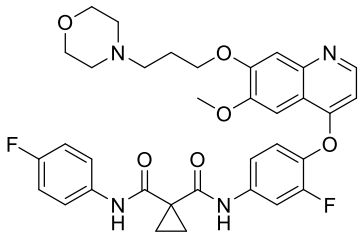
Product data sheet

MedKoo Cat#: 201372 Name: Foretinib CAS#: 849217-64-7 (free base) Chemical Formula: $C_{34}H_{34}F_2N_4O_6$ Exact Mass: 632.24464 Molecular Weight: 632.65	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Foretinib, also known as XL880 and GSK1363089, is an orally bioavailable small molecule with potential antineoplastic activity. MET/VEGFR2 inhibitor GSK1363089 binds to and selectively inhibits hepatocyte growth factor (HGF) receptor c-MET and vascular endothelial growth factor receptor 2 (VEGFR2), which may result in the inhibition of tumor angiogenesis, tumor cell proliferation and metastasis. The proto-oncogene c-MET has been found to be over-expressed in a variety of cancers.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	16.0	23.7
Ethanol	25.0	39.5

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.58 mL	7.90 mL	15.81 mL
5 mM	0.32 mL	1.58 mL	3.16 mL
10 mM	0.16 mL	0.79 mL	1.58 mL
50 mM	0.03 mL	0.16 mL	0.32 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Qian F, Engst S, Yamaguchi K, Yu P, Won KA, Mock L, Lou T, Tan J, Li C, Tam D, Lougheed J, Yakes FM, Bentzien F, Xu W, Zaks T, Wooster R, Greshock J, Joly AH. 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 Oct 15;69(20):8009-16. doi: 10.1158/0008-5472.CAN-08-4889. Epub 2009 Oct 6. PMID: 19808973.

2. Kataoka Y, Mukohara T, Tomioka H, Funakoshi Y, Kiyota N, Fujiwara Y, Yashiro M, Hirakawa K, Hirai M, Minami H. 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. 2012 Aug;30(4):1352-60. doi: 10.1007/s10637-011-9699-0. Epub 2011 Jun 8. PMID: 21655918.

In vivo study

1. Qian F, Engst S, Yamaguchi K, Yu P, Won KA, Mock L, Lou T, Tan J, Li C, Tam D, Lougheed J, Yakes FM, Bentzien F, Xu W, Zaks T, Wooster R, Greshock J, Joly AH. 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 Oct 15;69(20):8009-16. doi: 10.1158/0008-5472.CAN-08-4889. Epub 2009 Oct 6. PMID: 19808973.

7. Bioactivity

Biological target:

Foretinib is a multi-target tyrosine kinase inhibitor with IC50s of 0.4 nM and 0.9 nM for Met and KDR.

In vitro activity

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. To further delineate the cellular effect of EXEL-2880, VEGF-induced extracellular signal-regulated kinase phosphorylation was used to assess the effect of the compound on phosphorylation of KDR in human umbilical vein endothelial cells that resulted in an IC50 of 16 nmol/L. The ability of EXEL-2880 to inhibit HGF-stimulated migration and invasion was tested using in vitro assays. Murine B16F10 melanoma cells express high levels of Met, which becomes highly phosphorylated when the cells are treated with HGF (Fig. 3A). B16F10 cells plated in the top well of a Transwell chamber containing a barrier with 0.8 μm pores show very little ability to migrate to the bottom chamber. Addition of HGF to the bottom chamber greatly increased migration through the barrier over a 24 h period, which was blocked by EXEL-2880 with an IC50 value of 44 nmol/L (Fig. 3C). Addition of HGF to the bottom chamber again produced a large increase in the number of cells migrating through a Matrigel barrier in response to HGF, and EXEL-2880 inhibited this effect with an IC50 value of 25 nmol/L (Fig. 3D).

Reference: Cancer Res. 2009 Oct 15;69(20):8009-16. http://cancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=19808973

In vivo activity

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 (Fig. 5A). In separate experiments, a single oral dose of EXEL-2880 inhibited ligand (e.g., HGF or VEGF)–induced receptor phosphorylation of Met in liver and Flk-1/KDR in lung through 24 h. The potent and long-lasting pharmacodynamic activity of EXEL-2880 in B16F10 solid tumors prompted efficacy studies in this same model although under different experimental conditions. As shown in Fig. 5B, i.v. implantation of B16F10 cells leads to accumulation of tumor cells in the lung where they implant and grow as malignant nodules resembling a model of lung metastasis. 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 as determined by a reduction in lung wet weights (Fig. 5B). This reduction in lung wet weight was consistent with reductions in both the average size and the number of surface nodules in the lung. 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. In contrast, animals in the vehicle-treated control group exhibited a significant 2-fold increase in lung wet weight compared with animals treated with mock implantation (Supplementary Table S4). In a similar manner, EXEL-2880 treatment of mice bearing B16F10 solid tumors also resulted in dose-dependent tumor growth inhibition of 64% and 87% at 30 and 100 mg/kg, respectively (Supplementary Fig. S3). For both studies, administration of EXEL-2880 was well tolerated with no significant body weight loss.

Reference: Cancer Res. 2009 Oct 15;69(20):8009-16. http://cancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=19808973