Absence of Indicators of Hypercoagulability and Anti-phospholipid Syndrome in BXQ-350 First in Human Study.

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**Background:** Saposin C is a lysosomal activator protein that can be combined with a phosphatidylserine lipid to create a nanovesicle that targets cancer cells. Similar lipid nanovesicle preparations are linked to altered coagulation and anti-phospholipid syndrome (APS), thus coagulation parameters and immune markers for APS were explored in the first-in-human (FIH) trial of BXQ-350.

**Methods:** Data from 17 solid tumor/high grade glioma patients (59% M, 24-67 yrs) in the Phase 1a trial of BXQ-350 nanovesicles at IV doses of 0.7-2.4 mg/kg (NCT02859857) were examined for effects on plasma fibrinogen (PF), coagulation factors, prothrombin time (PT), aPPT, INR, and cardiolipins IgG, IgA, and IgM at days 1, 8, 15, 22, 29, 57, 85, 113, 141, and 171 (or off-study date). Mean and change from baseline (Day 0) ±2.0 units are reported.

**Results:** No clinically significant changes in coagulation or baseline PT or INR ±2.0 were observed. For doses 1.1-2.4 mg/kg, subclinical increases occurred at Day 57-171, including PF peak at Day 57 of 1.1 mg/kg (155±142.8 mg/dL) and Day 171 of 2.4 mg/kg (128.8±79.6 mg/dL). Subclinical aPTT peak was also observed Day 171 of 2.4 mg/dL (13.7±20.3 s), but not at other doses. No DLTs or severe adverse events related to BXQ-350 were reported.

**Conclusions:** Therapeutic BXQ-350 nanovesicle dosages did not cause APS or clinically significant hypercoagulability in humans. Further, AEs related to BXQ-350 were not due to hypercoagulability.

**Table. Δ Coagulability Factors**

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<tr>
<th>mg/kg</th>
<th>Day</th>
<th>PF</th>
<th>aPTT</th>
<th>IgG</th>
<th>IgM</th>
<th>IgA</th>
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<td>11.5±16</td>
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<tr>
<td>57</td>
<td>155±142.8</td>
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<td>171</td>
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<td>3.6±4</td>
<td>1±0.7</td>
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<td>7.6±11.9</td>
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<td>171</td>
<td>36.7±54.6</td>
<td>8.7±15.9</td>
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</tbody>
</table>

| 1.8 | 1 | - | - | 6±0 | 6.1±5.9 | - |
|   | 8 | 14.3±47 | - | 5±0 | - | 9.8±0 |
|   | 15 | 25±84.2 | 4.4±8.3 | - | - | - |
|   | 22 | 5.7±96 | 1.2±2.4 | 4±0 | - | - |
|   | 29 | 14±92.5 | 6.4±6 | - | - | - |
|   | 57 | 47.5±57.3 | - | - | - | - |
|   | 113 | 0 | - | 4±0 | 6±0 | - |
|   | 171 | 38.7±27.8 | - | 8±0 | 3.3±2.9 | - |

| 2.4 | 1 | - | 0 | 7.4±8.7 | 7±0 |
|   | 8 | 13.2±35.7 | - | 8.9±6.5 | - | 11.2±0 |
|   | 15 | 14.2±34.8 | 6±11.3 | - | - | - |
|   | 22 | 13±32.2 | - | 3.6±3 | 7±0 | - |
|   | 85 | 55±51.5 | 2.6±3.8 | - | - | - |
|   | 171 | 128.8±79.6 | 13.7±20.3 | 10±5.7 | 6±1.4 | - |

**Title:**
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