• Punctal Plug Delivery System

Sustained Drug Delivery for Ophthalmology

• Bob Butchofsky, CEO, Mati Therapeutics Inc.
Consistent efficacy and therapy control delivered easily and comfortably
Evolute® Punctal Plug Delivery System

Successful By Design

1. Easy to place and remove
2. Cosmetically invisible – easy to identify
3. Tolerable
4. Consistent, sustained efficacy
5. Use in multiple disease states
Evolute®: Familiar, Precise Insertion
Excellent Plug Retention Rates

U.S. Phase II Multi-center Trials – Lower Puncta

<table>
<thead>
<tr>
<th>Study</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12 or End of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glau 12 (n = 92)</td>
<td>98%</td>
<td>97%</td>
<td>96%</td>
</tr>
<tr>
<td>Glau 13 (n = 87)</td>
<td>98%</td>
<td>96%</td>
<td>92%</td>
</tr>
<tr>
<td>NPIF (n=55, end total 75)</td>
<td>NA</td>
<td>NA</td>
<td>98%</td>
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# Multiple Disease State Treatment Applications

## Multiple compounds can be formulated with Evolute® Punctal Plug Delivery System

<table>
<thead>
<tr>
<th>Glaucoma</th>
<th>Allergy</th>
<th>Anti-Inflammatory</th>
<th>Dry Eye</th>
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<tbody>
<tr>
<td><strong>Prostaglandins</strong>&lt;br&gt;- Latanoprost&lt;br&gt;- Travoprost&lt;br&gt;- Bimatoprost</td>
<td><strong>Antihistamines / Mast Cell Stabilizers</strong>&lt;br&gt;- Olopatadine&lt;br&gt;- Levocabastine&lt;br&gt;- alcaftadine</td>
<td><strong>Steroids</strong>&lt;br&gt;- Difluprednate&lt;br&gt;- Dexamethasone&lt;br&gt;- Loteprednol&lt;br&gt;- Fluorometholone</td>
<td><strong>Immunosuppressants</strong>&lt;br&gt;- Cyclosporine&lt;br&gt;- <strong>Integrin antagonist</strong>&lt;br&gt;- Lifitegrast</td>
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<tr>
<td><strong>Beta-Blockers</strong>&lt;br&gt;- Timolol&lt;br&gt;- Betaxolol&lt;br&gt;- Levobunolol</td>
<td><strong>Mast Cell Stabilizers</strong>&lt;br&gt;- Cromolyn&lt;br&gt;- Nedocromil</td>
<td><strong>OCT Demulcents / Oils / Emulsions</strong></td>
<td><strong>NSAIDs</strong>&lt;br&gt;- Nepafenac&lt;br&gt;- Bromfenac</td>
</tr>
<tr>
<td><strong>Alpha Agonists</strong>&lt;br&gt;- Brimonidine</td>
<td><strong>NCEs</strong>&lt;br&gt;- Rho Kinase Inhibitors&lt;br&gt;- Adenosine agonists</td>
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Ph II U.S. Multi-center 12 Week Results:

L-Evolute® with Previously Shown Elution Profile

Development data to date shows the T-Evolute® should out perform the L-Evolute® shown above in humans

All IOP included, regardless of plug loss/removal

*95% CI excludes 0, indicating a p-value of <.05
Animal model confirms greater efficacy of T-Evolute®
• Study Design
  • Double masked
  • Placebo controlled
    • Nepafenac Evolute® Vs Placebo Evolute®
  • Randomized 2 to 1 in favor of active
  • Post Operative Cataract Trial
  • End Points = Pain and Inflammation
  • Plugs Inserted 1-2 Days Pre-Op
  • N for interim analysis = 44 (29 N-Evolute® – 15 Placebo)
Nepafenac Evolute® Phase II Results

Percent of Patients with **No Pain**
Day 3 Post Op

66% in N-Evolute
25% in Placebo Evolute
Percent of Patients with **No Pain** Throughout Entire Trial Period

![Graph showing percent of patients with no pain for Nepafenac Evolute and Placebo Evolute. The graph indicates 43% of patients experienced no pain with Nepafenac Evolute, while 0% experienced no pain with Placebo Evolute.](image-url)
Nepafenac Evolute® Phase II Results

Percent of Patients with **None or Trace** Anterior Chamber Cells

**Day 3 Post Op**

- **N-Evolute**: 86%
- **Placebo Evolute**: 50%
Nepafenac Evolute® Phase II Results

Percent of Patients with None or Trace Anterior Chamber Flare
Day 3 Post Op

- 95% for N-Evolute
- 67% for Placebo Evolute
Nepafenac Evolute® Phase II Results

Percent of Patients with Uncorrected VA 20/50 or Better
Day 3 and Day 7 Post Op

- Day 3 Post Op: 71% (N-Evolute) vs. 50% (Placebo Evolute)
- Day 7 Post Op: 83% (N-Evolute) vs. 50% (Placebo Evolute)
Mati Therapeutics Inc. N-Evolute® Phase II Trial

• Adverse Events
  • Total of 11 Adverse Events Reported:
    • 7 N-Evolute® (24%)
    • 4 Placebo (27%)
  • No Serious AEs
  • No Unexpected AEs
Strong Intellectual Property Position

112 issued patents (11 issued in 2018)
61 pending applications
17 patent families

U.S. Patent, De Juan
“Use of ocular implants to deliver a therapeutic agent to the eye, either placed through the punctum or between the sclera and conjunctiva tissue layer.”
Evolute® Punctal Plug Delivery System

• Summary Of Benefits
  • Wide range of compounds
  • Flexible drug delivery profile
  • Non-invasive approach
  • Steady elution – unlike eye drops
  • Comfortable + excellent retention
    – 92% and 96% in last two clinical trials at 12 weeks
  • Cosmetically invisible / easily identifiable
  • Preservative free
  • “Passive” system for patients / physician controls compliance
  • Favorable reimbursement opportunity for MDs and ODs
  • Strong IP protection
Consistent efficacy and therapy control delivered easily and comfortably