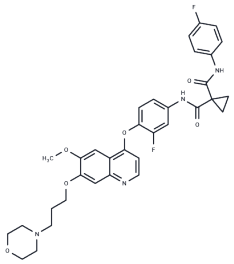
# Data Sheet (Cat.No.T3113)

TargetMol

## Foretinib

### Chemical Properties



CAS No. : 849217-64-7

Formula: C34H34F2N4O6

Molecular Weight: 632.65

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

### Biological Description

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| Description | Foretinib (GSK1363089) is a broad-spectrum tyrosine kinase inhibitor with IC50s of 0.4 nM and 0.9 nM for Met and KDR. |
| Targets(IC50) | c-Met/HGFR,Tie-2,VEGFR |
| In vitro | Foretinib (EXEL-2880) inhibits HGF receptor family tyrosine kinases with IC50 values of 0.4 nmol/L for Met and 3 nmol/L for Ron. EXEL-2880 also inhibits KDR, Flt-1, and Flt-4 with IC50 values of 0.9, 6.8, and 2.8 nmol/L, respectively. EXEL-2880 is a potent inhibitor of cellular Met with IC50 values of 23 and 21 nmol/L, respectively, in PC-3 prostate cells and murine B16F10 melanoma cells [1]. In MKN-45, 1 μM of foretinib inhibited phosphorylation of MET and downstream signaling molecules. Further, 1 μM of foretinib inhibited phosphorylation of FGFR2 and downstream molecules, suggesting that foretinib targets FGFR2 in KATO-III. Foretinib inhibits phosphorylation of epidermal growth factor receptor (EGFR), HER3 and FGFR3 via MET inhibition in MKN-45, and EGFR, HER3 and MET via FGFR2 inhibition in KATO-III [2]. |
| In vivo | A single 100 mg/kg oral gavage dose of EXEL-2880 resulted in substantial inhibition of phosphorylation of B16F10 tumor Met, which persisted through 24 h. Once daily oral gavage administration of EXEL-2880 resulted in a dose-dependent reduction in tumor burden of 31% and 62%, respectively, for doses of 30 and 100 mg/kg. The lung surface tumor burden, calculated by multiplying the total nodule count by the average nodule diameter for each tumor, was reduced by 50% and 58% following treatment with 30 and 100 mg/kg EXEL-2880, respectively [1]. The daily oral administration of foretinib (30 mg/kg) significantly inhibited the growth of tumor in all three of the tumor xenografts starting after only seven days of administration, and lasting throughout the experiment. Moreover, TEN cell tumor xenografts completely vanished in all specimens after 14 days of foretinib treatment [3]. |
| Kinase Assay | Kinase inhibition was investigated using one of three assay formats: [33P]phosphoryl transfer, luciferase-coupled chemiluminescence, or AlphaScreen tyrosine kinase technology. Further assay details are provided in Supplementary Section. IC50 values were calculated by nonlinear regression analysis using XLFit [1]. |
| Cell Research | PC-3 and B16F10 cells were seeded in 24-well plates overnight. The cells were then washed and incubated with serum-free medium for 3 h followed by a 1 h incubation with EXEL-2880 before addition of HGF (100 ng/mL) for 10 min. Met phosphorylation status was determined by ELISA analysis (Supplementary Data). For determination of |

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| Cell Research | VEGF-stimulated extracellular signal-regulated kinase phosphorylation, human umbilical vein endothelial cells were seeded in 96-well plates and incubated for 24 h and then serum-starved for another 24 h. A serial dilution of EXEL-2880 was added for 1 h before a 5 min stimulation with VEGF (20 ng/mL). Medium was removed, and the cells were fixed with Cytofix and then treated with 0.6% H2O2. Plates were blocked with 10% FBS and incubated with a mouse monoclonal anti-phosphorylated extracellular signal-regulated kinase p44/42 antibody (E10) followed by incubation with goat anti-mouse IgG-horseradish peroxidase and chemiluminescent detection. IC50 values were calculated based on triplicate experiments [1]. |
| Animal Research | B16F10 tumor cells (2 × 10^5) were implanted via i.v. tail vein injection into mice on day 0. EXEL-2880 or vehicle administration was initiated 3 days after implantation for 10 days followed by assessment of lung tumor burden. Lungs were excised, weighed, and zinc-fixed for 24 h, and the number of nodules formed on all lobe surfaces was counted using a Zeiss stereoscope. Lung nodule diameters were morphometrically measured on digitally captured images. Inhibition of tumor burden as measured by lung wet weight was calculated as follows: % tumor growth inhibition = [(compound treated-naive / vehicle-naive) × 100]. The results for each treatment group (n = 10 animals) were averaged, and statistical t test analysis was done comparing each treatment group to the vehicle-treated control [1]. |

## Solubility Information

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| Solubility | Ethanol: 63.3 mg/mL (100.06 mM),Sonication is recommended.<br>DMSO: 40 mg/mL (63.23 mM),Sonication is recommended.<br>(< 1 mg/ml refers to the product slightly soluble or insoluble) |
| In vivo Formulation | 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.16 mM),Sonication is recommended.<br>*Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.* |

Preparing Stock Solutions

| | 1mg | 5mg | 10mg |
|---|---|---|---|
| 1 mM | 1.5807 mL | 7.9033 mL | 15.8065 mL |
| 5 mM | 0.3161 mL | 1.5807 mL | 3.1613 mL |
| 10 mM | 0.1581 mL | 0.7903 mL | 1.5807 mL |
| 50 mM | 0.0316 mL | 0.1581 mL | 0.3161 mL |

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Qian F, et al. Inhibition of tumor cell growth, invasion, and metastasis by EXEL-2880 (XL880, GSK1363089), a novel inhibitor of HGF and VEGF receptor tyrosine kinases. Cancer Res, 2009, 69(20), 8009-8016.
Wang P, Zhang Y, Xiang R, et al.Foretinib is effective in acute myeloid leukemia by inhibiting FLT3 and overcoming secondary mutations that drive resistance to quizartinib and gilteritinib.Cancer Research.2024
Kataoka Y, et al. Foretinib (GSK1363089), a multi-kinase inhibitor of MET and VEGFRs, inhibits growth of gastric cancer cell lines by blocking inter-receptor tyrosine kinase networks. Invest New Drugs, 2011.
Cen S Y, Lin F, Li X, et al.Crizotinib and its enantiomer suppress ferroptosis by decreasing PE-O-PUFA content.Cell Death Discovery.2024, 10(1): 360.
Kogata Y, et al. Foretinib (GSK1363089) induces p53-dependent apoptosis in endometrial cancer. Oncotarget. 2018 Apr 27;9(32):22769-22784.