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产品名称：Asciminib
产品别名：ABL001

生物活性：

Description	Asciminib (ABL001) is a potent and selective allosteric Bcr-Abl inhibitor; inhibits Ba/F3 cells grown with an IC_{50} of 0.25 nM.
In Vitro	Asciminib binds to the myristoyl pocket of ABL1 and induces the formation of an inactive kinase conformation. NMR and biophysical studies confirm that asciminib binds potently (dissociation constant=0.5-0.8nM) and selectively to the myristoyl pocket of ABL1 and induces the inactive C-terminal helix conformation. Asciminib binding mimics the structural consequences of myristate binding to the N terminus of ABL1. Consistent with this binding site, asciminib exhibits the same non-ATP-competitive biochemical kinetics as the BCR–ABL inhibitor GNF-2 but with approximately 100-fold greater potency. Asciminib lacks activity against more than 60 kinases, including SRC, and is similarly inactive against G-protein-coupled receptors, ion channels, nuclear receptors and transporters. In BCR–ABL1-transformed Ba/F3 cells grown without IL-3, asciminib has an anti-proliferative with IC50 value of 0.25nM. In the CML blast-phase cell line KCL-22, asciminib inhibits phosphorylation of both STAT5 (Tyr694; pSTAT5) and BCR–ABL1 (Tyr245; pBCR–ABL1) after 1h using concentrations that correlate with those required for inhibition of cell proliferation. Asciminib is selectively active against all BCR–ABL1 lines (IC50 value of 1–20nM), irrespective of the presence of either the p210 or the p190 BCR–ABL1 isoform.[1].
In Vivo	Asciminib is undergoing clinical development testing in patients with CML and Philadelphia chromosome-positive acute lymphoblastic leukaemia. Single doses of 7.5, 15 and 30 mg/kg ABL001, administered to mice bearing KCL- 22 xenografts, inhibits pSTAT5 (Tyr694), which return to baseline at 10, 12 and 16-20h after administration of the dose, respectively. In mice implanted with KCL-22 tumors, the minimum dose of asciminib required for complete regression is 7.5 mg/kg twice a day (BID) or 30 mg/kg once a day (QD), and is tolerated at doses up to 250 mg/kg BID. Similarly, in xenografts derived from patients, treatment with 7.5 and 30 mg/kg asciminib leads to regressions that are maintained during dosing[1].

In Vitro:

DMSO : ≥ 100 mg/mL (222.30 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2230 mL	11.1151 mL	22.2301 mL
	5 mM	0.4446 mL	2.2230 mL	4.4460 mL
	10 mM	0.2223 mL	1.1115 mL	2.2230 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。 -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。

In Vivo:

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

Solvent&Solubility	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 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (5.56 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.56 mM，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，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.56 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.56 mM，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 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.56 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.56 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 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。
References	[1]. Wylie AA, et al. The allosteric inhibitor ABL001 enables dual targeting of BCR-ABL1. Nature. 2017 Mar 30;543(7647):733-737.

实验参考：

Cell Assay	Ba/F3 cells are treated with a range concentration of asciminib (0-10000 nM) for 48 h. Cell proliferation is measured using the Britelite luciferase detection assay[1].
Animal Administration	Mice: Asciminib efficacy in three patient-derived ALL systemic xenograft models (ALL-7015, AL-7119 and AL-7155) is assessed by FACS monitoring of the percentage of CD45+ cells per live cell in blood samples taken at varying time points after dosing with either 7.5 mg/kg BID (group 2) or 30 mg/kg BID (group 3) asciminib for 3 weeks[1].
References	[1]. Wylie AA, et al. The allosteric inhibitor ABL001 enables dual targeting of BCR-ABL1. Nature. 2017 Mar 30;543(7647):733-737.