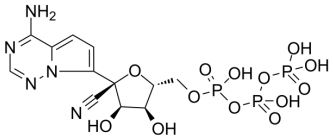
GS-443902

Cat. No.:	HY-126303
CAS No.:	1355149-45-9
Molecular Formula:	$C_{12}H_{16}N_5O_{13}P_3$
Molecular Weight:	531.2
Target:	DNA/RNA Synthesis; RSV; HCV; SARS-CoV; Drug Metabolite
Pathway:	Cell Cycle/DNA Damage; Anti-infection; Metabolic Enzyme/Protease
Storage:	-20°C, stored under nitrogen * The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

H_2O : 100 mg/mL (188.25 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8825 mL	9.4127 mL	18.8253 mL
	5 mM	0.3765 mL	1.8825 mL	3.7651 mL
	10 mM	0.1883 mL	0.9413 mL	1.8825 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

GS-443902 (GS-441524 triphosphate) is a potent viral RNA-dependent RNA-polymerases (RdRp) inhibitor with IC_{50}s of 1.1 μM, 5 μM for RSV RdRp and HCV RdRp, respectively. GS-443902 is the active triphosphate metabolite of Remdesivir[1][2].

IC_{50} & Target

IC50: 1.1 μM (RSV RdRp) and 5 μM (HCV RdRp)[1][2]

In Vitro

In a continuous 72 h incubation of 1 μM Remdesivir (GS-5734), the GS-443902 (GS-441524 triphosphate; Remdesivir metabolite; compound 4tp) level is measured at 2, 24, 48 and 72 h, and reaches a C_{max} of 300, 110, and 90 pmol/million cells in macrophages, HMVEC, and HeLa cells lines respectively[1].

GS-443902 (compound 8a) is a triphosphates (TP) derivative[2].

GS-443902 (NTP; 0.01, 0.1, 1, 10, 100 μM) inhibits RSV RdRp-catalysed RNA synthesis by incorporating into the nascent viral RNA transcript and causing its premature termination. GS-5734 selectively inhibits EBOV replication by targeting its RdRp and inhibiting viral RNA synthesis following efficient intracellular conversion to GS-443902[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Remdesivir (GS-5734; 10 mg kg; i.v.) rapidly distributes into peripheral blood mononuclear cells (PBMCs), and efficient conversion to GS-443902 (GS-441524 triphosphate; Remdesivir metabolite; NTP) is apparent within 2 h of dose administration in rhesus monkeys. In PBMCs, GS-443902 represents the predominant metabolite and is persistent with a $t_{1/2}$

	of 14 h and levels required for >50% virus inhibition for 24 hours[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2022 Nov 10;185(23):4347-4360.e17.
- Nat Commun. 2021 Oct 4;12(1):5811.
- Acta Pharm Sin B. 2021 Mar 22.
- Int J Mol Sci. 2022, 23(15), 8302.
- Chem Biol Interact. 2021 Apr 19;109480.

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REFERENCES

[1]. Siegel D, et al. Discovery and Synthesis of a Phosphoramidate Prodrug of a Pyrrolo[2,1-f][triazin-4-amino] Adenine C-Nucleoside (GS-5734) for the Treatment of Ebola and Emerging Viruses. Med Chem. 2017 Mar 9;60(5):1648-1661.

[2]. Cho A, et al. Synthesis and antiviral activity of a series of 1'-substituted 4-aza-7,9-dideazaadenosine C-nucleosides. Bioorg Med Chem Lett. 2012 Apr 15;22(8):2705-7.

[3]. Warren TK, et al. Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesus monkeys. Nature. 2016 Mar 17;531(7594):381-5.

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