holladay, MD
University of Texas

Paul Karpecki, OD
Indiana University

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Georgetown University

Peter Kaiser, MD
Harvard Medical School

Thomas Samuelson, MD
University of Minnesota

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Marguerite McDonald, MD
Columbia University
Ocuphire Board of Directors

Seasoned Directors With Decades Of Drug Development, M&A/Financings, And Ophthalmology

Cam Gallagher, MBA
Chair, Board Director

Mina Sooch, MBA
Vice-Chair, Board Director
President & CEO

James Manuso, PhD/MBA
Board Director

Talfinium Investments, Inc.

Sean Ainsworth, MBA
Lead Independent Director,
Board Director

Richard Rodgers, MBA
Board Director

Susan Benton, MBA
Board Director

Jay Pepose, MD, PhD
Board Director

Ocuphire

David Geffen
School of Medicine

UCLA

Washington University in St. Louis

Vellano Ventures

Apjohn Ventures

Gena Therapeutics

Gemphire Therapeutics

Anonza Therapeutics

Allergan

RetroSense Therapeutics

IMMUNOFOCUS

MOBILE

Pepose Vision

Wilmer Eye Institute

Washington University in St. Louis

Columbia Business School

astex 
pharmaceuticals

Galenica

Tesarin

MCi

Abraxis Bioscience

University of Minnesota

Carlson School of Management

Théa

Bausch + Lomb

Shire

44
Ocuphire Cadence Of Milestones

Multiple Data Catalysts On Path To NDA(s)

2021

- Report Positive Phase 3 Data for RM (MIRA-2)
- Report Positive Phase 2 Data for Presbyopia (VEGA-1)
- New Patent Claims for Presbyopia
- ASCRS 2021 Presentation for MIRA-2 & VEGA-1
- Manufacture 3xRegistration Batches for Nyxol Blow-Fill-Seal (BFS) Eye Drops
- Initiate 2nd Phase 3 RM and Pediatric RM trial

2022

- Report 2nd Phase 3 Data for RM
- Report Pediatric Data in RM
- Report Phase 3 Data for NVD
- Submit Nyxol NDA for RM
- Report Phase 2 Data for DR/DME
- Initiate Two Phase 3 Presbyopia Trials
- Initiate Phase 3 Chronic Safety Trial

Ongoing Partnering Discussions with Leading Ophthalmic Companies (including European and Asian Players)
# Ophthalmology – An Attractive Biotech Sector

## Deal Activity And FDA Approvals In Ophthalmology In 2021

### Deal Activity

<table>
<thead>
<tr>
<th>Date</th>
<th>Company</th>
<th>Transaction Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 2021</td>
<td>Alcon</td>
<td>$355M</td>
</tr>
<tr>
<td>September 2021</td>
<td>Regenxbio</td>
<td>$1.75B</td>
</tr>
<tr>
<td>October 2021</td>
<td>Théa</td>
<td>~$2B</td>
</tr>
<tr>
<td>December 2021</td>
<td>Novartis</td>
<td>~$1.5B</td>
</tr>
<tr>
<td>December 2021</td>
<td>Lineage</td>
<td>$670M</td>
</tr>
</tbody>
</table>

### New Product Approvals

7 of 60 Total FDA Drug Approvals in 2021 Were Ophthalmic Drugs

<table>
<thead>
<tr>
<th>Approval Date</th>
<th>Drug Name</th>
<th>Approval Type</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 2021</td>
<td>Ranibizumab</td>
<td>sNDA</td>
<td>~$2B</td>
</tr>
<tr>
<td>September 2021</td>
<td>Ranibizumab</td>
<td>sNDA</td>
<td>~$1.5B</td>
</tr>
<tr>
<td>September 2021</td>
<td>Genentech Lineage</td>
<td>sNDA</td>
<td>$670M</td>
</tr>
</tbody>
</table>

**Source:** 1. Endpoint Dec 29, 2021- Hitting a new record on drug approvals, the FDA offers a thumbs-up to another atopic dermatitis contender; OIS Year in Review 2021; Company press releases

---

**Aging Population**

**Active M&A**

**Lower Cost, Quick Enrolling, Short Duration Clinical Trials**

**Favorable Regulatory Environment**

---

**Lower Cost, Quick Enrolling, Short Duration Clinical Trials**

**Aging Population**

**Active M&A**

**Favorable Regulatory Environment**

---

**New Product Approvals**

- **Ranibizumab biosimilar**
  - Genentech
  - Lineage
  - Novartis

---

**Source:** 1. Endpoint Dec 29, 2021- Hitting a new record on drug approvals, the FDA offers a thumbs-up to another atopic dermatitis contender; OIS Year in Review 2021; Company press releases
OCUP – Market Snapshot

