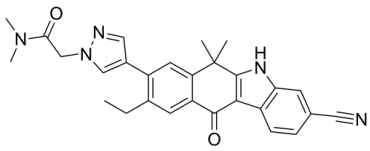
Data Sheet

Product Name:	JH-VIII-157-02
Cat. No.:	CS-0043469
CAS No.:	1639422-97-1
Molecular Formula:	$C_{28}H_{27}N_5O_2$
Molecular Weight:	465.55
Target:	Anaplastic lymphoma kinase (ALK)
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : ≥ 25 mg/mL



BIOLOGICAL ACTIVITY:

JH-VIII-157-02 is a structural analogue of alectinib, acts as an **ALK** inhibitor, and shows an **IC_{50}** of 2 nM for echinoderm microtubule-associated protein-like 4-ALK (EML4-ALK) G1202R in cells. IC50 & Target: IC50: 2 nM (EML4-ALK G1202R, cell assay), 2 nM (EML4-ALK^{wt}, cell assay), 2 nM (EML4-ALK C1156Y, cell assay), 2 nM (EML4-ALK F1174L, cell assay), 2 nM (EML4-ALK F1174L, cell assay)[1] ***In Vitro:*** JH-VIII-157-02 is a structural analogue of alectinib, acts as an ALK inhibitor, and shows an IC_{50} of 2 nM for echinoderm microtubule-associated protein-like 4-ALK (EML4-ALK) G1202R in cells. JH-VIII-157-02 also potently inhibits EML4-ALK ^{wt} (Eawt), EAC1156Y, EAF1174L, EAS1206Y (IC_{50}, 2 nM), EAG1269A (IC_{50}, 3 nM), EAL1196M (IC_{50}, 58 nM), EA1151Tins (IC_{50}, 107 nM), and EAL1152R (IC_{50}, 196 nM). Moreover, JH-VIII-157-02 has selectivity at other kinases, including IRAK1, CLK4, RET, RET V804L, RET V804M and IRAK 4, and the IC_{50}s are 14 nM, 14 nM, 3 nM, 13 nM, 12 nM, and 465 nM respectively. JH-VIII-157-02 exhibits inhibitory growth of cancer cell lines, such as H3122, DFCI76 (L1152R] with EC_{50}s of 5, 19 nM, respectively[1]. ***In Vivo:*** JH-VIII-157-02 exhibits good oral bioavailability following an oral dose of 10 mg/kg in mice. JH-VIII-157-02 also penetrates the CNS of mice[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]Cells are seeded at **4000 per well** in 96 well plates and exposed to **JH-VIII-157-02** in triplicate at **1 nM to 10 μM** for **72 hours**. Cell viability is evaluated using CellTiter-Glo Luminescent Cell Viability Assay. IC_{50} values are calculated by nonlinear regression (variable slope) using GraphPad Prism 5 software. Each experiment is repeated for at least twice[1].

References:

[1]. Hatcher JM, et al. Discovery of Inhibitors That Overcome the G1202R Anaplastic Lymphoma Kinase Resistance Mutation. J Med Chem. 2015 Dec 10;58(23):9296-9308.

CAIndexNames:

1H-Pyrazole-1-acetamide, 4-(3-cyano-9-ethyl-6,11-dihydro-6,6-dimethyl-11-oxo-5H-benzo[b]carbazol-8-yl)-N,N-dimethyl-

SMILES:

O=C(N(C)C)CN1N=CC(C2=C(CC)C=C3C(C(C)(C)C(NC4=C5C=CC(C#N)=C4)=C5C3=O)=C2)=C1

Caution: Product has not been fully validated for medical applications. For research use only.

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