INVESTOR CALL: IZERVAY™ (AVACINCAPTAD PEGOL INTRAVITREAL SOLUTION) GATHER2 2-YEAR DATA PRESENTED AT AAO 2023

November 6, 2023 (JST)
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DHAVAL DESAI

SENIOR VICE PRESIDENT AND CHIEF DEVELOPMENT OFFICER, IVERIC BIO, AN ASTELLAS COMPANY
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AAO UPDATE AND GATHER2
SUMMARY AND BACKGROUND
SUMMARY OF GATHER2: 2-YEAR DATA

Both monthly (EM) and every other month (EOM) IZERVAY reduced GA growth vs sham

Treatment effect more than doubled over 2 years compared to 1 year for IZERVAY

IZERVAY was well tolerated: over 2 years, there was 1 case of non-serious IOI, 1 case of culture-positive endophthalmitis, and no cases of ION or retinal vasculitis

In year 2, incidence of CNV was similar for sham vs IZERVAY EOM

Over 2 years, only a slight increased incidence of CNV was observed for pooled IZERVAY vs sham (11.6% vs 9.0%, respectively)

CNV, choroidal neovascularization; GA, geographic atrophy; IOI, intraocular inflammation; ION, ischemic optic neuropathy.
IZERVAY IS DESIGNED TO BE A SPECIFIC INHIBITOR OF COMPLEMENT C5

IZERVAY

Anti-C5 pegylated RNA aptamer

- Relatively small physical size
- Synthetic, as opposed to biological, production

Inhibition of C5 slows inflammation and cell death associated with development and progression of GA

GA, geographic atrophy.
IZERVAY ACHIEVED THE 12-MONTH PRESPECIFIED PRIMARY OBJECTIVE IN 2 PIVOTAL PHASE 3 STUDIES\textsuperscript{1,2}

\textbf{GATHER (1)}

- IZERVAY 2 mg (N=67)
- Sham (N=110)

Mean GA Growth (Slope) From Baseline (mm\textsuperscript{2} observed):

Baseline: 1.221
Month 12: 1.889

35.4\% reduction

Difference (95\% CI):
0.668 mm\textsuperscript{2} (0.205, 1.131)

\textit{p}=0.0050

\textbf{GATHER (2)}

- IZERVAY 2 mg (N=225)
- Sham (N=222)

Mean GA Growth (Slope) From Baseline (mm\textsuperscript{2} observed):

Baseline: 1.745
Month 12: 2.121

17.7\% reduction

Difference (95\% CI):
0.376 mm\textsuperscript{2} (0.122, 0.631)

\textit{p}=0.0039

\textit{CI}, confidence interval; GA, geographic atrophy.

GATHER2 IS A 2-YEAR, PHASE 3, INTERNATIONAL, MULTICENTER, PROSPECTIVE, RANDOMIZED, DOUBLE-MASKED, SHAM-CONTROLLED STUDY (NCT04435366)

**Year 1**

- **IZERVAY 2 mg (N=225)**
- **Sham (N=222)**

**Primary Analysis:** Mean rate of growth (slope) in GA area from baseline to month 12

**Year 2**

- **Re-randomized 1:1**
  - IZERVAY 2 mg EM (n=96)
  - IZERVAY 2 mg EOM (n=93)
- **Sham (n=203)**

**Year 2 Objectives:**
Evaluate efficacy and safety of re-randomized population of IZERVAY monthly (EM) and every other month (EOM) through year 2

**Statistical Methodology:**
To control for multiplicity, year 2 statistical significance was conducted sequentially on prespecified outcomes:
1. Reduction in GA growth for IZERVAY EM vs sham
2. Reduction in rate of persistent vision loss for IZERVAY pooled vs sham
3. Reduction in GA growth for IZERVAY EOM vs sham

**Note:** The 24-month objective used observed data. *448 randomized, with 447 treated (1 patient in sham did not receive treatment after randomization).**

