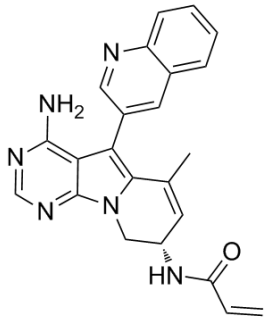
TAS6417

Cat. No.:	HY-112299
CAS No.:	1661854-97-2
Molecular Formula:	$C_{23}H_{20}N_6O$
Molecular Weight:	396.44
Target:	EGFR
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 125 mg/mL (315.31 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5224 mL	12.6122 mL	25.2245 mL
	5 mM	0.5045 mL	2.5224 mL	5.0449 mL
	10 mM	0.2522 mL	1.2612 mL	2.5224 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: **10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline**
   Solubility: ≥ 2.25 mg/mL (5.68 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: ≥ 2.25 mg/mL (5.68 mM); Clear solution
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 2.25 mg/mL (5.68 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TAS6417 is an **EGFR** inhibitor and an efficacious drug candidate for patients with NSCLC, with **IC_{50}** values ranging from 1.1-8.0 nM.

IC_{50} & Target

EGFR
1.1-8.0 nM (IC_{50})

In Vitro	TAS6417 inhibits the in vitro phosphorylation activity of EGFR and its mutants including an exon 20 insertion mutation, with IC_{50} values ranging from 1.1±0.1 to 8.0±1.1 nM. TAS6417 suppresses the growth of cells expressing exon 20 insertion mutations of the EGFR gene, with a GI_{50} value of 86.5±28.5 nM for LXF 2478L cells and 45.4±2.6 nM for NCI-H1975 EGFR D770_N771insSVD cells. TAS6417 also potently inhibits proliferation in other cell lines harboring activating mutations or acquired resistance mutations, with mean GI_{50} values of 1.92±0.21 nM to 7.12±0.60 nM. In contrast, the effect of TAS6417 on cell proliferation in normal human epidermal keratinocytes (NHEK-Neo), of which WT EGFR is implicates in the growth and survival, is moderate[1].
In Vivo	TAS6417 causes persistent tumor regression in vivo in EGFR exon 20 insertion-driven tumor models. TAS6417 inhibits mutant EGFR in tumors but not WT EGFR in skin tissues. TAS6417 prolongs survival of animals bearing lung cancer[1].

PROTOCOL

Animal Administration [1]	Mice[1] **Mice** bearing NCI-H1975 EGFR D770_N771insSVD xenografts are orally administered **TAS6417 (50, 100, 200 mg/kg)**. One and 2 hours after administration of TAS6417, xenograft tumors and skin tissues are collected[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Hasako S, et al. TAS6417, A Novel EGFR Inhibitor Targeting Exon 20 Insertion Mutations. Mol Cancer Ther. 2018 Aug;17(8):1648-1658.

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