



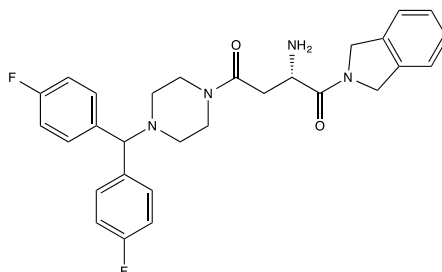
Catalog #10-4584

1G244

CAS# 847928-32-9

Lot # FBA3090

(S)-2-Amino-4-{4-[bis-(4-fluorophenyl)-methyl]piperazin-1-yl}-1-(1,3-dihydro-isoindol-2-yl)-butane-1,4-dione; PTX-1210



1G244 is a potent and selective inhibitor of the prolyl dipeptidases DPP8 ($IC_{50} = 14$ nM) and DPP9 ($IC_{50} = 53$ nM).^{1,2} It does not inhibit DPP2, DPP4 or fibroblast activation protein (FAP) at 100 μ M.^{1,2} 1G244 is a slow binding competitive inhibitor of DPP8 but a competitive and reversible inhibitor of DPP9.² Inhibition of DPP8/9 by 1G244 has been shown to cause pro-caspase-1-dependent pyroptosis in macrophages and monocytes.³ 1G244 also induced cell death in DPP8/9 knockout cells at higher concentration indicating there may be some off-target effects.³ 1G244 blocks adipogenesis in preadipocyte 3T3-L1 and 3T3-F422A cells.⁴ DPP8/9 inhibition attenuates PPAR γ 2 induction during preadipocyte differentiation.⁴ Because of its inhibitory effects on pro-inflammatory macrophages, 1G244 inhibition of DPP8/9 has been examined as a potential therapy for reducing atherosclerosis and/or in the prevention of plaque rupture.^{5,6} Cell permeable.

- 1) Jiaang *et al.* (2005), *Novel isoindoline compounds for potent and selective inhibition of prolyl dipeptidase DPP8*; Bioorg.Med.Chem.Lett. **15** 687
- 2) Wu *et al.* (2009), *Biochemistry, pharmacokinetics, and toxicology of a potent and selective DPP8/9 inhibitor*; Biochem.Pharmacol. **78** 203
- 3) Okondo *et al.* (2017), *DPP8/9 inhibition induces pro-caspase-1-dependent monocyte and macrophage pyroptosis*; Nat.Chem.Biol. **13** 46
- 4) Han *et al.* (2015), *Inhibition of dipeptidyl peptidase 8/9 impairs preadipocyte differentiation*; Sci.Rep. **5** 12348
- 5) Matheeussen *et al.* (2013), *Dipeptidyl peptidases in atherosclerosis: expression and role in macrophage differentiation, activation and apoptosis*; Basic Res.Cardiol. **108** 350
- 6) Waumans *et al.* (2016), *The Dipeptidyl Peptidases 4,8, and 9 in Mouse Monocytes and Macrophages: DPP8/9 Inhibition Attenuates M1 Macrophage Activation in Mice*; Inflammation **39** 413

PHYSICAL DATA

Molecular Weight:	504.57
Molecular Formula:	C ₂₉ H ₃₀ F ₂ N ₄ O ₂
Purity:	>98% by HPLC
	NMR: Conforms
Solubility:	DMSO (>20mg/mL)
Physical Description:	Off-white solid
Storage and Stability:	Store as supplied at -20°C for up to 1 year from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 2 months.

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