上海源叶生物科技有限公司
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产品名称：BI-3406
CAS 号：2230836-55-0
产品货号：S89064

生物活性：

Description	BI-3406 (compound I-6) 是一种具有口服活性，高效且选择性的 KRAS-SOS1 抑制剂，可抑制 KRAS 与 SOS1 之间相互作用，IC50 为 6 nM。BI-3406 有效地减少了 GTP 加载的 KRAS 的形成，并抑制了 MAPK 信号通路。BI-3406 具有抗癌活性。
IC50 & Target[1]	KRAS-SOS1 6 nM (IC_{50})

Cellular Effect

Cell Line	Type	Value	Description
A549	IC_{50}	106 nM	Antiproliferative activity against human A549 cells harboring KRAS G12S mutant assessed as inhibition of cell growth
A549	IC_{50}	263 nM	Antiproliferative activity against human A549 cells harboring KRAS G12S mutant assessed as inhibition of cell proliferation incubated for 7 days by CellTiterGlo-3D proliferation assay
ASPC1	IC_{50}	64.4 nM	Antiproliferative activity against human ASPC1 cells harboring KRAS G12D mutant assessed as inhibition of cell proliferation incubated for 7 days by CellTiterGlo-3D proliferation assay
DLD-1	IC_{50}	102 nM	Antiproliferative activity against human DLD-1 cells harboring G13D mutant assessed as inhibition of cell proliferation incubated for 7 days by celltiter-glo 3D assay
DLD-1	IC_{50}	169 nM	Antiproliferative activity against human DLD-1 cells harboring KRAS G13D mutant assessed as inhibition of cell growth
K562	IC_{50}	1.422 μM	Antiproliferative activity against human K562 cells incubated for 72 hrs by CCK8 assay
K562	IC_{50}	37 nM	Antiproliferative activity against human K562 cells assessed as reduction in cell viability measured after 72 hrs by CellTiter-Glo luminescent cell viability assay
LoVo	IC_{50}	142 nM	Antiproliferative activity against human LoVo cells harboring KRAS G13D mutant assessed as inhibition of cell proliferation incubated for 7 days by CellTiterGlo-3D proliferation assay
MIA PaCa-2	IC_{50}	24.8 nM	Antiproliferative activity against human MIA PaCa-2 cells harboring KRAS G12C mutant assessed as inhibition of cell proliferation incubated for 7 days by CellTiterGlo-3D proliferation assay
MIA PaCa-2	IC_{50}	29 nM	Antiproliferative activity against human MIA PaCa-2 cells incubated for 72 hrs by CCK8 assay
MIA PaCa-2	IC_{50}	30 nM	Antiproliferative activity against human MIA PaCa-2 cells harboring G12C mutant assessed as cell growth inhibition incubated for 7 days by Celltiter-Glo 3D cell viability assay
NCI-H358	IC_{50}	16.5 nM	Antiproliferative activity against human NCI-H358 cells harboring KRAS G12C mutant assessed as inhibition of cell proliferation incubated for 7 days by CellTiterGlo-3D

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				proliferation assay
	NCI-H358	IC_{50}	24 nM	Antiproliferative activity against human NCI-H358 cells assessed as reduction in cell viability
	NCI-H358	IC_{50}	26 nM	Antiproliferative activity against human NCI-H358 cells assessed as inhibition of cell proliferation incubated for 7 days by celltiter-glo 3D assay
	NCI-H358	IC_{50}	26 nM	Antiproliferative activity against human NCI-H358 cells harboring G12C mutant assessed as inhibition of cell proliferation incubated for 7 days by celltiter-glo 3D assay
	NCI-H358	IC_{50}	90 nM	Antiproliferative activity against human NCI-H358 cells harboring KRAS G12C mutant assessed as inhibition of cell proliferation incubated for 5 days by celltiter-glo 3D assay
	NCI-H441	IC_{50}	68 nM	Antiproliferative activity against human NCI-H441 cells harboring G12V mutant assessed as inhibition of cell proliferation incubated for 7 days by celltiter-glo 3D assay
	PANC-1	IC_{50}	17.8 nM	Antiproliferative activity against human PANC-1 cells harboring KRAS G12D mutant assessed as inhibition of cell proliferation incubated for 7 days by CellTiterGlo-3D proliferation assay
	PC-3	IC_{50}	1.37 μM	Synergistic antiproliferative activity against human PC-3 cells assessed as inhibition of cell growth incubated for 72 hrs in presence of gefitinib by MTT assay
	PC-3	IC_{50}	8.75 μM	Antiproliferative activity against human PC-3 cells assessed as inhibition of cell growth incubated for 72 hrs by MTT assay
	SW-620	IC_{50}	30.1 nM	Antiproliferative activity against human SW620 cells harboring KRAS G12V mutant assessed as inhibition of cell proliferation incubated for 7 days by CellTiterGlo-3D proliferation assay
	SW-620	IC_{50}	50.5 nM	Antiproliferative activity against human SW620 cells harboring KRAS G12V mutant assessed as inhibition of cell growth

In Vitro

BI-3406 是 KRAS 与其鸟嘌呤核苷酸交换因子 (GEF) SOS1 之间相互作用的抑制剂。BI-3406 不会阻断 KRAS 与 SOS2 的相互作用，但会在广泛的 KRAS 致癌变异体上引发活性，包括所有主要的 G12 和 G13 癌蛋白。在 KRAS G12 或 G13 突变细胞中，BI-3406 对这种信号级联的下调有效地限制了细胞增殖[2]。

