产品名称：Emricasan
产品别名：恩利卡生；PF 03491390; IDN-6556

生物活性：

Description	Emricasan (PF 03491390; IDN-6556) is an irreversible pan-caspase inhibitor.
IC_{50} & Target	Caspase
In Vitro	Emricasan (PF 03491390; IDN-6556) (50 μM; 24 hours) directly improves hepatocytes phenotype in primary rat cirrhotic hepatocytes[1]. . Emricasan (10-50 μM) has hepatoprotective effects in human liver cells[1].
In Vivo	Emricasan (PF 03491390; IDN-6556) is orally active that is retained in the liver for prolonged period of time. TUNEL-positive cells are considerably increased by five-fold in mice fed a HFD and are reduced under Emricasan treatment. In accordance with this observation caspase-3 and -8 are increased in HFD-fed mice by 1.5- and 1.3-fold respectively and are significantly decreased by Emricasan treatment[2]. When comparing efficacy by multiple routes of administration, Emricasan is administered i.p., p.o., i.m., or i.v. (0.03-3 mg/kg). Caspase 3-like activities, measured as DEVD-AMC cleavage, dose dependently decreased with a 92.5% reduction after the highest dose of Emricasan (3 mg/kg). Emricasan is initially tested in the α-Fas model of liver injury, marked hepatocellular apoptosis, and peak ALT activities within 6 h. Emricasan is administered i.p. immediately after administration of α-Fas, ALT activities, measured 6 h later, decreased in a dose-dependent manner with an ED50 value of 0.08 (0.06-0.12) mg/kg[3]. Emricasan is a highly selective pan-caspase inhibitor demonstrating irreversible inhibition and a significant first-pass effect. In both syngeneic mouse islets and human islets transplanted into immunodeficient mice, Emricasan (i.p., 20 mg/kg) given for 7 days post-transplant led to a significantly enhanced rate of diabetes reversal as compared to vehicle[4].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 42 mg/mL (73.75 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7559 mL	8.7796 mL	17.5593 mL
	5 mM	0.3512 mL	1.7559 mL	3.5119 mL
	10 mM	0.1756 mL	0.8780 mL	1.7559 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 (4.39 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.39 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 (4.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.39 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 (4.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.39 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]. Gracia-Sancho J, et al. Emricasan Ameliorates Portal Hypertension and Liver Fibrosis in Cirrhotic Rats Through a Hepatocyte-Mediated Paracrine Mechanism. Hepatol Commun. 2019 Apr 22;3(7):987-1000. [2]. Barreyro FJ, et al. The pan-caspase inhibitor Emricasan (IDN-6556) decreases liver injury and fibrosis in a murine model of non-alcoholic steatohepatitis. Liver Int. 2015 Mar;35(3):953-66. [3]. Hoglen NC, et al. Characterization of IDN-6556 (3-[2-(2-tert-butyl-phenylaminooxalyl)-amino]-propionylamino]-4-oxo-5-(2,3,5,6-tetrafluoro-phenoxy)-pentanoic acid): a liver-targeted caspase inhibitor. J Pharmacol Exp Ther. 2004 May;309(2):634-40. [4]. McCall M, et al. The caspase inhibitor IDN-6556 (PF3491390) improves marginal mass engraftment after islet transplantation in mice. Surgery. 2011 Jul;150(1):48-55. [5]. Tian J, et al. Combination of Emricasan with Ponatinib Synergistically Reduces Ischemia/Reperfusion Injury in Rat Brain Through Simultaneous Prevention of Apoptosis and Necroptosis. Transl Stroke Res. 2017 Nov 4.

实验参考：

Animal Administration	Mice[2] The male C57BL/6J mice are age-matched and used at approximately 12-16 weeks of age. Four groups are studied (n=60) with 15 mice per group. Groups 1 and 3 receive regular chow. Groups 2 and 4 receive HFD and 50 g/L (Sucrose) is added to drinking water for 20 weeks. Groups 3 and 4 receive Emricasan 0.3 mg/kg/day per os, and Group 1 and 2 receive the vehicle. The oral administration of Emricasan at doses of 0.3 mg/kg corresponds to the ED90 value to prevent liver injury in the model of α-Fas-induced liver injury. Total body weight is measured at 0, 5, 10, 15 and 20 weeks. Rats[3] The male Sprague-Dawley rats are cannulated in the carotid artery under isoflurane anesthesia and allowed to recover for at least 1 day before drug administration. Blood (100 μL/sample) is taken from the carotid cannula 2 to 240 min after administration of Emricasan (i.v., s.c., p.o., or i.p.). Serum is prepared and frozen immediately until analysis. In studies measuring drug concentrations in portal and systemic blood, individual rats are bled (three animals per time point) simultaneously from the

	portal vein and inferior vena cava. In the biliary excretion study, bile is collected from the common bile duct after i.v. and p.o. administration of Emricasan (10 mg/kg) over a 24-h period on ice and frozen until analysis.
References	[1]. Gracia-Sancho J, et al. Emricasan Ameliorates Portal Hypertension and Liver Fibrosis in Cirrhotic Rats Through a Hepatocyte-Mediated Paracrine Mechanism. Hepatol Commun. 2019 Apr 22;3(7):987-1000. [2]. Barreyro FJ, et al. The pan-caspase inhibitor Emricasan (IDN-6556) decreases liver injury and fibrosis in a murine model of non-alcoholic steatohepatitis. Liver Int. 2015 Mar;35(3):953-66. [3]. Hoglen NC, et al. Characterization of IDN-6556 (3-[2-(2-tert-butyl-phenylaminooxalyl)-amino]-propionylamino]-4-oxo-5-(2,3,5,6-te trafluoro-phenoxy)-pentanoic acid): a liver-targeted caspase inhibitor. J Pharmacol Exp Ther. 2004 May;309(2):634-40. [4]. McCall M, et al. The caspase inhibitor IDN-6556 (PF3491390) improves marginal mass engraftment after islet transplantation in mice. Surgery. 2011 Jul;150(1):48-55. [5]. Tian J, et al. Combination of Emricasan with Ponatinib Synergistically Reduces Ischemia/Reperfusion Injury in Rat Brain Through Simultaneous Prevention of Apoptosis and Necroptosis. Transl Stroke Res. 2017 Nov 4.