Ligand-biased signaling could have a significant impact on drug discovery programs in the pharmaceutical industry. As such, many investigators and screening campaigns are now being directed at a larger section of the signaling responses downstream of an individual G protein-coupled receptor. Biosensor-based platforms have been developed to capture signaling signatures. Despite the ability to use such signaling signatures, they may still be particular to an individual cell type and thus such platforms may not be portable from cell to cell, necessitating further cell-specific biosensor development. We have developed a complementary strategy based on capturing receptor-proximal conformational profiles using intra-molecular BRET-based sensors composed of a Renilla luciferase donor engineered into the carboxy-terminus and CCPGCC motifs which bind fluorescent hairpin arsenical dyes engineered into different positions into the receptor primary structure. I will discuss the design and optimization of such sensors to capture ligand bias and receptor dimerization-specific conformational crosstalk.