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产品名称：Acelarin
产品别名：NUC-1031

生物活性：

Description	Acelarin (NUC-1031) is a ProTide transformation and enhancement of the widely-used nucleoside analogue, gemcitabine.
IC_{50} & Target	EC50：0.2 nM (DNA synthesis inhibitor)[1]
In Vitro	Gemcitabine is a nucleoside analogue commonly used in cancer therapy but with limited efficacy due to a high susceptibility to cancer cell resistance. The addition of a phosphoramidate motif to the gemcitabine can protect it against many of the key cancer resistance mechanisms. A series of gemcitabine phosphoramidate prodrugs are synthesized and screened for cytostatic activity in a range of different tumor cell lines. Among the synthesized compounds, NUC-1031 is shown to be potent *in vitro*.
In Vivo	The ProTide demonstrates a significant reduction in tumor size against pancreatic xenograft models compared with the gemcitabine treated group, and less adverse effects on body weight, indicating a better safety profile. Data strongly suggests that the ProTides are not reliant on kinases or nucleoside transporters to exert their activity inside tumor cells and remain stable in the presence of deaminases. The ProTide NUC-1031 is currently advancing through phase I/II clinical studies and has already generated strong pharmacokinetic data that confirm significantly higher intracellular levels of gemcitabine triphosphate, together with promising early efficacy signals and a favorable safety profile. The phosphoramidate chemistry is potentially a great source of new and very effective anticancer agents, bringing a considerable array of advanced treatments specifically designed to overcome cancer resistance mechanisms that will benefit a greater proportion of patients[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 36 mg/mL (62.02 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7227 mL	8.6137 mL	17.2274 mL
5 mM	0.3445 mL	1.7227 mL	3.4455 mL
10 mM	0.1723 mL	0.8614 mL	1.7227 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: ≥ 2.08 mg/mL (3.58 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (3.58 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (3.58 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (3.58 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (3.58 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (3.58 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Slusarczyk M, et al. Application of ProTide technology to gemcitabine: a successful approach to overcome the key cancer resistance mechanisms leads to a new agent (NUC-1031) in clinical development. J Med Chem. 2014 Feb 27;57(4):1531-42.

实验参考：

Cell Assay	NUC-1031(5.0 mg) is dissolved in DMSO (0.050 mL) and D_2O (0.15 mL). After recording the control ^{31}P NMR at 37 °C, a previously defrosted human, rat, or dog serum (0.30 mL) is added to the sample, which is next submitted to the ^{31}P NMR experiments at 37°C. The spectra are recorded every 30 min over 13 h. ^{31}P NMR recorded data are processed and analyzed with the Bruker Topspin 2.1 program[1].
Animal Administration	Balb/c nude mice are female, six to eight week old, with the weight of 20 ± 2 g. They are intraperitoneally given NUC-1031 (i.p 0.228 mmol/kg, 132.3 mg/kg, 2×/WK) or vehicle for 2 weeks. NUC-1031 is dissolved in 40% Captisol solution. (40% Captisol is prepared by dissolving 20mg of Captisol with pure water, and made the final volume 50 mL. The solvent is filtered with 0.22 μm filter). Mice are monitored daily for body weight change and clinical symptoms for 2 weeks[1].
References	[1]. Slusarczyk M, et al. Application of ProTide technology to gemcitabine: a successful approach to overcome the key cancer resistance mechanisms leads to a new agent (NUC-1031) in clinical development. J Med Chem. 2014 Feb 27;57(4):1531-42.