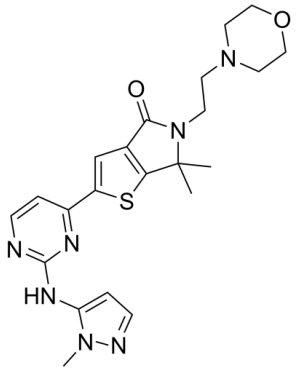
Data Sheet

Product Name:	Temuterkib
Cat. No.:	CS-6974
CAS No.:	1951483-29-6
Molecular Formula:	$C_{22}H_{27}N_7O_2S$
Molecular Weight:	453.56
Target:	ERK
Pathway:	MAPK/ERK Pathway; Stem Cell/Wnt
Solubility:	DMSO : 20 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

Temuterkib (LY3214996) is a highly selective inhibitor of **ERK1** and **ERK2**, with **IC_{50}** of 5 nM for both enzymes in biochemical assays. Temuterkib potently inhibits cellular p-RSK1 in BRAF and RAS mutant cancer cell lines. Temuterkib shows potent antitumor activities in cancer models with MAPK pathway alterations. IC50 & Target: IC50: 5 nM (ERK1/2)[1] ***In Vitro:*** Temuterkib is a highly selective inhibitor of ERK1 and ERK2, with IC_{50} of 5 nM for both enzymes in biochemical assays. Temuterkib potently inhibits cellular phospho-RSK1 in BRAF and RAS mutant cancer cell lines. In an unbiased tumor cell panel sensitivity profiling for inhibition of cell proliferation, tumor cells with MAPK pathway alterations including BRAF, NRAS or KRAS mutation are generally sensitivity to Temuterkib[1]. ***In Vivo:*** In tumor xenograft models, Temuterkib inhibits PD biomarker phospho-p90RSK1 in tumors and the PD effects are correlated with compound exposures and anti-tumor activities. Temuterkib shows either similar or superior anti-tumor activity as compared to other published ERK inhibitors in BRAF or RAS mutant cell lines and xenograft models. Oral administration of single-agent Temuterkib significantly inhibits tumor growth in vivo and is well tolerated in BRAF or NRAS mutant melanoma, BRAF or KRAS mutant colorectal, lung and pancreatic cancer xenografts or PDX models. Therefore, Temuterkib can be tailored for treatment of cancers with MAPK pathway alteration. In addition, Temuterkib has anti-tumor activity in a PLX4032-resistant A375 melanoma xenograft model due to MAPK reactivation, may have potential for treatment of melanoma patients who have failed BRAF therapies. More importantly, Temuterkib can be combined with investigational and approved agents in preclinical models, particularly KRAS mutant models. Combination treatment of Temuterkib and CDK4/6 inhibitor abemaciclib is well tolerated and results in potent tumor growth inhibition or regression in multiple in vivo cancer models, including KRAS mutant colorectal and non-small cell lung cancers[1].

References:

[1]. Shripad V. Bhagwat, et al. Abstract 4973: Discovery of LY3214996, a selective and novel ERK1/2 inhibitor with potent antitumor activities in cancer models with MAPK pathway alterations. Cancer Research. July 2017.

CAIndexNames:

4H-Thieno[2,3-c]pyrrol-4-one, 5,6-dihydro-6,6-dimethyl-2-[2-[(1-methyl-1H-pyrazol-5-yl)amino]-4-pyrimidinyl]-5-[2-(4-morpholinyl)ethyl]-

SMILES:

O=C(C(C=C(C1=NC(NC2=CC=NN2C)=NC=C1)S3)=C3C4(C)C)N4CCN5CCOCC5

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

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