OBJECTIVE OF THE RESEARCH WORK

To meet the expanding need for rapid and cost-effective analysis of drugs in biological matrices, suitable methods have to be made available. The ideal bioanalytical method should be able to quantitate desired level of analyte in intended matrix in a reproducible manner using the lowest sample volume possible. The method should be simple and robust meeting all the performance requirements as per validation guidelines.

This research work intends to develop fast and efficient methods for drugs from different therapeutic categories and validate them for the fundamental parameters of precision and accuracy, specificity, recovery, matrix effect and stability. These bioanalytical methods can be then applied for analysis of pharmacokinetic studies of these drugs.

- **PBG167** is a drug prescribed for the treatment of Alzheimer’s disease. Bioanalytical method with quantification ability lower than 0.5ng/ml is required to obtain the plasma concentration profiles in human subjects in pharmacokinetic studies. Reported methods of PBG167 have used HPLC based assays which lacked the required sensitivity and had longer runtimes. The LCMS based assays also had a runtime of around 3 minutes. Hence, a sensitive UPLC-MS/MS method with a shorter run time will be developed with the ability to quantitate upto 0.2ng/ml PBG167 in plasma. The method will be validated fully as per US FDA method validation guidelines.

- **PBG172** is used in the treatment of non-small cell lung cancer and pancreatic cancer. There are few reported methods of PBG172 in human plasma. The methods have used a larger sample volume for processing and estimation and had longer run-times. A sensitive bioanalytical method for estimation of PBG172 is required to support its pharmacokinetic studies. Hence, a UPLC-MS/MS method will be developed with single step extraction method using 125µl plasma combined with sensitive mass detection of the drug upto 20ng/ml. It will be aimed to develop the method with a shorter run time. The developed method will be validated according to US FDA method validation guidelines.

- **PBG187** is a corticosteroid based pro-drug with anti-inflammatory and immunosuppressive activities. Pharmacokinetic studies of PBG187 require the measurement of its active metabolite in human plasma below1ng/ml. Reported methods of PBG187 have either used HPLC assays with low sensitivity or LC-MS based assays with tedious sample preparation methods.
Hence, a UPLC-MS/MS method will be developed with an easier sample extraction procedure combined with sensitive mass detection of the metabolite up to 0.5 ng/ml. UPLC as the frontend inlet will help in reducing the runtime per injection thus increasing the speed of the analysis. The optimised method will be validated as per US FDA method validation guidelines.