LENZ THERAPEUTICS
Focused on innovative science to improve vision

Aceclidine - best-in-class Q2 2022 Phase 3 candidate to target presbyopia

- Exclusive and novel active ingredient
- Quickly improves near vision with a long duration
- No impact on distance vision and history of safe use in EU
- Potential for broadest target patient population

- Successful Phase 2
- Strong IP
- Completed FDA Type C
- Q2 2022 Phase 3 start
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
Solution

An eye drop to improve near vision while preserving distance vision.
Meet Aceclidine
Best-in-class potential

The first and only aceclidine-based eye drop with potential of providing all day seamless vision for the vast majority of presbyopes, with no preservatives.
How the eye focuses light for near and far vision

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

**Near vision:**
The lens changes shape, known as accommodation, to allow focus on close objects
Presbyopia is the age-related loss of near vision

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

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

- Contracted ciliary muscles
- Insufficient accommodation
- Contracted iris muscles
- Pinhole pupil
Research shows reducing the pupil diameter below 2mm dramatically increases depth-of-focus\textsuperscript{8,9}

“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

<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</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25,000 Circular</td>
<td>28</td>
</tr>
<tr>
<td>Pilocarpine</td>
<td>1,800</td>
<td>3,360 Longitudinal</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2,840 Circular</td>
<td>1.6</td>
</tr>
<tr>
<td>Carbachol</td>
<td>106</td>
<td>574 Longitudinal</td>
<td>5.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>560 Circular</td>
<td>5.3</td>
</tr>
</tbody>
</table>

EC50 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

Higher is better
Which allows it to uniquely avoid the myopic shift\(^4\)

<table>
<thead>
<tr>
<th>Miotic pinhole effect achieved (iris sphincter muscle)</th>
<th>Corresponding myopic shift (ciliary muscle)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2% Aceclidine</td>
<td>-0.13 Diopters myopia</td>
</tr>
<tr>
<td>1.40 mm</td>
<td>0.078 mm lens shift</td>
</tr>
<tr>
<td></td>
<td>0.07 mm increase lens thickness</td>
</tr>
<tr>
<td>2% Pilocarpine</td>
<td>-1.3 Diopters myopia</td>
</tr>
<tr>
<td>1.35 mm</td>
<td>0.234 mm lens shift</td>
</tr>
<tr>
<td></td>
<td>0.2 mm increase lens thickness</td>
</tr>
<tr>
<td>3% Carbachol</td>
<td>-1.15 Diopters myopia</td>
</tr>
<tr>
<td>1.63 mm</td>
<td>0.24 mm lens shift</td>
</tr>
<tr>
<td></td>
<td>0.26 mm increase lens thickness</td>
</tr>
<tr>
<td>All capable of pinhole effect</td>
<td>Lower is better</td>
</tr>
</tbody>
</table>

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

20/20
Perfect vision

20/50
1 Diopter myopic shift
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

Long Duration

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

* Based Phase 2 study endpoints for 1.75% 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 1.75% 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

<table>
<thead>
<tr>
<th>Pupil size over time</th>
<th>Predose</th>
<th>0.5 Hour</th>
<th>1 Hour</th>
<th>3 Hours</th>
<th>4 Hours</th>
<th>5 Hours</th>
<th>7 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pupil size in mm</td>
<td>5.1 mm</td>
<td>1.5 mm</td>
<td>1.5 mm</td>
<td>1.6 mm</td>
<td>1.7 mm</td>
<td>1.8 mm</td>
<td>2 mm</td>
</tr>
</tbody>
</table>

≥2 Line Improvement
- 81%
- 78%
- 69%
- 53%
- 64%
- 50%

≥3 Line Improvement
- 53%
- 47%
- 39%
- 17%
- 22%
- 22%

* Based on Phase 2 study endpoints for 1.75% Aceclidine-only study arm, mITT data
LENZ is preparing for a Q2 2022 pivotal phase 3

- Both use LENZ's proprietary, preservative free vehicle matrix to maximize comfort, efficacy and bioavailability

- Type C meeting completed

**LNZ100**
- 1.75% Aceclidine
  - Optimal concentration for pinhole effect
  - Minimal concern of induced myopia

**LNZ101**
- 1.75% Aceclidine + Brimonidine
  - Potential for increased duration
  - Added benefit of eye whitening
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
Aceclidine

Broad exclusivity protection

US
• 14 granted method of use and formulation patents
• 5 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
Expereined 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:

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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: LNZ-Tx.com
References

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