Product Data Sheet

Chemical Properties

Product Name: BMS-754807
Cas No.: 1001350-96-4
M.Wt: 461.49
Formula: C23H24FN9O

Chemical Name: (2S)-1-[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]pyrrolo[2,1-f][1,2,4]triazin-2-yl]-N-(6-fluoropyridin-3-yl)-2-methylpyrrolidine-2-carboxamide

Canonical SMILES: CC1(CCC1C2=NN3C=CC3C(=N2)NC4=NNC(=C4)C5CC5)C(=O)NC6=CN=C(C=C6)F

Solubility: ≥23.05mg/mL in DMSO
Storage: Store at -20°C
General tips: For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: Tyrosine Kinase
Pathways: IGF1R

Description:
BMS-754807 is a potent and small molecular inhibitor which targets the IGF-1R/IR family kinases with Ki <2 nmol/L[1]. The efficacy of BMS-754807 on normal tissues and tumor cell cycle is believed to be different from the effects of continuous inhibition by anti-IGF-1R antibodies.[2] BMS-754807 could effectively inhibit the growth of many human tumor types from in vitro
perspective, such as mesenchymal, hematopoietic and epithelial tumor cell lines with an IC50 value of 5–365 nmol/L. It can also induce sub-G1 fraction accumulation and an increase in poly ADP ribose polymerase and Caspase 3 cleavage, suggesting that it can lead to apoptosis in a human rhabdomyosarcoma cell line (Rh41). Furthermore, as a pyrrolotriazine and reversible ATP-competitive antagonist of IGF-1R, BMS-754807 was shown to inhibit the catalytic domain of the IGF-1R, and proved to inhibit the IGF-1R and IR activity by using the in-vitro kinase assays. Since the antibodies can bind to IGF-1R but not to IR, this could be regardere as an escape mechanism for IGF-II and insulin signaling.[3]

Reference:

Protocol

Cell experiment:

Cell lines IGF-1R-Sal, Rh41 and Geo cells
Preparation method The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting conditions 1 μM, (72 hours for cell proliferation inhibition; 1 hour for phosphorylation inhibition
Applications Cell proliferation was evaluated by incorporation of 3H-thymidine into DNA after exposure of cells to BMS-754807 with concentrations from 0.1 to 1000 nM. BMS-754807 inhibited cell proliferation with IC50 values of 7, 5 and 365 nM for IGF-1R-Sal, Rh41 and Geo cells, respectively. The IC50 values for inhibition of the pIGF-1R by BMS-754807 and downstream components (e.g., pAkt) were very similar. In contrast, there was greater inhibition against pMAPK in IGF-1R-Sal cells compared with Rh41 and Geo, indicating that additional compensatory pathways such as EGFR might be important in driving signals in both Rh41 and Geo cell types.
Animal experiment [3]:

<table>
<thead>
<tr>
<th>Animal models</th>
<th>Nude mice bearing various tumor xenografts (Sal-IGF, GEO, Colo205, JJN3, Rh41 or RD1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage form</td>
<td>Oral administration, 0.01 mL/g of body weight</td>
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<tr>
<td>Applications</td>
<td>BMS-754807 inhibited tumor growth in a selected group of epithelial (IGF-1R-Sal, GEO and Colo205), hematopoietic (JJN3) and mesenchymal (RD1 and Rh41) xenograft tumor models with TGI ranging from 53% to 115%. In the highly sensitive Rh41 rhabdomyosarcoma, BMS-754807 was effective at a dose level of 3.125 mg/kg twice daily and as low as 6.25 mg/kg once daily.</td>
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<tr>
<td>Other notes</td>
<td>Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.</td>
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</table>

Reference:

Caution

FOR RESEARCH PURPOSES ONLY.
NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Short term storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.