LENZ THERAPEUTICS

Focused on innovative science to improve vision

Lead late-stage candidate – aceclidine to target presbyopia

• Exclusive and novel active ingredient
• Quickly improves near vision with a long duration
• No impact on distance vision
• History of safe use in Europe for glaucoma
• Potential for broadest target patient population

• Successful Phase 2
• $47M Series A
• New, experienced leadership
• Strong IP
• Catalyst rich
Problem

Presbyopia, the inevitable loss of near vision

Research shows adults over 45 lose on average 1.5 lines of near vision per 6 years\(^1\)

Most of us first start noticing this as...
- We hold our phones farther from our eyes
- We have difficulty reading a menu in a dimly lit restaurant
Struggle

Impacts over 120M people in the US

1.4M New presbyopes every year\textsuperscript{2,3}

Imperfect treatment options

Aesthetic compromises and inconvenience

Invasive and limited surgical solutions with inherent risk
An eye drop to improve near vision while preserving distance vision
Potential for best-in-class treatment

The first and only aceclidine-based eye drop with promise to provide seamless vision for the vast majority of all presbyopes

- Made possible by aceclidine, our novel active ingredient
- Quickly achieved near vision for on demand needs with a long duration*
- No impact on distance vision in standard and night conditions*
- Potential for broadest target patient population

* Based on Phase 2 study endpoints for aceclidine-only study arm
How the eye focuses light for near and far vision

**Distance vision:**
The lens is in its native shape which enables far vision

Relaxed ciliary muscles

Thin lens

**Near vision:**
The lens changes shape, known as accommodation, to allow focus on close objects

Contracted ciliary muscles

Thick lens
Presbyopia is the age-related loss of near vision

**Problem:**

The lens hardens with age, limiting accommodation and shifting near vision focus

- Contracted ciliary muscles
- Insufficient accommodation

**Solution:**

A pinhole pupil only allows light that will focus on the retina as a surrogate for accommodation

- Contracted iris muscles
- Pinhole pupil
Research shows reducing the pupil diameter below 2mm drastically increases depth-of-focus

“Although differences between studies, DOF increases rapidly as the pupil diameter is reduced below 2mm”

- W. Neil Charman
Key side effect to avoid is the myopic shift

**Risk:**
Triggering the iris for pinhole effect while overstimulating the ciliary muscle causing unwanted refractive change

**Problem:**
Resulting in improved near vision at the expense of impaired distance vision
Research shows aceclidine targets iris sphincter without overstimulating the ciliary muscle\(^7\)

<table>
<thead>
<tr>
<th></th>
<th>Iris sphincter muscle EC(_{50}) (nmol/l)</th>
<th>Ciliary muscle EC(_{50}) (nmol/l)</th>
<th>Independence ratio iris to ciliary EC(_{50})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aceclidine</td>
<td>900</td>
<td>20,000 Longitudinal 25,000 Circular</td>
<td>22 28</td>
</tr>
<tr>
<td>Pilocarpine</td>
<td>1,800</td>
<td>3,360 Longitudinal 2,840 Circular</td>
<td>1.9 1.6</td>
</tr>
<tr>
<td>Carbachol</td>
<td>106</td>
<td>574 Longitudinal 560 Circular</td>
<td>5.4 5.3</td>
</tr>
</tbody>
</table>

Higher is better

EC\(_{50}\) is the amount of drug required to elicit 50% of the maximum muscle response, research based on 29 pairs of eyes and donor ages ranging from 41 - 89
Which allows it to uniquely avoid the myopic shift\(^4\)

Miotic pinhole effect achieved (iris sphincter muscle)

- **2% Aceclidine**: 1.40 mm
  - -0.13 Diopters myopia
    - 0.078 mm lens shift
    - 0.07 mm increase lens thickness

- **2% Pilocarpine**: 1.35 mm
  - -1.3 Diopters myopia
    - 0.234 mm lens shift
    - 0.2 mm increase lens thickness

- **3% Carbachol**: 1.63 mm
  - -1.15 Diopters myopia
    - 0.24 mm lens shift
    - 0.26 mm increase lens thickness

All capable of pinhole effect

Corresponding myopic shift (ciliary muscle)

- **2% Pilocarpine**: 1.35 mm
- **3% Carbachol**: 1.63 mm

Academic research on general miotics, concentrations in research not necessarily under development. Pinhole data at 45 minutes. Diopters myopia, lens thickness and lens shift measurements for ages 40 – 60 years old.
One diopter of myopic shift is meaningful.
Addressable market is largest when pinhole effect is decoupled from myopic shift

