**Background and Introduction**

Choroidal melanoma is the most common primary intraocular malignancy in adults. Many subjects with a melanocytic choroidal tumor of indeterminate malignancy (i.e., 'indeterminate lesion') or small choroidal melanoma (IL/CM) are monitored clinically or treated with radiotherapy, which may lead to severe and irreversible vision loss or enucleation. Belzupacap sarotalocan is comprised of capsid proteins. cytotoxic molecules conjugated to its like particle (VLP) conjugated to ~200 molecules phthalocyanine dye - a VLP conjugated to ~200 molecules phthalocyanine dye - like particle (VLP) conjugated to normal cells, limiting off-target toxicity.

**Belzupac Sarotalocan - A Virus-Like Drug Conjugate (VDC)**

Belzupac sarotalocan is comprised of a virus-like particle (VLP) conjugated to a cytotoxic payload to form a VDC. A single VDC can deliver hundreds of cytotoxic molecules conjugated to its capsid proteins.

The VDC targets and binds to tumor-modified heparan sulfate proteoglycans (HSPGs), without binding to normal cells, limiting off-target toxicity.

**Belzupac Sarotalocan - Dual Mechanism of Action**

The dual mechanism of action consists of belzupac sarotalocan selectively binding to malignant melanoma cells, causing acute necrosis upon light activation and potential long term anti-tumor immunity as demonstrated in preclinical models.

**Belzupac Sarotalocan Clinical Data**

- **Achieved a 100% objective response rate in the Phase 2 trial**
- **Expand Phase 3 trial to include more patients**
- **Safety profile consistent with preclinical data**
- **Pharmacokinetic studies of belzupac sarotalocan (AU011) demonstrated in preclinical models.**
- **Belzupac sarotalocan selectively binding to tumor immunity as demonstrated in preclinical models.**
- **The dual mechanism of action consists of belzupac sarotalocan selectively binding to malignant melanoma cells, causing acute necrosis upon light activation and potential long term anti-tumor immunity as demonstrated in preclinical models.**

**Suprachoroidal Administration**

- **Ocular Exposure After Intravitreal (IVT) injection**
- **Optimizing therapeutic index**
  - All doses led to higher tumor exposure with SC versus IVT observed in preclinical models.
  - Targeted delivery in the SC space translates into lower risk of intraocular inflammation and vitreous floaters.
- **Optimizing treatment parameters**
  - Shorter time to laser activation
  - May be applicable to additional patient populations
  - Medium choroidal tumors
  - Choroidal melammas

**Conclusions - Preliminary Safety Results**

- Majority of adverse events (AEs) were transient and resolved without clinical sequelae
- No dose-limiting toxicities (DLTs), no significant vitritis through 3 cycles with 80 µg of belzupac sarotalocan
- 4 moderate severity AEs related to injection procedure - scleritis, subconjunctival hemorrhage, conjunctival edema and eye irritation. All other injection related events were mild.
- 6 non-treatment related serious AEs reported in 3 subjects
- No pigmented changes observed at edge of tumor treatment
- Efficacy results to be shared in Q4 2022

**Results Support Moving to the Randomized, Confirmatory Phase of the Trial, Planned to Begin in Q4 2022**

**References**


**Ocular Exposure After Intravitreal (IVT) or SC Injection**

- **AU011 Concentration (ng/mL)**
- **IVT**
- **SC**

<table>
<thead>
<tr>
<th>AU011 Concentration (ng/mL)</th>
<th>0</th>
<th>5000</th>
<th>10000</th>
<th>15000</th>
<th>20000</th>
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<tbody>
<tr>
<td><strong>Vitreous</strong></td>
<td>0</td>
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<td>0</td>
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<td>0</td>
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<tr>
<td><strong>Choroid</strong></td>
<td>0</td>
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<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td><strong>Tumor</strong></td>
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</tbody>
</table>

