

Acoziborole

Catalog No: tcsc0016944



Available Sizes

Size: 1mg

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg



Specifications

CAS No:

1266084-51-8

Formula:

$C_{17}H_{14}BF_4NO_3$

Pathway:

Anti-infection

Target:

Parasite

Purity / Grade:

>98%

Solubility:

DMSO : ≥ 125 mg/mL (340.51 mM)

Alternative Names:

SCYX-7158;AN5568

Observed Molecular Weight:

367.1

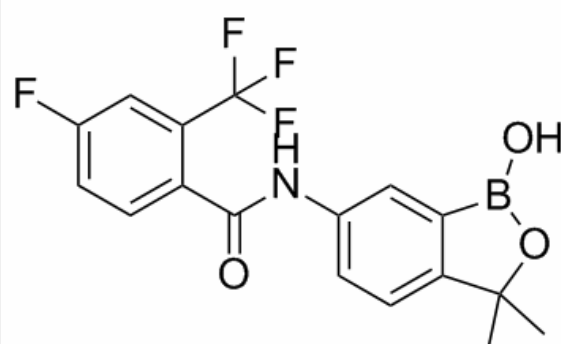
Product Description

SCYX-7158 is an effective, safe and orally active treatment for human african trypanosomiasis (**HAT**). In the ***T. b. brucei*** S427 strain, the **MIC** value for SCYX-7158 is 0.6 µg/mL.

IC50 & Target: MIC: SCYX-7158 (*T. b. brucei* S427 strain)^[1]

In Vitro: SCYX-7158 is active in vitro against relevant strains of *Trypanosoma brucei*, including *T. b. rhodesiense* and *T. b. gambiense*. In whole cell assays, SCYX-7158 exhibits potent activity against representative *T. b. brucei*, *T. b. rhodesiense* and *T. b. gambiense* strains. IC₅₀ values for SCYX-7158 are approximately 0.07 µg/mL to 0.37 µg/mL following incubation of the parasite strains with SCYX-7158 for 72 h. In the *T. b. brucei* S427 strain, the MIC value for SCYX-7158 is 0.6 µg/mL, approximately two times the IC₅₀ measured for this strain. In contrast to the potent activity of SCYX-7158 against trypanosomes, no significant inhibition of cell proliferation is observed in an in vitro mammalian cell (L929 mouse cell line) assay at drug concentrations up to 50 µg/mL. The potential for SCYX-7158 to inhibit cytochrome P450 (CYP) enzymes is evaluated using P450-Glo assays for the human isoforms CYP3A4, CYP1A2, CYP2C19, CYP2C9 and CYP2D6. The IC₅₀ values for SCYX-7158 in these assays are all above 10 µM^[1].

In Vivo: In uninfected mice, 4.3 mg/kg intravenous dose of SCYX-7158 show an apparent elimination half-life ($t_{1/2}$) of 26.6 h; systemic clearance (CL) of 0.089 L/h/kg; a volume of distribution (Vd_{ss}) of 1.69 L/kg and area under the concentration-time curve ($AUC_{0-24\ h}$) of 48 h•µg/mL. Following an oral dose of 13.4 mg/kg, which corresponds to the lowest efficacious dose in the murine stage 2 HAT model, SCYX-7158 is rapidly absorbed, as a C_{max} of 6.96 µg/mL is achieved in plasma at 6 h after dose, with an oral clearance (CL/F) value of 0.163 L/h/kg, an $AUC_{0-24\ h}$ of 82 h•µg/mL and absolute oral bioavailability of 55%. After a 26 mg/kg oral dose, which corresponds to the dose giving a 100% cure rate in the murine stage 2 HAT model, C_{max} increases to 9.8 µg/mL and the $AUC_{0-24\ h}$ is 113 h•µg/mL. In uninfected rats, following oral administration of SCYX-7158 at a nominal dose of 25 mg/kg (dose affording a 100% cure rate in mice), C_{max} increases approximately 2 fold more than that in mice (C_{max} =18.2 µg/mL) and $AUC_{0-24\ h}$, and hence oral clearance, improves approximately 4 fold ($AUC_{0-24\ h}$ 291 h•µg/mL and CL/F=0.092 L/kg/h). The time to maximum concentration is similar to that in mice (t_{max} =8 h). Uninfected male and female cynomolgus monkeys are treated with SCYX-7158 at 2 mg/kg (IV) on study day 1 and 10 mg/kg (NG) on study day 8. SCYX-7158 exhibits excellent plasma pharmacokinetics, with CL of 0.022 L/h/kg; Vd_{ss} of 0.656 L/kg and area under the concentration-time curve 78.8 h•µg/mL, and 94.4 for $AUC_{0-24\ h}$ and AUC_{0-inf} , respectively, following intravenous administration^[1].



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