**Product Name**: GNF-5837  
**Catalog Number**: T6097  
**CAS Number**: 1033769-28-6  
**Molecular Formula**: C28H21F4N5O2  
**Molecular Weight**: 535.49

**Description**: GNF-5837 is a specific, and orally bioavailable pan-TRK inhibitor for TrkA/TrkB (IC50: 8/12 nM).

**Storage**: 2 years -80°C in solvent; 3 years -20°C powder;

**Solubility**

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Concentration (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSO</td>
<td>53.6 (100 mM)</td>
</tr>
<tr>
<td>Ethanol</td>
<td>5.4 (10 mM)</td>
</tr>
</tbody>
</table>

(< 1 mg/ml refers to the product slightly soluble or insoluble)

**Receptor (IC50)**

<table>
<thead>
<tr>
<th>Receptor</th>
<th>IC50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kit</td>
<td>0.91 μM</td>
</tr>
<tr>
<td>PDGFRβ</td>
<td>0.87 μM</td>
</tr>
<tr>
<td>TrkA</td>
<td>8 nM</td>
</tr>
<tr>
<td>TrkB</td>
<td>12 nM</td>
</tr>
<tr>
<td>TrkC</td>
<td>7 nM</td>
</tr>
</tbody>
</table>

**In vitro Activity**

In Ba/F3 cells overexpressing the constitutively active Tel-TRKC fusion, GNF-5837 shows potent anti-Trk activity and potent antiproliferation activity with IC50 of 0.042 μM. [1]

**In vivo Activity**

In both male Balb/c mice and Sprague–Dawley rats, GNF-5837 has the low drug clearance, and moderate bioavailability. In mice bearing Rie xenografts expressing TrkA and NGF, GNF-5837 (100 mg/kg/d p.o.) significantly inhibits tumor growth. [1]

**Kinase Assay**

Inhibition of biochemical TrkA, TrkB and TrkC: TrkA and TrkC biochemical assays are carried out by HTRF method. The reaction mixtures contains 1 μM peptide substrate, 1 μM ATP, and either 1.8 nM TrkA or 34 nM TrkC in the reaction buffer (50mM HEPES pH 7.1, 10mM MgCl2, 2 mM MnCl2, 0.01% BSA, 2.5 mM DTT and 0.1 mM Na3VO4) at a final volume of 10 μL. All reactions are carried out at room temperature in white ProxiPlate™ 384-well Plus plates and are quenched with 5 μL of 0.2mM EDTA at 60 min. Five μL of the detection reagents (2.5 ng PT66K and 0.05 μg SAXL per well) are added, the plates are incubated at room temperature for 1 h and then read in EnVision reader. Compounds are diluted into assay mixture (final DMSO 0.5%), and IC50 values are determined by 12-point (from 50 to 0.000282 μΜ) inhibition curves in duplicate under the assay conditions. TrkB biochemical assay is carried out by caliper microfluidic method. The reaction mixtures contained 1 μM peptide substrate, 10 μM ATP, and 2 nM TrkB in a reaction buffer containing 100 mM HEPES, pH 7.5, 5 mM MgCl2, 0.01% Triton X-100, 0.1% BSA, 1 mM DTT, 10 μMNa3VO4, and 10 μM Beta-Glycerophosphate. The reactions are carried out at room temperature for 3 hrs, and the products are determined by Caliper EZ-reader. Compounds are diluted into assay mixture (final DMSO 1%), and IC50 values are determined by 12-point (from 50 to 0.000282 μΜ) inhibition curves in duplicate under the assay conditions.

**Cell Assay**

Compounds are tested for their ability to inhibit the proliferation of wt Ba/F3 cells and Ba/F3 cells transformed with constituatively expressed luciferase reporter and BCR-ABL or Tel-KDR or other Tel fusion kinases. Parental Ba/F3 cells are maintained in media containing recombinant mouse IL3 and the kinase transformed Ba/F3 cells are maintained in media without IL-3. 7.5 nL of compounds are spotted to each well of 1536-well assay plates by Liquid handling System Echo 555 (Labcyte). 700 cells are then plated into each well of the assay plates in 7 μL culture media per well and compounds are tested at 0.17 nM to 10 μM in 3-fold serial dilutions. The cells were then incubated for 48 hours at 37 °C. 3 μL of Bright-Glo® is added to each well and the plates are read using ViewLux. (Only for Reference)

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**Datasheet version 1.3**

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**Contact**

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Cell line: Wt Ba/F3 cells and Ba/F3 cells transformed with constitutively expressed luciferase reporter and BCR-ABL or Tel-KDR or other Tel fusion kinases

**Animal Experiment**
Animal Model: Mice bearing Rie xenografts expressing TrkA and NGF.

**Reference**

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