**BACKGROUND**

RORγ is a nuclear receptor transcription factor that modulates gene expression

- RORγ is the master transcription factor for Th17/Tc17 differentiation
- RORγ modulates expression of genes operating in pathways that enhance immunity and decrease immune suppression
- Th17/Tc17 cells have demonstrated durable anti-tumor efficacy

IL-17 is associated with good prognosis in some cancers

**LYCERA RORγ AGONISTS**

Selective small molecule RORγ agonists lead optimization

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<thead>
<tr>
<th>Compound</th>
<th>Selective Agonist</th>
<th>Selective Agonist</th>
<th>Selective Agonist</th>
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<tbody>
<tr>
<td>A</td>
<td>16 (160%)</td>
<td>1600 (150%)</td>
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<tr>
<td>B</td>
<td>300 (150%)</td>
<td>440 (151%)</td>
<td></td>
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<tr>
<td>C</td>
<td>70 (166%)</td>
<td>200 (160%)</td>
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**SUMMARY OF KEY FINDINGS**

RORγ small molecule agonists:

- Have activities consistent with established RORγ biology
- Combine multiple anti-tumor mechanisms into a single therapeutic
- Demonstrate single agent activity in several models without evidence of enhanced tumor growth
- Manifest anti-tumor activity only in immune competent mice

High potency, bioavailable compounds are rapidly advancing as a promising immunotherapy approach

**RESULTS**

RORγ agonists enhance anti-tumor effector T cell functions

RORγ agonists increase anti-tumor cytokines (p < 0.01 all changes)

Adoptive transfer of RORγ agonist-treated Tc17 cells has superior anti-tumor effects

Oral administration of RORγ agonist inhibits tumor growth

**4T1 mammary carcinoma**

Increased IL-17, RORγ and IFNγ and Decreased CD73 in Tumors of Agonist-Treated Mice (Day 23)

**MC38 colon carcinoma**

RORγ agonist does not inhibit MC38 colon carcinoma in SCID mice

MC38 cells were implanted subcutaneously in C57BL6 mice. Group C was donor B6 mice starting from day 1.