Solvent&Solubility

细胞实验:

Ethanol 中的溶解度 ：100 mg/mL (216.23 mM; 超声助溶)

DMSO 中的溶解度 ：100 mg/mL (216.23 mM; 超声助溶; 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO）

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.1623 mL	10.8117 mL	21.6235 mL
	5 mM	0.4325 mL	2.1623 mL	4.3247 mL
	10 mM	0.2162 mL	1.0812 mL	2.1623 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month (stored under nitrogen)。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

动物实验：

请根据您的 实验动物和给药方式 选择适当的溶解方案。

以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用；

以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

方案 一

请依序添加每种溶剂： 10% DMSO → 40% PEG300 → 5% Tween-80 → 45% Saline

Solubility: ≥ 2.5 mg/mL (5.41 mM); 澄清溶液

此方案可获得 ≥ 2.5 mg/mL（饱和度未知）的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；再向上述体系中加入 50 μL Tween-80，混合均匀；然后再继续加入 450 μL 生理盐水 定容至 1 mL。

生理盐水的配制：将 0.9 g 氯化钠，溶解于 ddH₂O 并定容至 100 mL，可以得到澄清透明的生理盐水溶液。

方案 二

请依序添加每种溶剂： 10% DMSO → 90% (20% SBE-β-CD in Saline)

Solubility: 2.5 mg/mL (5.41 mM); 澄清溶液; 超声助溶

此方案可获得 2.5 mg/mL 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液 中，混合均匀。

2 g SBE-β-CD（磺丁基醚 β-环糊精）粉末定容于 10 mL 的生理盐水中，完全溶解至澄清透明。

方案 三

请依序添加每种溶剂： 10% DMSO → 90% Corn Oil

Solubility: ≥ 2.5 mg/mL (5.41 mM); 澄清溶液

此方案可获得 ≥ 2.5 mg/mL（饱和度未知）的澄清溶液，此方案实验周期在半个月以上的动物实验酌情使用。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。

方案 四

请依序添加每种溶剂： 10% EtOH → 40% PEG300 → 5% Tween-80 → 45% Saline

Solubility: ≥ 2.5 mg/mL (5.41 mM); 澄清溶液

此方案可获得 ≥ 2.5 mg/mL（饱和度未知）的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 EtOH 储备液加到 400 μL PEG300 中，混合均匀；再向上述体系中加入 50 μL Tween-80，混合均匀；然后再继续加入 450 μL 生理盐水 定容至 1 mL。

生理盐水的配制：将 0.9 g 氯化钠，溶解于 ddH₂O 并定容至 100 mL，可以得到澄清透明的生理盐水溶液。

方案 五

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	请依序添加每种溶剂： 10% EtOH → 90% (20% SBE-β-CD in Saline) Solubility: ≥ 2.5 mg/mL (5.41 mM); 澄清溶液 此方案可获得 ≥2.5 mg/mL（饱和度未知）的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 EtOH 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液 中，混合均匀。 2 g SBE-β-CD（磺丁基醚 β-环糊精）粉末定容于 10 mL 的生理盐水中，完全溶解至澄清透明。 方案 六 请依序添加每种溶剂： 10% EtOH → 90% Corn Oil Solubility: ≥ 2.5 mg/mL (5.41 mM); 澄清溶液 此方案可获得 ≥2.5 mg/mL（饱和度未知）的澄清溶液，此方案实验周期在半个月以上的动物实验酌情使用。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 EtOH 储备液加到 900 μL 玉米油中，混合均匀。
参考文献	[1]. Michael Gmachl, et al. Novel benzylamino substituted quinazolines and derivatives as sos1 inhibitors. WO2018115380A1. [2]. Marco H Hofmann, et al. Abstract PL06-01: Discovery of BI-3406: A potent and selective SOS1::KRAS inhibitor opens a new approach for treating KRAS-driven tumors. December 2019.

完整储备液配制表：

请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month (stored under nitrogen)。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
Ethanol/ DMSO	**1 mM**	2.1623 mL	10.8117 mL	21.6235 mL	54.0587 mL
	5 mM	0.4325 mL	2.1623 mL	4.3247 mL	10.8117 mL
	10 mM	0.2162 mL	1.0812 mL	2.1623 mL	5.4059 mL
	15 mM	0.1442 mL	0.7208 mL	1.4416 mL	3.6039 mL
	20 mM	0.1081 mL	0.5406 mL	1.0812 mL	2.7029 mL
	25 mM	0.0865 mL	0.4325 mL	0.8649 mL	2.1623 mL
	30 mM	0.0721 mL	0.3604 mL	0.7208 mL	1.8020 mL
	40 mM	0.0541 mL	0.2703 mL	0.5406 mL	1.3515 mL
	50 mM	0.0432 mL	0.2162 mL	0.4325 mL	1.0812 mL
	60 mM	0.0360 mL	0.1802 mL	0.3604 mL	0.9010 mL
	80 mM	0.0270 mL	0.1351 mL	0.2703 mL	0.6757 mL
	100 mM	0.0216 mL	0.1081 mL	0.2162 mL	0.5406 mL