**GA, geographic atrophy.**
GATHER2 2-YEAR DATA

ERIN HENRY
VICE PRESIDENT, PRODUCT STRATEGY AND INNOVATION,
IVERIC BIO, AN ASTELLAS COMPANY
IZERVAY REDUCED GA GROWTH WHEN DOSED EM AND EOM VS SHAM

- Monthly IZERVAY 2 mg months 0-12

<table>
<thead>
<tr>
<th>IZERVAY 2 mg</th>
<th>Percent reduction</th>
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<tbody>
<tr>
<td>EM</td>
<td>14% reduction</td>
</tr>
<tr>
<td>EOM</td>
<td>19% reduction</td>
</tr>
</tbody>
</table>

aP-value is nominal. Note: This analysis is based on a mixed model assuming constant growth rate from baseline to month 24.

CI, confidence interval; EM, every month; EOM, every other month.
TREATMENT EFFECT MORE THAN DOUBLED WITH IZERVAY OVER 2 YEARS COMPARED TO 1 YEAR

**Difference in Mean Rate of GA Growth From Baseline Compared to Sham (Observed; mm²)**

- **IZERVAY 2 mg EM (n=96)**
  - Baseline to Month 12: 0.31
  - Baseline to Month 24: 0.81

- **IZERVAY 2 mg EOM (n=93)**
  - Baseline to Month 12: 0.41
  - Baseline to Month 24: 1.04

Note: This is a simplified piecewise slope spline Mixed model with Repeated Measures analysis. The analysis is based on a mixed effects model for repeated measures assuming a piecewise linear growth slope every 6 months. The EOM group received monthly IZERVAY in the first year. EM, every month; EOM, every other month.
NO STATISTICALLY SIGNIFICANT DIFFERENCE IN ≥15-LETTER PERSISTENT VISION LOSS BETWEEN IZERVAY AND SHAM

~ Mean change in BCVA and LL-BCVA from baseline between IZERVAY and sham was similar at two-years

Note: Persistent vision loss was defined as loss ≥15 letters in BCVA at 2 consecutive visits. Mean BCVA change from baseline at month 24 was -7.309 for ACP 2 mg (N=225) and -6.475 for sham (N=222). Mean LL-BCVA change from baseline at month 24 was -10.583 for ACP 2 mg (N=225) and -9.096 for sham (N=222). BCVA, best-corrected visual acuity; CI, confidence interval; LL-BCVA, low-luminance BCVA.
TREATMENT EMERGENT ADVERSE EVENTS (TEAEs) OVER 2 YEARS WERE SIMILAR AND CONSISTENT WITH YEAR 1

<table>
<thead>
<tr>
<th></th>
<th>IZERVAY (N=225)</th>
<th>Sham (N=222)</th>
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<tbody>
<tr>
<td>TEAEs, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ocular in study eye</td>
<td>144 (64.0)</td>
<td>107 (48.2)</td>
</tr>
<tr>
<td>Non-ocular</td>
<td>172 (76.4)</td>
<td>160 (72.1)</td>
</tr>
<tr>
<td>Serious TEAEs, n (%)</td>
<td>60 (26.7)</td>
<td>51 (23.0)</td>
</tr>
<tr>
<td>Ocular in study eye</td>
<td>4 (1.8)</td>
<td>2 (0.9)</td>
</tr>
<tr>
<td>Non-ocular</td>
<td>55 (24.4)</td>
<td>49 (22.1)</td>
</tr>
<tr>
<td>TEAEs leading to study drug discontinuation, n (%)</td>
<td>11 (4.9)</td>
<td>9 (4.1)</td>
</tr>
<tr>
<td>Ocular in study eye</td>
<td>4 (1.8)</td>
<td>0</td>
</tr>
<tr>
<td>Non-ocular</td>
<td>7 (3.1)</td>
<td>9 (4.1)</td>
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</tbody>
</table>

