

## Product Data Sheet

Product Name: JW 55  
Cat. No.: GC12869

### Chemical Properties

Cas. No. 664993-53-7

Chemical Name N-[4-[[4-(4-methoxyphenyl)oxan-4-yl]methylcarbamoyl]phenyl]furan-2-carboxamide

SMILES COC1=CC=C(C=C1)C2(CCOCC2)CNC(=O)C3=CC=C(C=C3)NC(=O)C4=CC=CO4

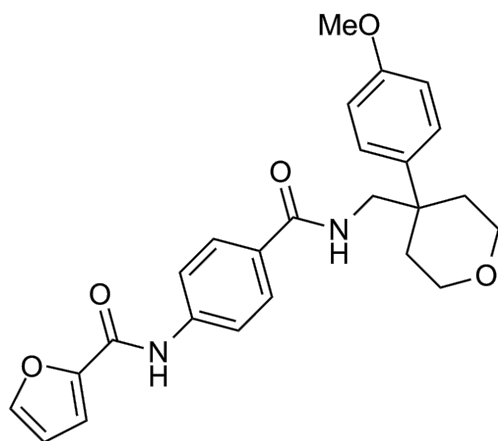
Formula  $C_{25}H_{26}N_2O_5$  M.Wt 434.48

Solubility  $\geq 19.25\text{mg/mL}$  in DMSO,  $\geq 3.53$  mg/mL in EtOH with ultrasonic Storage Store at 4°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



### Protocol

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

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**Cell experiment:** A total of 1,000 SW480 or RKO cells are seeded in 96-well plates. The day after, the cell culture medium is exchanged to solutions that contained 0.1% DMSO or 10  $\mu$ M JW55 for RKO cells and 0.1% DMSO or 10, 5, or 1  $\mu$ M JW55 for SW480 cells. All samples consist of a minimum of 6 replicates. The plate is incubated in an IncuCyte inside a cell culture incubator. Images are captured every second hour to monitor proliferation[1].

**Animal experiment:** Mice[1] Seven 12-week old female ApcCKO/CKO/Lgr5-CreERT2 mice are injected intraperitoneally with 25 mg/kg of Tamoxifen diluted in an ethanol and corn oil (ratio 1:4). The mice are randomized into 2 groups and treated with either JW55 (100 mg/kg) or vehicle (DMSO). Daily per oral applications started the day after and continued for 3 weeks. The mouse body weight is measured twice a week. The mice are sacrificed and the intestines are dissected, washed in PBS, and fixed in formaldehyde [10% solution (v/v) in PBS]. The small intestines are stained using 1% methylene blue prepared in 10% paraformaldehyde (PFA)/PBS solution. Small ileum Swiss-rolls are embedded in paraffin sectioned and stained with hematoxylin and eosin. Fixed colons are embedded in paraffin, sectioned and stained with an anti- $\beta$ -catenin antibody. The number and size of the intestinal lesions are quantified by the Ellipse program.

### References:

[1]. Waaler J, et al. A novel tankyrase inhibitor decreases canonical Wnt signaling in colon carcinoma cells and reduces tumor growth in conditional APC mutant mice. Cancer Res. 2012 Jun 1;72(11):2822-32.

### Background

IC50: 1.9  $\mu$ M (TNK S1); 0.83  $\mu$ M (TNK S2)

Increased nuclear accumulation of  $\beta$ -catenin, a mediator of canonical Wnt signaling, is found in numerous tumors and is frequently associated with tumor progression and metastasis. Inhibition of

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Wnt/b-catenin signaling therefore is an attractive strategy for anticancer drugs.

**In vitro:** In a previous study, the authors identified a novel small molecule inhibitor of the  $\beta$ -catenin signaling pathway, JW55, that functions via inhibition of the PARP domain of tankyrase 1 and tankyrase 2 (TNKS1/2), regulators of the b-catenin destruction complex. Inhibition of TNKS1/2 poly(ADP-ribosyl)ation activity by JW55 led to stabilization of AXIN2, a member of the b-catenin destruction complex, followed by increased degradation of b-catenin. In a dose-dependent manner, JW55 inhibited canonical Wnt signaling in colon carcinoma cells that contained mutations in either the APC (adenomatous polyposis coli) locus or in an allele of b-catenin [1].

**In vivo:** JW55 was reported to reduce XWnt8-induced axis duplication in *Xenopus* embryos and tamoxifen-induced polyposis formation in conditional APC mutant mice. These findings provide a novel chemotype for targeting canonical Wnt/b-catenin signaling through inhibiting the PARP domain of TNKS1/2 [1].

**Clinical trial:** JW55 is currently in the preclinical development and no clinical trial is ongoing.

### Reference:

[1] Waaler J, Machon O, Tumova L, Dinh H, Korinek V, Wilson SR, Paulsen JE, Pedersen NM, Eide TJ, Machonova O, Gradl D, Voronkov A, von Kries JP, Krauss S. A novel tankyrase inhibitor decreases canonical Wnt signaling in colon carcinoma cells and reduces tumor growth in conditional APC mutant mice. *Cancer Res.* 2012;72(11):2822-32.

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