

## Small Molecules

### XAV939

WNT pathway inhibitor; Inhibits TNKS1 and TNKS2

Catalog #	72672	1 mg
	72674	10 mg
	100-1052	25 mg



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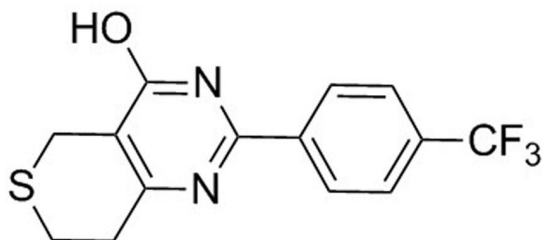
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## Product Description

XAV939 is an inhibitor of WNT signaling. WNT proteins are small secreted proteins that are active in embryonic development, tissue homeostasis (Clevers), and tumorigenesis (Polakis; Reya et al.). WNT proteins bind to receptors on the cell surface, initiating a signaling cascade that leads to  $\beta$ -catenin accumulation and downstream gene transcription. The WNT signaling pathway is regulated through degradation of the downstream effector,  $\beta$ -catenin, via a complex consisting of the tumor suppressor, APC, AXIN, and glycogen synthase kinase 3 (GSK3). AXIN is the concentration-limiting factor for this degradation complex. Initially identified as telomere-associated proteins (Smith), tankyrases promote AXIN ubiquitination, possibly through poly-ADP-ribosylation (PARsylation; Huang et al.). XAV939 is a potent, small molecule inhibitor of tankyrase (TNKS) 1 and 2 ( $IC_{50}$  = 11 and 4 nM, respectively; Huang et al.). By inhibiting TNKS activity, XAV939 increases the protein levels of the AXIN-GSK3 $\beta$  complex and promotes the degradation of  $\beta$ -catenin in SW480 cells (Huang et al.), thereby inhibiting WNT pathway downstream actions.

Molecular Name:	XAV939
Alternative Names:	Not applicable
CAS Number:	284028-89-3
Chemical Formula:	C <sub>14</sub> H <sub>11</sub> F <sub>3</sub> N <sub>2</sub> OS
Molecular Weight:	312.3 g/mol
Purity:	≥ 98%
Chemical Name:	2-[4-(trifluoromethyl)phenyl]-1,5,7,8-tetrahydrothiopyrano[4,3-d]pyrimidin-4-one
Structure:	



## Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect from prolonged exposure to light. Stable as supplied for 12 months from date of receipt.
Solubility:	· DMSO ≤ 6.4 mM For example, to prepare a 1 mM stock solution in DMSO, resuspend 1 mg in 3.20 mL of fresh DMSO.

Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported, however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application.

Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

## Published Applications

### DIFFERENTIATION

- Induces cardiomyogenesis in mesoderm progenitor cells derived from mouse embryonic stem cells (Wang et al.).
- In combination with the SMAD inhibitors LD193189 (Catalog #72146) and SB431542 (Catalog #72232), promotes induction of forebrain fates in human pluripotent stem cell lines (Maroof et al.).

### CANCER RESEARCH

- Inhibits colony formation of APC-deficient,  $\beta$ -catenin-dependent DLD-1 colorectal cancer cells (Huang et al.).

## References

- Clevers H. (2006) Wnt/beta-catenin signaling in development and disease. *Cell* 127(3): 469–80.
- Huang S-MA et al. (2009) Tankyrase inhibition stabilizes axin and antagonizes Wnt signalling. *Nature* 461(7264): 614–20.
- Maroof AM et al. (2013) Directed differentiation and functional maturation of cortical interneurons from human embryonic stem cells. *Cell Stem Cell* 12(5): 559–72.
- Polakis P. (2000) Wnt signaling and cancer. *Genes Dev* 14(15): 1837–51.
- Reya T & Clevers H. (2005) Wnt signalling in stem cells and cancer. *Nature* 434(7035): 843–50.
- Smith S. (1998) Tankyrase, a poly(ADP-ribose) polymerase at human telomeres. *Science* 282(5393): 1484–7.
- Wang H et al. (2011) Cardiac induction of embryonic stem cells by a small molecule inhibitor of Wnt/ $\beta$ -catenin signaling. *ACS Chem Biol* 6(2): 192–7.

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