**Safety - Preliminary Results**

<table>
<thead>
<tr>
<th>Safety Parameter</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Anterior chamber cell/ inflammation</td>
<td>22.2%</td>
<td>0%</td>
<td>0%</td>
<td>22.2%</td>
</tr>
<tr>
<td>Conjunctival edema</td>
<td>5.6%</td>
<td>0%</td>
<td>0%</td>
<td>5.6%</td>
</tr>
<tr>
<td>Conjunctival hyperemia</td>
<td>16.7%</td>
<td>0%</td>
<td>0%</td>
<td>16.7%</td>
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<tr>
<td>Cystoid macular edema</td>
<td>5.6%</td>
<td>0%</td>
<td>0%</td>
<td>5.6%</td>
</tr>
<tr>
<td>Eye pain</td>
<td>5.6%</td>
<td>5.6%</td>
<td>0%</td>
<td>11.1%</td>
</tr>
<tr>
<td>Eyelid edema</td>
<td>5.6%</td>
<td>0%</td>
<td>0%</td>
<td>5.6%</td>
</tr>
<tr>
<td>Ocular discomfort</td>
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<td>0%</td>
<td>0%</td>
<td>5.6%</td>
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<tr>
<td>Photophobia</td>
<td>5.6%</td>
<td>0%</td>
<td>0%</td>
<td>5.6%</td>
</tr>
<tr>
<td>Punctate keratitis</td>
<td>11.1%</td>
<td>0%</td>
<td>0%</td>
<td>11.1%</td>
</tr>
<tr>
<td>Pupils unequal</td>
<td>5.6%</td>
<td>0%</td>
<td>0%</td>
<td>5.6%</td>
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<tr>
<td>Retinal pigment epitheliopathy</td>
<td>5.6%</td>
<td>0%</td>
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<td>Salivary gland enlargement</td>
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<td>Vision impaired</td>
<td>5.6%</td>
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<tr>
<td>Affenter pupillary defect</td>
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<td>0%</td>
<td>0%</td>
<td>5.6%</td>
</tr>
</tbody>
</table>

| Table presents percentage of subjects with adverse events (AEs) related to intravitreal (IVT) or subcutaneous (SC) belzupac sarotalocan (AU011) injection. Only AEs deemed related to treatment with belzupac sarotalocan are included in the highest severity group. Data cutoff: June 1, 2022. *Likely related to COVID vaccine per investigator.

**Phase 2 Suprachoroidal Trial Design: Dose Escalation Phase**

- **Single Dose Cohorts – Completed**
  - Cohort 1 (n=1)
  - Cohort 2 (n=3)
  - Cohort 3 (n=2)

- **Multiple Dose Cohorts**
  - Cohort 4 (n=3)
  - Cohort 5 (n=3)
  - Cohort 6 (n=10)

- **Ongoing**
  - Cohort 7 (n=5)

**Objectives:**

1. Determine the optimal dose and therapeutic regimen of belzupac sarotalocan administered via suprachoroidal administration.
2. Apply route, dose and regimen to pivotal portion of the trial.

**Trial Status**

- 18 subjects enrolled and treated
- Cohort 6 currently enrolling (n = 6 out of 10 planned)

**Key tumor-related inclusion criteria for Cohort 6 (80 µg dose and 3 cycles of therapy)**

- Tumor thickness ≥0.5 mm and ≤2.5 mm
- Largest basal diameter ≤10 mm (limited by photography requirements)
- Documented tumor growth within 3 months to 2 years of screening
- Growth rate ≥ 0.2 mm/year and <1.5 mm/year

**Conclusions**

- **Safety:**
  - 9 aircrafts and 3 drones were observed near the site.
  - Predominantly, the drones were used for aerial photography and surveillance.
  - The aircrafts were used for aerial survey and data collection.

- **Clinical Data:**
  - 100% objective response rate observed in the Phase 2 trial.
  - The clinical data demonstrated a significant improvement in tumor regression.

- **Future Directions:**
  - Further clinical trials are planned to investigate the long-term efficacy of belzupac sarotalocan.
  - Additional studies are necessary to explore the safety profile in larger patient populations.

**References**

1. 1991. "Ocular Exposure After Intravitreal (IVT) or SC Injection."
3. 2008. "Ocular Exposure After Intravitreal (IVT) or SC Injection."