Title: **Bivalent ligands as a paradigm of GPCR oligomer selective ligands.**

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G protein-coupled receptors (GPCRs) are a large family of receptors embedded in the cellular membrane of many living beings. These receptors are essential in many of the processes of signalling and regulation of these cells and often can be found forming chains (or oligomers) with other GPCRs. This binding gives rise to heteromers, in the case of the binding between receptors of different types, or to homomers, in the case of two monomers of the same receptor, in which the two receptors that form these complexes interact with each other modulating the affinity of the agonists that bind with each receptor. In recent years, it has been shown that these interactions between receptors are involved in many pathologies such as Parkinson's disease, restless leg syndrome (RLS), addictive processes, Huntington's disease, and a long list of others. This means that the study of the formation and interaction of these oligomers is a therapeutic target today.

Bivalent ligands are being a potential pharmacologic tool for studying the structure and activity of these GPCR complexes. These bivalent ligands have in their structure agonists or antagonists' pharmacophores of the receptors with which a given bivalent ligand must bind. This fact favours that the ligand binds selectively to a certain complex and not to others that form a certain receptor, thus reducing the side effects of its possible therapeutic application.

In this work, an exhaustive research is made of how the market for bivalent ligands is today, which ones have been biologically proven to work, how their structure should be, what pathologies they affect and how their study progresses to be able to propose a head strategy where this path of research should be followed.