The aim of the Project is to develop a group of non-basic ligands of serotonin receptor 5-HT_7 with improved metabolic stability, derivatives of 2-(6-oxo-3-phenyl-1,6-dihydropyridazin-1-yl)-N-phenylacetamide. Both of the above-mentioned compounds properties are of great importance in terms of development of new biologically active substances. The former one (low basicity) can help in getting rid of side effects, whereas metabolic stability is important for inducing biological response prior to compound decomposition.

The Project will use the state-of-the art computational strategies, being now the inherent part of every stage of drug design pipelines. Their application is aimed to minimize the time and costs and maximize the effectiveness at the same time the process of search for new biologically active substances. Various methods help in the identification of new potentially active compounds, optimization of their physicochemical and pharmacokinetic profiles, but the important step of data management also cannot be neglected. This widespread use of computational methods gave roots to the field of computer-aided drug design (CADD).

The two most popular paths of the search for new ligands involve their search in various databases of existing compounds or their *de novo* generation using various combinatorial approaches. In the Project, both of these strategies will be used. Combinatorial approaches will involve simple changes of substituents, and the application of machine learning methods to optimize chemical composition of compounds. The compounds activity towards 5-HT_7R will be evaluated in both *ligand-* and *structure-based* approaches. Moreover, methodologies for *in silico* evaluation of metabolic stability will be developed. In addition to assessment of the considered parameter, the tool that will developed within the Project will provide the set of structural modifications optimizing the compound structure in terms of metabolic stability. Compounds with the highest potential of possessing desired biological activity and the best scores in the metabolic stability assessment will evaluated in *in vitro* experiments in terms of their affinity to 5-HT_7R and metabolic stability. The latter parameter will be evaluated at the Faculty of Pharmacy University of Bari, which is the Partner in the Project.

The core of computational methodologies used in the Project will be machine learning - extremely important tools in the era of the exponential growth of the amount of information. As they are able to deal with large-scale, high-dimensional data, their application in various fields will get wider. As the predictions made by machine learning methods can often reduce laboratory experiments, their application in drug design campaigns can lower the costs of the search for new potential medicines. They are often used in drug design pipelines, not only for the search of new potentially active ligands, but also for the optimization of their physicochemical and pharmacokinetic properties, and for such tasks they will be also applied in the presented Project.