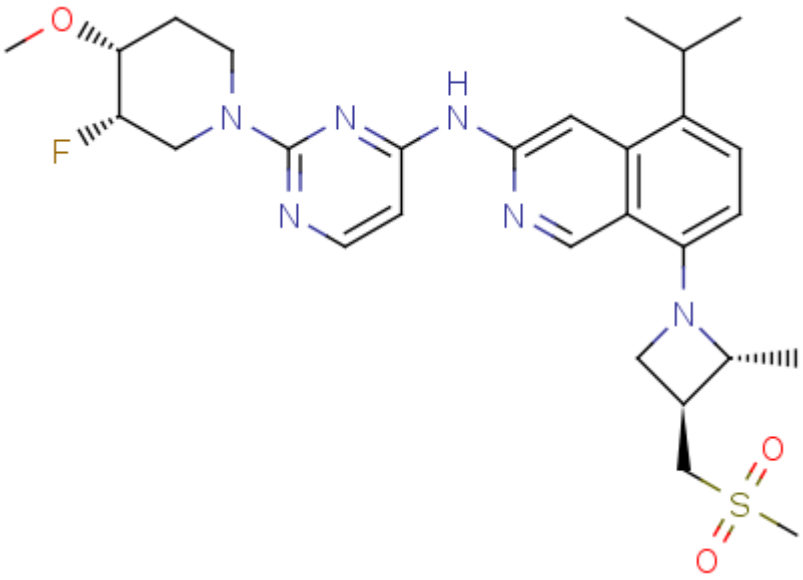
Name: BLU-945 Cat#: EX-A6018

Target: EGFR
Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK

Chemical Structure:



Chemical Name	N-(2-((3S,4R)-3-fluoro-4-methoxypiperidin-1-yl)pyrimidin-4-yl)-5-isopropyl-8-((2R,3S)-2-methyl-3-((methylsulfonyl)methyl)azetidin-1-yl)isoquinolin-3-amine

Molecular Weight	556.70	Storage	3 years -20°C powder 6 months -80°C in solvent Away from light
Formula	C28H37FN6O3S		
CAS No.	2660250-10-0	Synonyms	BLU945; BLU 945

Solubility (25°C) *	In vitro	DMSO	DMSO : >=100 mg/mL (179.65 mM; Need ultrasonic)
		Ethanol	N/A
		Water	N/A
	In vivo (should be freshly prepared each time)	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% Saline	

		Solubility: 2.5 mg/mL (4.49 mM); Suspended solution; Need ultrasonic 2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in Saline) Solubility: 2.08 mg/mL (3.74 mM); Suspended solution; Need ultrasonic

* <1 mg/ml means slightly soluble or insoluble.
* Please note that Selleck tests the solubility of all compounds in-house, and the actual solubility may differ slightly from published values. This is normal and is due to slight batch-to-batch variations.

Preparing Stock Solutions:

Mass / Volume / Concentration	1 mg	5 mg	10 mg
1 mM	1.7963 mL	8.9815 mL	17.9630 mL
5 mM	0.3593 mL	1.7963 mL	3.5926 mL
10 mM	0.1796 mL	0.8981 mL	1.7963 mL

DMSO :

*The above data is based on the product molecular weight 556.70.

Biological Activities:

Description	BLU-945 is a potent, highly selective, reversible and orally active epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKIs). BLU-945 can effectively inhibit EGFR with L858R and/or exon 19 deletion mutation, T790M mutation and C797S mutation. BLU-945 can be used for the research of lung cancer including non-small cell lung cancer (NSCLC)[1][2][3].
In Vitro	BLU-945 has inhibitory activity against the EGFRm/T790M double and EGFRm/T790M/C797Striple mutants with IC50 value range from 1.2-4.4 nM[1]. BLU-945 (0- 10 mM, 4 h) inhibit EGFR phosphorylation in the EGFR L858R/T790M/C797S, and EGFR ex19del/T790M/C797S mutant cell lines[1].
In Vivo	BLU-945 (oral, 0-100 mg/kg; bid) demonstrates potent, robust EGFR pathway inhibition and anti-tumor activity in triple mutant Osimertinib (HY-15772)-resistant Ba/F3 CDX and PDCX models[1] . Animal Model: triple-mutant osimertinib-resistant Ba/F3 CDX and PDCX models[1]. Dosage: 0-100 mg/kg

Administration:	oral, twice daily
Result:	Showed significant tumor regression in an osimertinib-resistant EGFR ex19del/T790M/C797S PDCX.

References

[1]. Meredith S Eno, et al. Discovery of BLU-945, a Reversible, Potent, and Wild-Type-Sparing Next-Generation EGFR Mutant Inhibitor for Treatment-Resistant Non-SmallCell Lung Cancer. J Med Chem. 2022 Jul 28;65(14):9662-9677.

[2]. Sun Min Lim, et al. BLU-945, a fourth-generation, potent and highly selective epidermal growth factor receptor tyrosine kinase inhibitor with intracranial activity, demonstrates robust in vivo anti-tumor activity in models of osimertinib-resistant non-small cell lung cancer.

[3]. John Emmerson Campbell, et al. Inhibitors of mutant forms of egfr. Patent WO2021133809A1.

[4]. Elaine Shum. et al. A phase 1/2 study of BLU-945 in patients with common activating EGFRmutant non-small cell lung cancer (NSCLC) (SYMPHONY trial-in-progress).