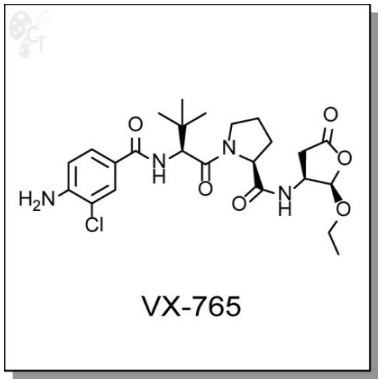
Product Specification Sheet

Product Name: VX-765

Catalog Number: C8976



Technical information:

Chemical Formula:	$C_{24}H_{33}ClN_4O_6$
CAS #:	273404-37-8
Molecular Weight:	509
Purity:	> 98%
Appearance:	white solid
Solubility:	Soluble in DMSO up to 50 mM
Chemical Name:	(S)-1-((S)-2-(4-amino-3-chlorobenzamido)-3,3-dimethylbutanoyl)-N-((2R,3S)-2-ethoxy-5-oxotetrahydrofuran-3-yl)pyrrolidine-2-carboxamide
Storage:	Store solid powder at 4°C desiccated; Store DMSO solution at -20°C.
Shelf Life:	In the unopened package, powder is stable for 1 year and DMSO solution is stable for 6 months under proper storage condition.

Handling:

- To make 10 mM stock solution, add 0.196mL of DMSO for each mg of VX-765.
- For DMSO solution, briefly spin the vial at 500 rpm in a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity:

VX-765 is an orally-available prodrug of VRT-043198, an inhibitor of interleukin-converting enzyme / caspase-1 subfamily caspases. VRT-043198 shows Ki values of 0.8 nM and <0.6 nM for ICE/caspase-1 and caspase-4, respectively, with >100-fold selectivity over other non-ICE subfamily caspases. VRT-043198 showed no significant activity towards trypsin or cathepsin B. (1)

VRT-043198 inhibits IL-1b release from both PBMCs and whole blood with IC50 values of 0.67 and 1.9 uM, respectively. Additionally in stimulated PBMCs, VRT-043198 dose-dependently inhibited IL-1b, IL-18, and IFN-g, without affecting TNF-a release. In a hypoxia-induced apoptosis assay employing the NT2 human neuroblastoma cell line, VRT-043198 did not alter ischemia-induced apoptosis up to concentrations of 100 uM. (1)

According to Vertex's news release , VX-765 has been shown to inhibit acute seizures in preclinical models of acute epilepsy and has shown activity in preclinical models of chronic epilepsy that do not respond to standard anti-epileptic drugs. (2)

Reference:

1. Wannamaker et al., (S)-1-((S)-2-{[1-(4-Amino-3-chloro-phenyl)-methanoyl]-amino}-3,3-dimethyl-butanoyl)-pyrrolidine-2-carboxylic acid ((2R,3S)-2-ethoxy-5-oxo-tetrahydro-furan-3-yl)-amide (VX-765), an Orally Available Selective Interleukin (IL)-Converting Enzyme/
Caspase-1 Inhibitor, Exhibits Potent Anti-Inflammatory Activities by Inhibiting the Release of IL-1b and IL-18. J. Pharmacol. Exp. Ther. 2007, 321(2), 509-516. Pubmed ID: 17289835

2. http://investors.vrtx.com/releasedetail.cfm?ReleaseID=555967

To reorder: http://www.cellagentech.com/VX-765/
For Technical Support: technical@cellagentech.com

Chemicals are sold for research use only, not for clinical or diagnostic use.