**Active Trading Volume And Sufficient Cash Runway Through 2Q 2023**

<table>
<thead>
<tr>
<th>Ticker</th>
<th>OCUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price</td>
<td>$3.73</td>
</tr>
<tr>
<td>Market Cap</td>
<td>$64.8 M</td>
</tr>
<tr>
<td>Shares Outstanding</td>
<td>18.8 M</td>
</tr>
<tr>
<td>Cash</td>
<td>$24.5 M</td>
</tr>
<tr>
<td>Cash Runway</td>
<td>Sufficient into 2Q 2023</td>
</tr>
<tr>
<td>Average Daily Volume</td>
<td>390 K</td>
</tr>
<tr>
<td>Short Interest</td>
<td>868 K; 5.1% of Float</td>
</tr>
</tbody>
</table>

As of 12-31-21

| Shares Outstanding   | 18.8 M                      |
| Cash Runway          | Sufficient into 2Q 2023     |
| Average Daily Volume | 390 K                       |
| Short Interest       | 868 K; 5.1% of Float        |

As of 12-31-21

| Shares Outstanding   | 18.8 M                      |
| Cash Runway          | Sufficient into 2Q 2023     |
| Average Daily Volume | 390 K                       |
| Short Interest       | 868 K; 5.1% of Float        |

As of 12-31-21 (unaudited)

| Shares Outstanding   | 18.8 M                      |
| Cash Runway          | Sufficient into 2Q 2023     |
| Average Daily Volume | 390 K                       |
| Short Interest       | 868 K; 5.1% of Float        |

As of 12-15-21

Research Analyst Coverage on OCUP

<table>
<thead>
<tr>
<th>Research Analyst Coverage on OCUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>John Newman</td>
</tr>
<tr>
<td>Canaccord Genuity</td>
</tr>
<tr>
<td>Kristen Kluska</td>
</tr>
<tr>
<td>Cantor Fitzgerald</td>
</tr>
<tr>
<td>James Molloy</td>
</tr>
<tr>
<td>Alliance Global Partners</td>
</tr>
<tr>
<td>Prakhar Agrawal</td>
</tr>
<tr>
<td>Jones Trading</td>
</tr>
<tr>
<td>Matthew Caufield</td>
</tr>
<tr>
<td>H. C. Wainwright</td>
</tr>
</tbody>
</table>
NVD Endpoint: 5% Low Contrast Visual Acuity (LCVA) Chart

*FDA Accepted Endpoint For Contrast Sensitivity Assessment*

**Primary Endpoint of Nyxol LYNX-1 Trial**

Percent of subjects with $\geq 3$ lines of improvement in mesopic low contrast best-corrected distance visual acuity (7 days)

*Inclusion Criteria includes subjects with baseline mesopic LCVA of 20/100 or worse*
## DR/DME Endpoint: Diabetic Retinopathy Severity Scale (DRSS)

*FDA Accepted Endpoint For DR (EYLEA® in PANORAMA Pivotal Trial)*

### Primary Endpoint of APX3330 ZETA-1 Trial

Percent of patients with a $\geq 2$ step improvement on the DRSS score at week 24

<table>
<thead>
<tr>
<th>DRSS Score</th>
<th>Description</th>
<th>Retinal Image</th>
<th>Patients included in the ZETA-1 Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (10)</td>
<td>DR Absent</td>
<td>Healthy blood vessels with no bulges</td>
<td>5, 6 (47, 53)</td>
</tr>
<tr>
<td>2 (20)</td>
<td>Microaneurysm only</td>
<td>Small bulges in blood vessel walls as well as other signs in the retina</td>
<td>7 – 13 (60, 61, 65, 71, 75, 85, 90)</td>
</tr>
<tr>
<td>3 (35)</td>
<td>Mild NPDR</td>
<td>More changes in the blood vessels in the retina and small spots of blood can become more visible</td>
<td>Moderately Severe NPDR</td>
</tr>
<tr>
<td>4 (43)</td>
<td>Moderate NPDR</td>
<td>More blood vessels in larger areas of the retina show changes</td>
<td>PDR – Mild, Moderate, and Severe</td>
</tr>
<tr>
<td>5, 6</td>
<td>Moderately Severe NPDR</td>
<td>Many of the blood vessels in the retina show visible changes</td>
<td></td>
</tr>
<tr>
<td>7 – 13</td>
<td>Increased growth of new, damaged blood vessels</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*A 13-point Scale Outlining the Various Stages of Diabetic Retinopathy*