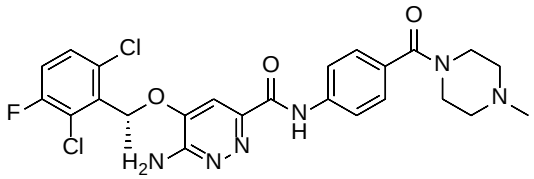
Product data sheet

MedKoo Cat#: 206616 Name: X-376 CAS#: 1365267-27-1 (X376) Chemical Formula: $C_{25}H_{25}Cl_2FN_6O_3$ Exact Mass: 546.1349 Molecular Weight: 547.41	
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:
X-376 is an ALK inhibitor and potentially useful in non-small cell lung cancer. Caution: Many vendora are mistakenly selling X-376 as Ensartinib (X396, X-396, X 396). The structure is slightly different (see Cat#206013)

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	100.0	182.68
Ethanol	13.0	23.75

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.83 mL	9.13 mL	18.27 mL
5 mM	0.37 mL	1.83 mL	3.65 mL
10 mM	0.18 mL	0.91 mL	1.83 mL
50 mM	0.04 mL	0.18 mL	0.37 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. Lovly CM, Heuckmann JM, de Stanchina E, Chen H, Thomas RK, Liang C, Pao W. Insights into ALK-driven cancers revealed through development of novel ALK tyrosine kinase inhibitors. Cancer Res. 2011 Jul 15;71(14):4920-31. doi: 10.1158/0008-5472.CAN-10-3879. Epub 2011 May 25. PMID: 21613408; PMCID: PMC3138877.

In vivo study

1. Lovly CM, Heuckmann JM, de Stanchina E, Chen H, Thomas RK, Liang C, Pao W. Insights into ALK-driven cancers revealed through development of novel ALK tyrosine kinase inhibitors. Cancer Res. 2011 Jul 15;71(14):4920-31. doi: 10.1158/0008-5472.CAN-10-3879. Epub 2011 May 25. PMID: 21613408; PMCID: PMC3138877.

7. Bioactivity
Biological target: X-376 is an ALK tyrosine kinase inhibitor with an IC50 of 0.61 nM.

In vitro activity

To compare the in vitro effects of X-376 versus PF-1066, the ability of both agents to inhibit the growth of four different cancer cell lines known to harbor ALK fusions or point mutations was tested. In H3122 lung cancer cells harboring EML4-ALK E13;A20 (variant 1), X-376 was 3-fold more potent than PF-1066 (IC50: PF-1066 180nM, X-376 77nM) (Fig. 2A and Table 2). Similar results

were obtained with H2228 lung cancer cells (Fig. 2B), SUDHL-1 lymphoma cells (Fig. 2C), and SY5Y neuroblastoma cells (Fig. 2D), which harbor an EML4-ALK E6a/b;A20 (variant 3a/b) fusion, an NPM-ALK fusion, and an activating point mutation within the ALK kinase domain (F1174L) (12), respectively. In H3122 cells, the relative decrease in cell growth seen with X-376 treatment correlated with increased apoptosis, as assessed by fluorescence-activated cell sorting for Annexin V and propidium iodide (Fig. 2E).

Reference: Cancer Res. 2011 Jul 15;71(14):4920-31. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3138877/

In vivo activity

Nude mice harboring H3122 xenografts were treated with either X-376 at 50mg/kg bid. X-376 significantly delayed the growth of tumors compared to vehicle (Fig. 3A). At the dose used in these xenograft experiments, plasma levels inversely correlated with cellular potency. X-376 appeared well-tolerated in vivo. Mouse weight was unaffected by the treatment (Fig. 3B).

Reference: Cancer Res. 2011 Jul 15;71(14):4920-31. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3138877/