Developing a brand-new drug takes an enormous amount of time, money and efforts. However, there is a wide consensus that new drugs in many therapeutic areas are urgently needed, meaning that it is crucial to advance strategies to reduce time frame, decrease costs and improve success rates.

The most fruitful basis for the discovery of a new drug is to start with an old drug. — Sir James Black, 1988 Nobel Prize

Disillusioned with HTS and struggling to bring new chemical entities to market, many companies are turning back to Sir James’ wisdom. In this perspective, we support strategies such as drug repurposing, fragment-based drug discovery (FBDD) and selective optimization of a side activity (SOSA approach), a range of valuable tools based on marketed drugs that have been developed at Prestwick. The design, properties and advantages of these tools are presented and discussed in the present poster.

**Drug Repurposing**

**Prestwick Chemical Library**: A High Valuable Tool

What is Drug Repurposing?

Repurposing is defined as developing new uses for drug beyond its original approved indication.

Selected by a team of medicinal chemists and pharmacists for high chemical and pharmacological diversity, as well as for known bioavailability and safety in humans, the Prestwick Chemical Library is a unique collection of 1,280 off-patent small molecules, 95% approved drugs.

**Repurposing in Multiple Therapeutic Areas**

- 1978 FDA approved: Antiepileptic CNS
  - Valproic acid
  - Phase II, 2017: Head and neck cancer Oncology
  - Phase II, 2018: HDAC inhibitor Anti-infective

**Repurposing of a Withdrawn Drug**

- Approved in 1950s: Antihistaminic, Sedative
  - Thalidomide
  - 1998 FDA approved: Treat leprosy
  - 2012 FDA approved: Multiple myeloma

**Repurposing as Orphan Drug**

- 2008 FDA approved: Cholesterol lowering effects
  - Simvastatin
  - Duchenne Muscular Dystrophy: phase III
  - 2007 EMA approved: Leber’s hereditary optic neuropathy

**SOSA (Selective Optimization of Side Activity) Approach**

**Panel of Prestwick Drug Libraries: Key Tools**

- Time and cost shortened
- Free space for patenting
- Increased probability of obtaining safe, soluble and oral bioavailable leads

Prestwick Chemical has developed a range of valuable drug libraries:

- **Prestwick Chemical Library**: 1,280 drugs with high pharmacological diversity
- **Prestwick CNS Drug Library**: 320 drugs with proven pharmacological effects on the central nervous system
- **Prestwick GPCR Drug Library**: 265 drugs interacting primarily with GPCRs
- **Prestwick Ion Channel Drug Library**: 106 drugs interacting primarily with ion channels

**Example: Inversion of the Activity Profile of Minaprine**

- Minaprine (Cantor®) = Prestw-65
- Modified Analogue: Dopaminergic: 0 Serotoninergic: 0 Cholinergic: ++

**Fragment Based Drug Discovery**

**Prestwick Drug-Fragment Library: An Innovative Tool**

What is FBDD?

It starts with identification of small molecules that bind with weak affinity but high quality interactions to the target. It is followed by optimization to low compounds with high affinity and selectivity.

Prestwick Chemical medicinal chemists designed a unique collection of 1,464 small molecules (MW<300) arising from the smart fragmentation of 1,500 approved drugs (up to year 2016).

**Spectacular Occurrence of Prestwick Fragments in 2017 FDA-Approved Drugs**

- 85% of the 2017 FDA-approved*164 drugs contain at least one of the Prestwick Drug-Fragments confirming that expansion of drug fragment hits is likely to give molecules with appropriate ADME properties during lead optimization.

**Spectacular Occurrence of Prestwick Fragments**

Small antibiotic drug Sulfabenzamide (Prestw-Frag-2345), FDA approved in 1945, is present as core fragment in Venetoclax, an aneuploidy agent approved by FDA in 2016.

**Conclusion**

In drug discovery process, starting with approved drugs or fragments of approved drugs increases hit quality and the probability of obtaining safe, soluble and oral bioavailable leads. To support this strategy, Prestwick Chemical has developed a wide panel of compound libraries with the Prestwick Chemical Library® and the Prestwick Drug Fragment Library as flagship products.