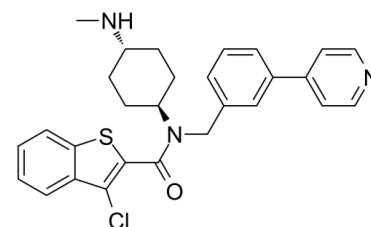


Data Sheet

Product Name:	SAG
Cat. No.:	CS-4176
CAS No.:	912545-86-9
Molecular Formula:	C ₂₈ H ₂₈ ClN ₃ OS
Molecular Weight:	490.06
Target:	Smo
Pathway:	Stem Cell/Wnt
Solubility:	DMSO : ≥ 38 mg/mL (77.54 mM)



BIOLOGICAL ACTIVITY:

SAG is a potent **Smo receptor** agonist which activates the Hedgehog signaling pathway with a K_d of 59 nM. IC₅₀ & Target: K_d: 59 nM (Smo)^[1] **In Vitro:** SAG acts downstream of Ptch1 in the Hh pathway and counteracts cyclopamine inhibition of Smo. SAG induces firefly luciferase expression in Shh-LIGHT2 cells with an EC₅₀ of 3 nM and then inhibits expression at higher concentrations. In Smo-expressing Cos-1 cells, SAG yields an apparent dissociation constant (K_D) of 59 nM for the SAG/Smo complex^[1]. SAG and purmorphamine override the inhibitory effect of robotnikinin since Smo functions downstream of Shh/Ptc1^[2]. **In Vivo:** In CD-1 mice, SAG (1.0 mM) or NELL-1 (600 µg/ml) alone results in increased bone formation at 4 and 8 weeks, but significantly greater bone formation with both components combined (SAG + NELL-1). The combination of the two compounds exhibits a significant increase in new bone formation, accompanied by increased defect vascularization^[3]. SAG (15, 17, or 20 mg/kg, i.p.) induces pre-axial polydactyly prevalently. The highest SAG dose is effective in ca. 80% of the embryos and increased Gli1 and Gli2 mRNA expression in the limb bud, with Gli1 mRNA being the most upregulated^[4].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: SAG is formulated in lactated Ringer's solution.^[4] GD 9:6 hr females are weighed, given a single intraperitoneal SAG injection (6, 6, and 7 for the 15, 17, and 20 mg/kg doses, respectively) or vehicle (lactated Ringer's solution; 9 litters), and returned to their home cage. GD 9:6 is a sensitive period for inducing forelimb malformations by retinoic acid and ethanol administration. For SAG dose-response studies, GD 15 embryos are collected, examined for the number and appearance of the digits on each limb. For whole-mount in situ hybridization studies, embryos are collected at GD 9:10 hr in ice-cold RNase-free phosphate-buffered saline (PBS), fixed in 4% paraformaldehyde, rinsed with PBS, dehydrated in methanol and stored at -20°C.

References:

- [1]. Chen JK, et al. Small molecule modulation of Smoothened activity. Proc Natl Acad Sci U S A. 2002 Oct 29;99(22):14071-6.
- [2]. Stanton BZ, et al. A small molecule that binds Hedgehog and blocks its signaling in human cells. Nat Chem Biol. 2009 Mar;5(3):154-6.
- [3]. Lee S, et al. Combining Smoothened Agonist (SAG) and NEL-like protein-1 (NELL-1) Enhances Bone Healing. Plast Reconstr Surg. 2017 Feb 13
- [4]. Fish EW, et al. Preaxial polydactyly following early gestational exposure to the smoothened agonist, SAG, in C57BL/6J mice. Birth Defects Res A Clin Mol Teratol. 2016 Nov 1

CAIndexNames:

Benzo[b]thiophene-2-carboxamide, 3-chloro-N-[trans-4-(methylamino)cyclohexyl]-N-[[3-(4-pyridinyl)phenyl]methyl]-

SMILES:

O=C(C1=C(C)C2=CC=CC=C2S1)N([C@H]3CC[C@H](NC)CC3)CC4=CC=CC(C5=CC=NC=C5)=C4

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

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA