

**P004** Bivalent GPCR ligands  
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A series of bivalent  $\beta_2$ -adrenergic antagonists containing between 2 and 12 polyethylene glycol linker units were designed and synthesised on the basis of a model of the receptor dimer and were tested for their pharmacological activity. None of the bivalent antagonists showed agonistic activity. An unusual relationship between the length of the linker and the potency of the bivalent ligand was observed. Moreover, for compounds with linker length 4 and 5, unusual behaviour was observed, namely that the affinity of the antagonists for the receptor increased as the concentration increased. Molecular modelling, has been used to build models of the  $\beta_2$ -adrenergic receptor, to assess the utility of the receptor in virtual screening and to address the binding modes of the bivalent ligands. The molecular modelling indicates that the compounds bind entirely with a single receptor, rather than bind to 2 receptors, but the role of dimerization in conferring the enhanced potency at the optimal linker length is discussed.