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产品名称：ALS-8176
产品别名：Lumicitabine；ALS-008176

生物活性：

Description	Lumicitabine (ALS-008176) is an inhibitor of the respiratory syncytial virus (RSV) polymerase.
In Vitro	Lumicitabine is an orally bioavailable prodrug of the novel RSV replication inhibitor ALS-008112, a cytidine nucleoside analogue[1].
In Vivo	Lumicitabine demonstrates excellent anti-RSV efficacy and safety in a phase 2 clinical RSV challenge study. It exhibits good oral bioavailability and a high level of 2c-TP *in vivo*. Lumicitabine has excellent stability profiles in formulations (>24 h storage stability in 0.5% methylcellulose aqueous formulation at rt) and simulats gastric and intestinal fluids (half-life >2 h). Its solubility is adequate to support oral administration in solutions with relatively low percentage of organic solvent and in aqueous suspensions. High levels of NMP and NTP are obtained following oral administration of Lumicitabine to monkeys[2]. In an adult human challenge study, Lumicitabine has shown efficacy against RSV infection[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (115.24 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3049 mL	11.5245 mL	23.0489 mL
	5 mM	0.4610 mL	2.3049 mL	4.6098 mL
	10 mM	0.2305 mL	1.1524 mL	2.3049 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 (5.76 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.76 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 (5.76 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.76 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 (5.76 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.76 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]. DeVincenzo JP, et al. Activity of Oral ALS-008176 in a Respiratory Syncytial Virus Challenge Study. N Engl J Med. 2015 Nov 19;373(21):2048-58. [2]. Wang G, et al. Discovery of 4'-chloromethyl-2'-deoxy-3',5'-di-O-isobutyryl-2'-fluorocytidine (ALS-8176), a first-in-class RSV polymerase inhibitor for treatment of human respiratory syncytial virus infection. J Med Chem. 2015 Feb 26;58(4):1862-78.

实验参考：

Animal Administration	Rats: Lumicitabine are formulated as solutions in PEG400-based vehicles. Pharmacokinetic studies are conducted at 5 mg/kg and for oral PK studies the prodrugs are administered at 5 mg/kg parent nucleoside equivalent doses. Blood samples are typically collected at various time points up to 24 h post dose for rat[2]. Monkeys: Lumicitabine are formulated as solutions in PEG400-based vehicles. Pharmacokinetic studies are conducted at 5 mg/kg and for oral PK studies the prodrugs are administered at 5 mg/kg parent nucleoside equivalent doses. Blood samples are typically collected at various time points up to 12 h post dose for Monkeys[2].
References	[1]. DeVincenzo JP, et al. Activity of Oral ALS-008176 in a Respiratory Syncytial Virus Challenge Study. N Engl J Med. 2015 Nov 19;373(21):2048-58. [2]. Wang G, et al. Discovery of 4'-chloromethyl-2'-deoxy-3',5'-di-O-isobutyryl-2'-fluorocytidine (ALS-8176), a first-in-class RSV polymerase inhibitor for treatment of human respiratory syncytial virus infection. J Med Chem. 2015 Feb 26;58(4):1862-78.