GLPG1790: the first Ephrin (EPH) receptor tyrosine kinase inhibitor for the treatment of triple negative breast cancer

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Abstract

GLPG1790 – IC50 (nM)

<table>
<thead>
<tr>
<th>GLPG1790</th>
<th>IC50 (nM)</th>
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<tbody>
<tr>
<td>EPHA2</td>
<td>1</td>
</tr>
<tr>
<td>EPHA4</td>
<td>11</td>
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<tr>
<td>EPHA4</td>
<td>77</td>
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<tr>
<td>EPHA2</td>
<td>864</td>
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**Biochemical selectivity profile**

GLPG1790 is a low nM inhibitor of several EPH receptor kinases as determined in a biochemical assay.

**Cellular pharmacology**

- GLPG1790 inhibits MDA-MB-231 human breast cancer cell growth in vitro in 3D growth assay

**In vivo efficacy and target engagement**

- In vivo efficacy in MDA-MB-231 xenograft model
- GLPG1790 completely blocks established tumor growth in the MDA-MB-231 nude mouse xenograft model at 30 mg/kg, qd. Efficacy similar to a high dose of Paclitaxel. No body weight loss or clinical signs were observed (not shown).
- GLPG1790 in vivo target engagement and pharmacodynamic effects in MDA-MB-231 xenograft model

**Conclusions**

All together these data support the development of GLPG1790 in triple negative breast cancer. This novel mechanism-of-action is under investigation in other cancer types overexpressing EPHs (melanoma, ovarian, prostatic and colorectal cancers). Recent successful developments in oncology have relied on careful patient selection based on target expression. Efforts are now underway to identify biomarkers of tumor cell sensitivity and target expression in patient derived material.

**References**