

## Product Data Sheet

Product Name: SAG 21k

Cat. No.: GC50135

### Chemical Properties

Cas. No. 946002-48-8

SMILES COC1=C(CN([C@@H]2CC[C@H](NC)CC2)C(C3=C(Cl)C4=C(C(F)=CC=C4F)S3)=O)C=C(C5=CC=NC=C5)C=C1

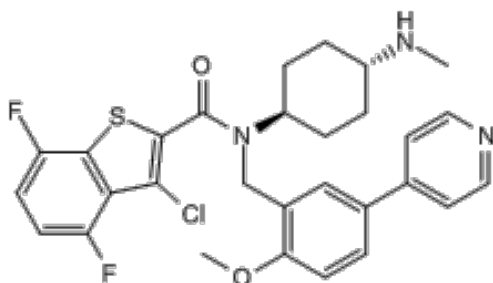
Formula  $C_{29}H_{28}ClF_2N_3O_2S$  M.Wt 556.07

Solubility DMSO : 40 mg/mL (71.93 mM; ultrasonic and warming and heat to 60°C) Storage Store at -20°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

#### Cell experiment [1]:

Cell lines HCC1954 cells

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

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**Preparation Method** HCC1954 cells were grown in DMEM media supplemented with 10% FBS, 1% sodium pyruvate, and 2mM L-glutamine. The trastuzumab-resistant HCC1954 cells were generated by exposing the cells to increased doses (0.1-10 $\mu$ M) of trastuzumab for 3 months. The trastuzumab-resistant HCC1954 cells were treated with 1 $\mu$ M SAG 21k for 24 hours, and then RNA was extracted for analysis.

**Reaction Conditions** 1 $\mu$ M; 24h

**Applications** SAG 21k treatment significantly enhanced the expression of Nanog, Sox2, Bmi1, and Oct4 in trastuzumab-resistant HCC1954 cells.

### Animal experiment [2]:

**Animal models** C57BL/6 mice

**Preparation Method** C57BL/6 mice (25-30g) were kept in temperature-controlled (21°C-25°C) and humidity-maintained (40%-70%) rooms with a 12-h light/dark cycle. Water and food were provided freely. Replace the regular drinking water of the mice with DSS solution (5%) for one week. Then, inject SAG 21k intraperitoneally into the mice at a dose of 0.5mg/kg, once every 12 hours for one week. The control group of mice will be injected with PBS. Collect the colon tissues of the mice for analysis and daily monitor the body weight of the mice.

**Dosage form** 0.5mg/kg; twice a day for 7 days; i.p.

**Applications** SAG 21k treatment alleviated the acute colitis induced by DSS in mice and inhibited the weight loss.

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### References:

- [1] Er I, Boz Er A B. Hedgehog pathway is a regulator of stemness in HER2-positive trastuzumab-resistant breast cancer[J]. International Journal of Molecular Sciences, 2024, 25(22): 12102.
- [2] Lee J J, Rothenberg M E, Seeley E S, et al. Control of inflammation by stromal Hedgehog pathway activation restrains colitis[J]. Proceedings of the National Academy of Sciences, 2016, 113(47): E7545-E7553.

### Background

SAG 21k is a potent and orally bioavailable Hedgehog signaling activator with an EC<sub>50</sub> value of 0.4nM [1]. SAG 21k can induce a myofibroblast-like phenotype and promote the increased expression of  $\alpha$ -smooth muscle actin ( $\alpha$ SMA) and type I collagen (Col I) in the extracellular matrix[2]. SAG 21k has been widely used in mouse models to inhibit the formation of intramuscular fat and promote regenerative muscle growth[3].

In vitro, SAG 21k treatment (1 $\mu$ M) for 24h significantly induced the upregulation of Hedgehog response genes (Bmp4, Gli1, Gli2, Hhip, Ptch1, Ptch2) in Trastuzumab-resistant SKBR3 and HCC1954 cells, and promoted the expression of Nanog, Sox2, Bmi1 and Oct4[4]. The 24-hour treatment of 10nM SAG 21k promoted the migration of endoneurial fibroblasts and increased the expression of VEGF-A[5].

In vivo, SAG 21k treatment via intraperitoneal injection at a dose of 5mg/kg/day for one week promoted bone formation in segmental bone defects of mice and increased bone volume[6]. Daily intraperitoneal injection of SAG 21k (0.5mg/kg) twice a day for one week can alleviate the acute colitis induced by dextran sulfate sodium (DSS) in mice and increase the survival rate of the mice[7].

### References:

- [1] Brunton S A, Stibbard J H A, Rubin L L, et al. Potent agonists of the Hedgehog signaling pathway[J]. Bioorganic & medicinal chemistry letters, 2009, 19(15): 4308-4311.
- [2] Lee J J, Perera R M, Wang H, et al. Stromal response to Hedgehog signaling restrains pancreatic cancer progression[J]. Proceedings of the National Academy of Sciences, 2014, 111(30): E3091-E3100.

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- [3] Liu X, Choi J, Moussa A, et al. Abstract Tu0084: Cilia-dependent Hedgehog Signaling Act as A Guardian against Limb Ischemia-induced Fatty Fibrosis[J]. Arteriosclerosis, Thrombosis, and Vascular Biology, 2025, 45(Suppl\_1): ATu0084-ATu0084.
- [5] Faniku C, Kong W, He L, et al. Hedgehog signaling promotes endoneurial fibroblast migration and Vegf-A expression following facial nerve injury[J]. Brain research, 2021, 1751: 147204.
- [4] Er I, Boz Er A B. Hedgehog pathway is a regulator of stemness in HER2-positive trastuzumab-resistant breast cancer[J]. International Journal of Molecular Sciences, 2024, 25(22): 12102.
- [6] Rundle C H, Gomez G A, Pourteymoor S, et al. Sequential application of small molecule therapy enhances chondrogenesis and angiogenesis in murine segmental defect bone repair[J]. Journal of Orthopaedic Research®, 2023, 41(7): 1471-1481.
- [7] Lee J J, Rothenberg M E, Seeley E S, et al. Control of inflammation by stromal Hedgehog pathway activation restrains colitis[J]. Proceedings of the National Academy of Sciences, 2016, 113(47): E7545-E7553.

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