Note: n = study eyes with events.
### SERIOUS OCULAR TEAEs – NO NEW SAFETY SIGNALS IN YEAR 2

<table>
<thead>
<tr>
<th>Serious ocular TEAEs in study eye, n (%)</th>
<th>IZERVAY 2 mg (N=225)</th>
<th>Sham (N=222)</th>
<th>IZERVAY 2 mg EM (n=96)</th>
<th>IZERVAY 2 mg EOM (n=93)</th>
<th>Sham (n=203)</th>
<th>IZERVAY 2 mg (N=225)</th>
<th>Sham (N=222)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choroidal neovascularization</td>
<td>2 (0.9)</td>
<td>1 (0.5)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2 (0.9)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Visual acuity reduced</td>
<td>0</td>
<td>1 (0.5)a</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (0.5)a</td>
</tr>
<tr>
<td>Visual acuity reduced transiently</td>
<td>0</td>
<td>1 (0.5)a</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (0.5)a</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>0</td>
<td>0</td>
<td>1 (1.0)b</td>
<td>0</td>
<td>0</td>
<td>1 (0.4)b</td>
<td>0</td>
</tr>
<tr>
<td>Subluxated intraocular lens</td>
<td>0</td>
<td>0</td>
<td>1 (1.0)</td>
<td>0</td>
<td>0</td>
<td>1 (0.4)</td>
<td>0</td>
</tr>
</tbody>
</table>

**Year 1**

**Year 2**

**Total**

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**Note:** Choroidal neovascularization = eMNV, neMNV, peripapillary NV.

**Em, every month; eMNV, exudative macular neovascularization; MNV, macular neovascularization; EOM, every other month; neMNV, nonexudative MNV; NV, neovascularization; TEAE, treatment emergent adverse event.**

### CHOROIDAL NEOVASCULARIZATION (CNV)

<table>
<thead>
<tr>
<th></th>
<th>Year 1&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Year 2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IZERVAY 2 mg</td>
<td>Sham</td>
<td></td>
</tr>
<tr>
<td>(N=225)</td>
<td>(N=222)</td>
<td>(n=203)</td>
<td>(N=225)</td>
</tr>
<tr>
<td>CNV in study eye, n (%)</td>
<td>15 (6.7)</td>
<td>9 (4.1)</td>
<td>7 (7.3)</td>
</tr>
</tbody>
</table>

**Incidence of CNV in year 2 was similar for sham and the IZERVAY groups**

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**Note:** Choroidal neovascularization = eMNV, neMNV, peripapillary NV. 
EM, every month; eMNV, exudative macular neovascularization; MNV, macular neovascularization; EOM, every other month; neMNV, nonexudative MNV; NV, neovascularization.

### ADVERSE EVENTS OF SPECIAL INTEREST

#### Over 2 years
- 1 case of non-serious intraocular inflammation, reported as trace vitreous cells
- 1 case of culture-positive endophthalmitis
- No cases of ischemic optic neuropathy and occlusive or non-occlusive retinal vasculitis

#### Table

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<thead>
<tr>
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<th>Year 1</th>
<th>Year 2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IZERVAY 2 mg (N=225)</td>
<td>Sham (N=222)</td>
<td>IZERVAY 2 mg EM (n=96)</td>
</tr>
<tr>
<td>Intraocular inflammation</td>
<td>0</td>
<td>0</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>0</td>
<td>0</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Ischemic optic neuropathy</td>
<td>0</td>
<td>0</td>
<td>0</td>
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**Note:**
- Culture positive.
- EM, every month; EOM, every other month.
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LIFECYCLE MANAGEMENT UPDATE

**GATHER2**
Ongoing open-label study capturing long-term safety data

**LABEL**
Anticipate FDA filing submission for label update on treatment duration and regimen in Q4 FY2023

**EMA**
The Marketing Authorization Application for ACP was accepted on 17 Aug 2023

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FDA, Food and Drug Administration; EMA, European Medicines Agency; ACP, avacincaptad pegol.