Allometric Scaling of Preclinical Pharmacokinetic and Toxicokinetic Parameters to Predict Clinical Pharmacokinetics of BXQ-350 Saposin C Protein-Phosphatidylserine Nanovesicles.

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**Background:** Interspecies allometric scaling is used to extrapolate pharmacokinetics (PK) from preclinical data to human PK and dosing. Efficacy of BXQ-350, a novel Saposin C phosphatidylserine lipid nanovesicle therapy that targets tumor cell phospholipids, has been demonstrated in murine tumors, and pharmacokinetic and toxicokinetic (PK/TK) parameters have been derived in animal models. This study compares predictions based on allometric scaling of animal PK/TK data with FIH data for BXQ-350.

**Methods:** PK was assessed over 24 hr after IV BXQ-350 doses in mice (30 mg/m2) and rats/monkeys (60 mg/m2). TK was assessed at day 1 and 24 in rats/monkeys (24, 72 and 240 mg/m2 5 days/wk). Saposin C was analyzed by ELISA, and noncompartmental PK methods were used. Preclinical PK/TK was allometrically scaled to predict human PK and exposure (AUC) at 0.7-2.4 mg/kg therapeutic doses. Values were compared to actual FIH Phase 1 data (NCT02859857).

**Results:** Human clearance, terminal volume of distribution (Vz), half-life, and AUC (at 0.7 and 2.4 mg/kg doses) were within predicted ranges, though human ranges were somewhat narrower for clearance (63-114 vs 81-102 mL/kg/hr), Vz (135-650 vs 285-380 mL/kg), and half-life (0.8-4.5 vs 2.0-3.4 hr). Notably, actual vs predicted AUC hr*ng/mL at 0.7 and 2.4 mg/kg were not significantly different (7,100 vs 6,100 and 38,000 vs 36,000, respectively). Efficacy occurred in murine models at 4-16 mg/kg (AUC 7,400-29,600), aligned with human exposure at 0.7-2.4 mg/kg doses.

**Conclusions:** Allometric scaling of animal PK/TK data provided reasonable estimates of human PK and exposure (AUC) for BXQ-350 and can thus be expected to have good predictive utility for extrapolating drug dose and pharmacokinetic parameters.

**Table.** Predicted vs Actual PK/TK

<table>
<thead>
<tr>
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<th>Predicted¹</th>
<th>Actual²</th>
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</thead>
<tbody>
<tr>
<td>Clearance, mL/kg/hr</td>
<td>63-114</td>
<td>81-102</td>
</tr>
<tr>
<td>Volume of distribution (Vz), mL/kg</td>
<td>135-650</td>
<td>285-380</td>
</tr>
<tr>
<td>Half-life, hrs</td>
<td>0.8-4.5</td>
<td>2-3.4</td>
</tr>
<tr>
<td>AUC at 0.7 mg/kg, hr*ng/mL</td>
<td>6100</td>
<td>7100</td>
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<tr>
<td>AUC at 2.4 mg/kg, hr*ng/mL</td>
<td>36000</td>
<td>38000</td>
</tr>
</tbody>
</table>

Murine Efficacy-associated AUC (~4-16 mg/kg), hr*ng/mL  
7,400-29,600 -

1 3-animal composite PK/TK models

2 High/low geometric mean for 0.7-2.4 mg/kg Phase 1 cohorts

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