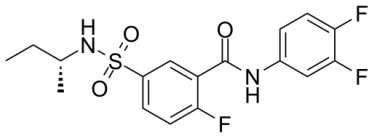
Data Sheet

Product Name:	AB-423
Cat. No.:	CS-0043473
CAS No.:	1572510-80-5
Molecular Formula:	$C_{17}H_{17}F_3N_2O_3S$
Molecular Weight:	386.39
Target:	HBV
Pathway:	Anti-infection
Solubility:	DMSO : ≥ 100 mg/mL (258.81 mM)



BIOLOGICAL ACTIVITY:

AB-423 is an inhibitor of **HBV capsid** assembly, and potent inhibits HBV replication with EC_{50}/EC_{90} of 0.08-0.27 μM/0.33-1.32 μM in cells. IC50 & Target: HBV capsid[1] **In Vitro:** AB-423 is an inhibitor of HBV capsid assembly. AB-423 shows inhibitory effect on rcDNA production in AML12-HBV10 and HepDE19 cells with EC_{50}s of □0.260 μM. AB-423 also suppresses cccDNA formation-dependent HBeAg production in the HepBHAe82 assay with an EC_{50} of 0.267 μM and inhibits HBV DNA levels in culture supernatants of HepG 2.2.15 cells with an EC_{50} of 0.134 μM. However, AB-423 has no cytotoxicity in any of the three cell lines[1]. **In Vivo:** AB-423 (30 and 100 mg/kg, p.o. bid) blocks HBV replication in a mouse model of HBV. AB-423 (100 mg/kg, p.o. bid) with entecavir (ETV, 100 ng/mg, qd, p.o.) or 0.1 mg/kg dose of ARB-1467 potently inhibits serum HBV DNA in an HDI model of HBV in immunodeficient NOD-SCID mice[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: AB-423 is dissolved in DMSO[1].[1]To test the compound combinations, **HepBHAe82 (50,000 cells/well)** are plated in 96-well tissue-culture treated microtiter plates in DMEM/F12 medium supplemented with 10% fetal bovine serum, 1% penicillin-streptomycin and tetracycline (1 μg/mL), and incubated in a humidified incubator at 37°C and 5% CO_2 overnight. On the next day, the cells are switched to fresh medium and treated with inhibitor A and inhibitor B, at concentration range in the vicinity of their respective EC_{50} values. The inhibitors are either diluted in 100% **DMSO** (ETV, TDF and **AB-423**) or growth medium (ARB-1467 and ARB-1740) and the final DMSO concentration in the assay is **≤0.5%**. The two inhibitors are tested both singly as well as in combinations determine their effects on inhibition of rcDNA production. The final DMSO concentration in the assay is 0.5%. The plates are incubated for 9 days in a humidified incubator at 37°C and 5% CO_2. Following a 9 day-incubation, medium is removed, and cells are subjected to RNA extraction to measure the cccDNA-dependent precore mRNA level[1].

Animal Administration: AB-423 is formulated in saline[1].[1]Mice[1]

Prior to start of treatment, 10 micrograms of the plasmid pHBV1.3 is administered to **NOD.CB17-Prkdcscid/J mice** via hydrodynamic injection (HDI; rapid high volume injection into the tail vein; n = 6 to 8 animals per group). This plasmid carries a 1.3-fold overlength copy of a HBV genotype D genome which, when expressed, generates hepatitis B viral particles and other HBV products. **AB-423** is administered via **oral gavage** at **30 or 100 mg/kg twice-daily for 7 consecutive days**, starting on Day 0. Entecavir (ETV) at 100 ng/kg once-daily for 7 consecutive days, starting on Day 0. ARB-1467 is administered as a single intravenous bolus tail vein injection at 0.1 mg/kg on Day 0. Blood is collected on Days 0 (pre-dose), 4 and 7 for HBV biomarker analysis. Serum HBV DNA concentration in mice is measured from total extracted DNA using a quantitative PCR assay using primer/probe sequences[1].

References:

[1]. Mani N, et al. Preclinical profile of AB-423, an inhibitor of Hepatitis B virus pgRNA encapsidation. Antimicrob Agents Chemother. 2018 Mar 19.

CAIndexNames:

Benzamide, N-(3,4-difluorophenyl)-2-fluoro-5-[[[(1R)-1-methylpropyl]amino]sulfonyl]-

SMILES:

O=C(NC1=CC=C(F)C(F)=C1)C2=CC(S(=O)(N[C@H](C)CC)=O)=CC=C2F

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