### Results (Continued)

**Intracocular Pressure Reduction**

- **Primary efficacy endpoint:** mean diurnal IOP on Day 28.
- **Secondary efficacy endpoints:** mean change in diurnal IOP; mean change at each diurnal time point (8 AM, 10 AM, and 4 PM); mean change from baseline IOP.
- **Efficacy analyses are presented for the modified Intent To Treat population (mITT).**

**Mean Diurnal IOP**

**Baseline IOPs 22-36 mmHg**

- Both AR-13324 0.01% and 0.02% produced large reductions in IOP (p<0.0001)
- AR-13324 0.02% reduced mean diurnal IOP by 5.7 and 6.2 mmHg
- Latanoprost reduced mean diurnal IOP by 6.8 and 7.1 mmHg

**Change in Mean IOP at Each Visit**

**Baseline IOPs 22-36 mmHg**

- AR-13324 0.02% reduced mean IOP 5.2 - 6.6 mmHg across all on-treatment time points
  - AR-13324 0.01%: 5.4 - 6.1 mmHg reduction
  - Latanoprost: 6.1 - 7.5 mmHg reduction
- AR-13324 0.02% efficacy unchanged from Day 7 to Day 28 (38.00 time point)
- AR-13324 and latanoprost show similar duration of effect beyond Day 28 (36 hrs and 60 hrs after final Day 27 PM dose)

**Efficacy in Patients with Moderately Elevated Baseline IOPs**

- Efficacy analyses were repeated for a protocol-specified subgroup of patients with baseline IOPs of 22-26 mmHg at all time points

**Change in Mean IOP at Each Visit**

**Subgroup with Baseline IOPs 22-26 mmHg**

- AR-13324 0.02% reduced mean IOP 5.2 - 6.4 mmHg throughout all on-treatment time points
  - Same efficacy as in mITT population
  - Latanoprost reduced mean IOP by 5.2 - 6.9 mmHg
  - <1 mmHg less effective than in mITT
- AR-13324 0.02% efficacy statistically equivalent to latanoprost on Day 28 (mean diurnal IOP within 0.2 mmHg, p=0.754)

### Results (Continued)

**Safety**

- **Adverse Events**
  - No drug-related SAEs were reported. One subject was discontinued for a drug-related AE (AR-13324 0.02%).
  - The most frequently reported AEs were conjunctival/ocular hyperemia.
  - There were no systemic safety issues of note.

### Number of Subjects with Treatment-Related Adverse Events

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n=74</th>
<th>n=75</th>
<th>n=72</th>
<th>n=77</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eye Disorders</strong></td>
<td>45 (54.7%)</td>
<td>42 (52.3%)</td>
<td>9 (11.6%)</td>
<td>20 (25.8%)</td>
</tr>
<tr>
<td><strong>Conjunctival Hyperemia</strong></td>
<td>28 (36.8%)</td>
<td>34 (42.7%)</td>
<td>12 (15.1%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>IOP Increase</strong></td>
<td>71 (9.3%)</td>
<td>6 (7.9%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Lacrimation</strong></td>
<td>5 (6.5%)</td>
<td>4 (5.0%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Foreign Body Sensation</strong></td>
<td>5 (6.9%)</td>
<td>3 (3.9%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Vision Blurred</strong></td>
<td>3 (4.2%)</td>
<td>2 (2.6%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Eye Pruritus</strong></td>
<td>2 (2.7%)</td>
<td>1 (1.4%)</td>
<td>2 (2.6%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Eye Discharge</strong></td>
<td>1 (1.3%)</td>
<td>0</td>
<td>1 (1.3%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Photophobia</strong></td>
<td>0</td>
<td>2 (2.6%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Visual Acuity Reduced</strong></td>
<td>0</td>
<td>1 (1.4%)</td>
<td>1 (1.3%)</td>
<td>0</td>
</tr>
</tbody>
</table>

**Administration Site Conditions**

| Incision site pain | 5 (6.7%) | 9 (12.2%) | 4 (5.2%) | 0 |

**Biomicroscopy**

- The only drug-related finding of note was conjunctival hyperemia.
- AR-13324-associated hyperemia was mild to moderate and appeared to diminish over the course of the study:
  - Day 7, 08:00: 28%, 35% and 4% for AR-13324 0.01%, AR-13324 0.02% and latanoprost.
  - Day 30, 08:00: 18%, 24% and 11% for AR-13324 0.01%, AR-13324 0.02% and latanoprost.
- The incidence of hyperemia by biomicroscopy during the day was lower than the total incidence of hyperemia reported as AEs, indicating that hyperemia noted by patients after evening dosing was transient and often resolved overnight.

### Conclusions

- AR-13324 0.01% and AR-13324 0.02% produced clinically and statistically significant reductions in IOP.
- AR-13324 0.02% was less effective than latanoprost by approximately 1 mm Hg in patients with unmedicated IOPs in the range of 22 – 36 mm Hg.
- AR-13324 0.02% had equivalent efficacy to latanoprost (within 0.2 mm Hg) in patients with baseline IOPs of 22 – 26 mm Hg.
- AR-13324 0.02% maintained similar efficacy regardless of baseline IOP, whereas latanoprost was less effective at baseline IOPs of 22 – 26 mm Hg. Both latanoprost and timolol have been previously reported to show less absolute lowering of IOP in patients with lower baseline IOPs.
- The only drug-related adverse event of note was conjunctival hyperemia which for the majority of patients was mild to moderate and transient.