Product Data Sheet

Product Name: Tankyrase Inhibitors (TNKS) 22
Cat. No.: GC15041

Chemical Properties

Cas. No.			
Chemical Name	3-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)-N-((1r,4r)-4-(5-phenyl-1,3,4-oxadiazol-2-yl)cyclohexyl)propanamide		
SMILES	O=C1NC(SCCC(N[C@H]2CC[C@H](C3=NN=C(C4=CC=CC=C4)O3)CC2)=O)=NC5=CC=CC=C51		
Formula	$C_{25}H_{25}N_5O_3S$	M.Wt	475.56
Solubility	<4.76mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Tankyrase Inhibitors (TNKS) 22		

Protocol

Cell experiment [1]:

Cell lines	SW480-TBC cell lines
Preparation method	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.

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Reaction Conditions	24 h; IC50=3.7nM
Applications	Tankyrase Inhibitors (TNKS) 22, lead-optimized phenyloxadiazole compounds, has a good enzymatic potency and cellular potency with IC50 value of 3.7 nM in the SW480-TBC cellular assay. The compound demonstrated excellent potencies in TNKS2 autoparsylation assay and the two additional functional cellular assays.

Animal experiment [1]:

Animal models	Athymic nude mice.
Dosage form	10 and 50 mg/kg; q.d.; oral taken
Applications	Tankyrase Inhibitors (TNKS) 22 was evaluated for Wnt-pathway specific pharmacological activity in mouse tumor pharmacodynamic (PD) models. Upon once daily oral administration (at 10 and 50 mg/kg) to mice (n=4) bearing human DLD-1 tumors for 3 days, both compounds exhibited statistically significant, dose-dependent axin2 accumulation (2.7-to 3.5-fold) and inhibition of STF (51−58%) at day 3 (24 h after the last dose) .
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1] Hua Z, Bregman H, Buchanan J L, et al. Development of Novel Dual Binders as Potent, Selective, and Orally Bioavailable Tankyrase Inhibitors[J]. Journal of medicinal chemistry, 2013, 56(24): 10003-10015.

Background

Tankyrase Inhibitors (TNKS) 22 is a potent, selective and orally bioavailable inhibitor of tankyrase with IC50 value of 0.1nM [1].

Tankyrase 1 and tankyrase 2 are members of PARP family. They can use NAD+ as substrates to transfer ADP-ribose polymers onto tagert proteins. The tankyrase are found to bind to PARSylate axin proteins which are the negative regulator of Wnt pathway. It makes tankyrase to be targets in treatment for adenomatous polyposis coli. Tankyrase inhibitors 22 is an optimization of the previous hit compound inhibitor 8 with improved potency and selectivity. It has excellent effects in both tankyrase assay and cellular assay (total β-catenin degradation assay in SW480 cells) with IC50 values of 0.1nM and 3.7nM, respectively. In addition, it is found to be a dual binder with both the nicotinamide pocket and the induced pocket of the enzymes [1].

In the in vivo studies in rodents, tankyrase inhibitors 22 is found to potently inhibit TNKS2 autoparsylation with IC50 value of 4.1nM. It also causes stabilization and accumulation of axin protein in SW480 cells with EC50 value of 3.9nM. In DLD-1 cells with truncated APC, the inhibitor inhibits the STF reporter transcription with IC50 value of 0.6nM suggesting its downstream inhibitory activity on Wnt-associated transcription [1].

References:
[1] Hua Z, Bregman H, Buchanan J L, et al. Development of Novel Dual Binders as Potent, Selective, and Orally Bioavailable Tankyrase Inhibitors. Journal of medicinal chemistry,

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