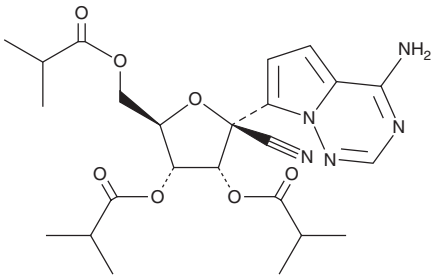
PRODUCT INFORMATION

GS-621763

Item No. 34125

CAS Registry No.:	2563617-99-0
Formal Name:	6-((1E,3Z,6Z,9Z)-pentadeca-1,3,6,9-tetraen-1-yl)tetrahydro-2H-pyran-2-one
Synonym:	GS-441524 *tris*-isobutyryl ester
MF:	$C_{24}H_{31}N_5O_7$
FW:	501.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 246 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

GS-621763 is supplied as a crystalline solid. A stock solution may be made by dissolving the GS-621763 in the solvent of choice, which should be purged with an inert gas. GS-621763 is soluble in organic solvents such as DMSO and dimethyl formamide. The solubility of GS-621763 in these solvents is approximately 10 mg/ml.

GS-621763 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, GS-621763 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. GS-621763 has a solubility of approximately 0.16 mg/ml in a 1:5 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

GS-621763 is an orally bioavailable prodrug form of the antiviral nucleotide analog GS-443902, which is also an active metabolite of remdesivir (Item No. 30354).[1,2] Upon intestinal absorption, GS-621763 is metabolized into the intermediate metabolite GS-441524 (Item No. 30469), which is then further metabolized to the active nucleotide triphosphate GS-443902 in cells where it induces RNA chain termination and inhibits viral polymerases.[2] It reduces the cytopathic effect of respiratory syncytial virus (RSV) in infected HEp-2 cells (EC_{50} = 0.26 µM), as well as reduces viral titers in Vero E6 cells infected with various clinical isolates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; EC_{50}s = 0.11-0.73 µM). GS-621763 (10 mg/kg) inhibits viral transmission in ferrets infected with the SARS-CoV-2 variant of concern (VOC) P.1, also known as the gamma variant.[2]

Reference

1. Mackman, R.L., Hui, H.C., Perron, M., *et al.* Prodrugs of a 1'-CN-4-aza-7,9-dideazaadenosine C-nucleoside leading to the discovery of remdesivir (GS-5734) as a potent inhibitor of respiratory syncytial virus with efficacy in the african green monkey model of RSV. *J. Med. Chem.* **64(8)**, 5001-5017 (2021).
2. Cox, R.M., Wolf, J.D., Lieber, C.M., *et al.* Oral prodrug of remdesivir parent GS-441524 is efficacious against SARS-CoV-2 in ferrets. *Nat. Commun.* **12(1)**, 6415 (2021).

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