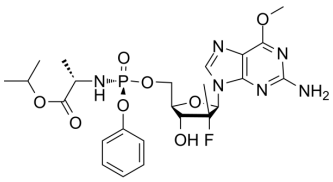
PSI-353661

Cat. No.:	HY-14391
CAS No.:	1231747-08-2
Molecular Formula:	$C_{24}H_{32}FN_6O_8P$
Molecular Weight:	582.52
Target:	HCV
Pathway:	Anti-infection
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	PSI-353661 (GS-558093) is a purine nucleotide NS5B polymerase inhibitor against HCV infection. PSI-353661 shows EC_{90}s of 8 nM and 11 nM for wild type and S282T resistant replicons of HCV. PSI-353661 can produce high concentrations of the active triphosphate in primary human hepatocytes[1][3].
IC_{50} & Target	NS5B polymerase[3]
In Vitro	PSI-353661 exhibits strong inhibition of HCV in the cell-based replicon assay, with EC_{90}s of 8 nM and 11 nM for wild type and S282T resistant replicons[1]. PSI-353661 (24 h) produces high concentrations of (0.44 mM) triphosphate (TP) level in primary human hepatocytes[1]. PSI-353661 (4 days) inhibits viral replication with EC_{50} and EC_{90} value of 0.0030 μM and 0.0085 μM for genotype 1b replicon cells[2]. PSI-353661 (8 days) shows little cytotoxicity in Huh7, HepG2, BxPC3, and CEM cells, with IC_{50} more than 80 μM[2]. PSI-353661 (8-160 nM, 2 weeks) clears HCV replicon RNA and prevents viral rebound[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PSI-353661 (50 mg/kg, p.o., together with 400 mg/kg of Telaprevir (HY-10235), daily for 4 weeks) is effective against human hepatocyte chimeric mice infected with HCV[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Human hepatocyte chimeric mice infected with HCV
Dosage:	50 mg/kg, together with 400 mg/kg of Telaprevir
Administration:	Oral administration (p.o.)
Result:	Achieved sustained eradication of the mutant virus or the end-of-treatment response. Reduced serum levels of HCV RNA.

REFERENCES

[1]. Wonsuk Chang, et al. Discovery of PSI-353661, a Novel Purine Nucleotide Prodrug for the Treatment of HCV Infection. ACS Med Chem Lett. 2010 Dec 17;2(2):130-5.

[2]. Furman PA, et al. Activity and the metabolic activation pathway of the potent and selective hepatitis C virus pronucleotide inhibitor PSI-353661. Antiviral Res. 2011 Aug;91(2):120-32.

[3]. Yugo Kai, et al. Emergence of hepatitis C virus NS5A L31V plus Y93H variant upon treatment failure of daclatasvir and asunaprevir is relatively resistant to ledipasvir and NS5B polymerase nucleotide inhibitor GS-558093 in human hepatocyte chimeric mice.

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