Presbyopia market segments

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 – 54 yrs</td>
<td>31%</td>
</tr>
<tr>
<td>55 – 64 yrs</td>
<td>30%</td>
</tr>
<tr>
<td>Over 65 yrs</td>
<td>39%</td>
</tr>
</tbody>
</table>

Aceclidine

- Broad addressable market
- Optimal concentration for pinhole effect
- Minimal concern of induced myopia
**Phase 2**

Met endpoints for near vision improvement

**Rapid Onset / On Demand**

81% gained at least 2 lines within 30 minutes
53% gained at least 3 lines within 30 minutes

<table>
<thead>
<tr>
<th>Time</th>
<th>Aceclidine</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 Hour</td>
<td>53%</td>
<td>2%</td>
</tr>
<tr>
<td>1 Hour</td>
<td>47%</td>
<td>2%</td>
</tr>
<tr>
<td>3 Hours</td>
<td>39%</td>
<td>0%</td>
</tr>
<tr>
<td>4 Hours</td>
<td>17%</td>
<td>0%</td>
</tr>
<tr>
<td>5 Hours</td>
<td>22%</td>
<td>0%</td>
</tr>
<tr>
<td>7 Hours</td>
<td>22%</td>
<td>0%</td>
</tr>
</tbody>
</table>

P Values <0.0001

**Long Duration**

50% maintained 2-line improvement at least 7 hours
22% maintained 3-line improvement at least 7 hours

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<tr>
<td>1 Hour</td>
<td>78%</td>
<td>12%</td>
</tr>
<tr>
<td>3 Hours</td>
<td>69%</td>
<td>10%</td>
</tr>
<tr>
<td>4 Hours</td>
<td>53%</td>
<td>10%</td>
</tr>
<tr>
<td>5 Hours</td>
<td>64%</td>
<td>10%</td>
</tr>
<tr>
<td>7 Hours</td>
<td>50%</td>
<td>12%</td>
</tr>
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P Values <0.0002

* Based Phase 2 study endpoints for Aceclidine-only study arm, mITT data
Phase 2
Met endpoint for no impact to distance vision with trend towards net gain

No change in best corrected **normal light** distance visual acuity (P ≥ 0.99 placebo vs Aceclidine at all time points)

No change in best corrected **low luminance** distance visual acuity (P ≥ 0.25 placebo vs Aceclidine at all time points)

Well tolerated with most common side effect being mild discomfort on instillation and **no serious adverse events**

* Based on Phase 2 study endpoints for Aceclidine-only study arm, mITT data
Phase 2
Maintained pupil size in target sweet spot for 7 hours

Average pupil size reduced from 5.1 mm to 1.5 mm at 30 minutes

Average pupil size maintained in sweet spot of 1.5mm to 2 mm for 7 hours

Pupil size correlates to lines of near vision improvement

* Based on Phase 2 study endpoints for Aceclidine-only study arm, mITT data
Aceclidine

Broad exclusivity protection

US
- 12 granted method of use and formulation patents
- 6 patent applications under review

Ex-US
- 13 granted method of use and formulation patents
- 33 patent applications under review

FDA exclusivity provided by NCE status upon approval
Aceclidine

Safety history

History of use in Europe for Glaucoma

• Approved for Glaucoma in Europe in 1970's\(^6\)
• Approved at higher concentration and QID dosing\(^6\)
• Rapid anterior chamber penetration
• Well tolerated with no tachyphylaxis
• No US DMF submission and therefore a US NCE
Experienced leadership

Management:
- Eef Schimmelpennink
  President and CEO
- Shawn Olsson
  Chief Commercial Officer
- Marc Odrich, MD
  Chief Medical Officer
- Gerald Horn, MD
  Senior Scientific Advisor & Founder

Board:
- Clare Ozawa, PhD
  Managing Director, Versant
- Zach Scheiner, PhD
  Principal, RA Capital
- Jim McCollum
  Founder
- Frederic Guerard
  Graybug, CEO
- Eef Schimmelpennink
  LENZ, President and CEO

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  Medical Director
  Dell Laser
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  Discover Vision Centers
- Terry Kim, MD
  Prof. of Ophthalmology
  Duke University
- Colman Kraff, MD
  Kraff Eye Institute
- Robert Osher, MD
  Cincinnati Eye Institute
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* Based on Phase 2 data

Focused on innovative science to improve vision
LENZ Therapeutics is a late-stage clinical company developing innovative ophthalmic pharmaceutical products that improve vision. Our lead program is an aceclidine based eye drop designed to restore the loss of near vision associated with presbyopia. Presbyopia impacts almost two billion people globally and more than 120 million people in the US. LENZ Therapeutics is headquartered in San Diego, California, and is backed by multiple blue-chip venture capital investors.

For more information please visit: LENZ-Tx.com
References

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