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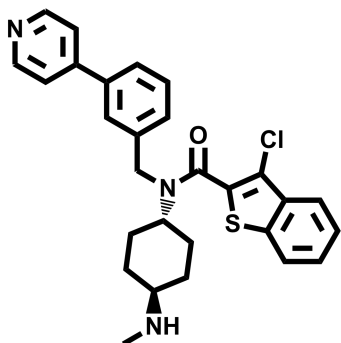
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Hedgehog Agonist SAG

Chemical Name: 3-chloro-N-((1r,4r)-4-(methylamino)cyclohexyl)-N-(3-(pyridin-4-yl)benzyl)benzo[b]thiophene-2-carboxamide



Molecular Weight:	490.06
Formula:	C ₂₈ H ₂₈ ClN ₃ OS
Purity:	≥ 98%
CAS#:	364590-63-6
Solubility:	DMSO up to 50 mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

Biological Activity:

SAG is a potent, selective, and cell-permeable small-molecule agonist of the Hedgehog pathway. It modulates the coupling of Smo with its downstream effector by interacting with the Smo heptahelical domain (KD = 59 nM). SAG induces Hedgehog pathway activation with an EC₅₀ of ~3 nM in NIH 3T3-derived Shh-LIGHT2 cells and counteracts Cyclopamine-KAAD inhibition of Smo. It was reported that SAG acts as an activator at low concentrations and as an inhibitor at high concentrations (>1 μM). In recent studies, SAG was shown to prevent glucocorticoid-induced neonatal cerebellar injury, and trigger rapid metabolic rewiring via AMPK.

How to Use:

In vitro: SAG was used at 200 nM to induce Hh pathway activation.

In vivo: n/a

Reference:

1. Frank-Kamenetsky M, et al. Small-molecule modulators of Hedgehog signaling: identification and characterization of Smoothed agonists and antagonists. (2002) *Journal of Biology* (1): 10.2-10.19.
2. Chen JK, et al. Small molecule modulation of Smoothed activity.(2002) *Proc Natl Acad Sci U S A*. 99(22):14071-6.
3. Chen W, et al. Activity-dependent internalization of smoothed mediated by beta-arrestin 2 and GRK2. (2004) *Science*. 306(5705):2257-60.
4. Dyer LA, et al. BMP signaling modulates hedgehog-induced secondary heart field proliferation. (2010) *Dev Biol*. 348(2):167-76.
5. Heine VM, et al. A small-molecule smoothed agonist prevents glucocorticoid-induced neonatal cerebellar injury. (2011) *Sci Transl Med*. 3(105).
6. Teperino R, et al. Hedgehog partial agonism drives Warburg-like metabolism in muscle and brown fat. (2012) *Cell*. 151(2):414-26.

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