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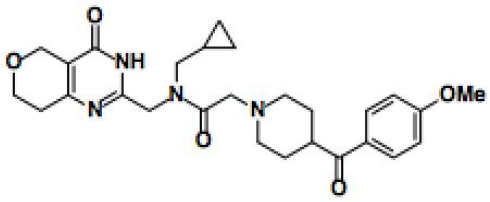
Wnt / Tankyrase Inhibitor – NVP-TNKS656

Chemical Name: N-(cyclopropylmethyl)-2-(4-(4-methoxybenzoyl)piperidin-1-yl)-N-((4-oxo-3,5,7,8-tetrahydro-4H-pyrano[4,3-d]pyrimidin-2-yl)methyl)acetamide



Molecular Weight:	494.59
Formula:	$C_{27}H_{34}N_4O_5$
Purity:	≥98%
CAS#:	1419949-20-4
Solubility:	DMSO up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

NVP-TNKS656 is a highly potent, selective and oral bioavailable tankyrase inhibitor with IC_{50} of 6 nM for TNKS2. It has 300-fold selectivity against PARP1 and PARP2. In MMTV-Wnt1 tumor models, NVP-TNKS656 was dosed to mice orally to stabilize Axin1 protein and reduce the Wnt/beta-catenin target gene Axin2 mRNA level by 70-80%. In colorectal cancer PDX models, NVP-TNKS656 reduces nuclear β-catenin, reverts such resistance, and represses tumor growth.

How to Use:

In vitro: NVP-TNKS656 was used at 10 μM in vitro and cellular assays.

In vivo: In MMTV-Wnt1 tumor bearing athymic nude mice, NVP-TNKS656 was dosed to mice orally at 100-350 mg/Kg once per day to stabilize Axin1 protein and reduce the Wnt/beta-catenin target gene Axin2 mRNA level by 70-80%. In colorectal cancer PDX models, NVP-TNKS656 reduces nuclear β-catenin, reverts such resistance, and represses tumor growth.

Reference:

1. Shultz MD, et al. Identification of NVP-TNKS656: the use of structure-efficiency relationships to generate a highly potent, selective, and orally active tankyrase inhibitor. (2013) J Med Chem. 56(16):6495-511.
2. Arqués O, et al. Tankyrase Inhibition Blocks Wnt/β-Catenin Pathway and Reverts Resistance to PI3K and AKT Inhibitors in the Treatment of Colorectal Cancer. (2016) Clin Cancer Res. 22(3):644-56.