INTRODUCTION
The Prestwick Chemical Library® (PCL) is Prestwick’s flagship product dedicated to screening. It is a collection of 1280 molecules comprising 100% approved drugs (FDA, EMEA and other agencies) selected for their high chemical and pharmacological diversity. These off-patent drugs have known bioavailability and safety data in humans are available. The PCL was designed to reduce the risk of “low quality” hits and therefore of the cost of the initial screening, and appears to be an efficient smart library for hit discovery. The library is used:
- primarily for molecular and phenotypic screening in order to repositioning
- for finding hits which may enter an optimization program
- for assay validation
- more recently for the finding of stem cell differentiation modulators
The PCL comes in different formats with a fully-annotated database.

PHYSICOCHEMICAL PROPERTIES AND CHEMICAL DIVERSITY
Analysis of the physicochemical properties shows that 83% of the library compounds match with Lipinski drug-like parameters. In whereas clogP and MW cover a large range of value, half of the compounds respect Hans and Oprea lead-like parameters used for the lead selection process. Chemical diversity of a library could be assessed by using the Delimited Reference Chemical Subspaces (DRCS) method. The DRCS analysis of the PCL revealed that it covers a well-distributed chemical space compared to other libraries.

PHARMACOLOGICAL DIVERSITY
Analysis of PCL therapeutic data (WHO ATC classification and therapeutic class distribution) shows that the library covers all main ATC groups. More than half of the drugs within the library are dedicated to CNS, cardiovascular, metabolism and endocrine diseases. Associated pharmacological targets were identified using ChEMBL database and revealed that most of the targets are related to enzymes and GPCRs. More than 100 different targets were found in the PCL: Histamine H1, H2 receptors, voltage-gated sodium channel and cytochrome P450 were the most represented targets.

FORMATS AND DATABASE
The PCL is delivered with a fully-annotated database available in several electronic formats (SDF, XLS, DB, DWAR). The database includes information such as structure, chemical name, literature reference, physicochemical properties, targets, therapeutic class and effect, pharmacokinetics data and reported side effects. The database has been recently highly updated by using several public sources.

DRUG REPURPOSING
Finding new uses for old drugs can be an efficient strategy in drug discovery/development. The significant advantage is that since the repositioned drug has fully evaluated, safety data are known and so the early cost and time needed to bring a drug to market could be spared. Over the past decade, the PCL use has proven to be a valuable tool for drug development (160+ bibliographic references) and has allowed to identify new indications and mechanisms of action for several PCL compounds (see table).

CONCLUSION & PERSPECTIVES
The ensuing poster was performed to highlight the benefits of the Prestwick Chemical Library®. The PCL is a screening collection arising from medicinal chemistry expertise that presents a large degree of chemical and pharmacological diversity despite the relatively small number of compounds. Over the past 16 years, the PCL use has shown high efficiency for the identification of new hits and biochemical mechanisms. The PCL database represents so far the best and most annotated database delivered with a screening library.

REFERENCES
5. Wiley Online Library.