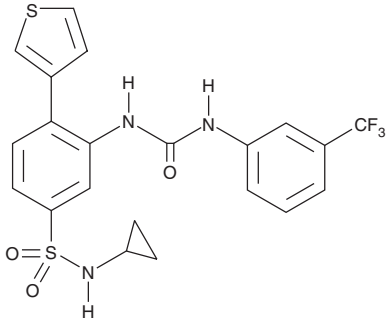
PRODUCT INFORMATION

AGI-6780

Item No. 14639

CAS Registry No.:	1432660-47-3
Formal Name:	N-cyclopropyl-4-(3-thienyl)-3-[[[[3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-benzenesulfonamide
MF:	$C_{21}H_{18}F_3N_3O_3S_2$
FW:	481.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 245 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

AGI-6780 is supplied as a crystalline solid. A stock solution may be made by dissolving the AGI-6780 in the solvent of choice. AGI-6780 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of AGI-6780 in ethanol is approximately 5 mg/ml and approximately 30 mg/ml in DMSO and DMF.

AGI-6780 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, AGI-6780 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. AGI-6780 has a solubility of approximately 0.2 mg/ml in a 1:4 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Isocitrate dehydrogenases (IDHs) are NAD^+ and $NADP^+$-dependent enzymes in the tricarboxylic acid cycle that catalyze oxidative decarboxylation of isocitrate producing α-ketoglutarate (2-OG) and carbon dioxide. IDH1 and IDH2 are mutated in >70% of lower grade gliomas.[1] The most common mutations map to arginine residues in the catalytic pockets of IDH1 (R132) or IDH2 (R140 and R172) and impart new gain of function catalytic activity leading to the NADPH-dependent conversion of 2-OG to 2-hydroxyglutarate (2-HG).[2-4] AGI-6780 is a potent, selective inhibitor of mutant IDH2 with an IC_{50} value of 23 nM.[5] It binds allosterically at the dimer interface of mutant IDH2-R140Q, inhibiting 2-HG formation in human glioblastoma U87 and TF-1 cells expressing IDH2-R140Q with IC_{50} values of 11 and 18 nM, respectively.[5] In primary human acute myelogenous leukemia cells, AGI-6780 suppressed cell growth and induced differentiation of immature blast cells toward macrophage and granulocytic lineages.[5]

References

1. Turcan, S., Rohle, D., Goenka, A., *et al. Nature* **483(7390)**, 479-483 (2012).
2. Reitman, Z.J. and Yan, H. *J. Natl. Cancer Inst.* **102(13)**, 932-941 (2010).
3. Dang, L., White, D.W., Gross, S., *et al. Nature* **462(7274)**, 739-744 (2009).
4. Koivunen, P., Lee, S., Duncan, C.G., *et al. Nature* **483(7390)**, 484-488 (2012).
5. Wang, F., Travins, J., DeLaBarre, B., *et al. Science* **340(6132)**, 622-626 (2013).

WARNING
THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA
This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent *via* email to your institution.

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