Key Finder™ Libraries

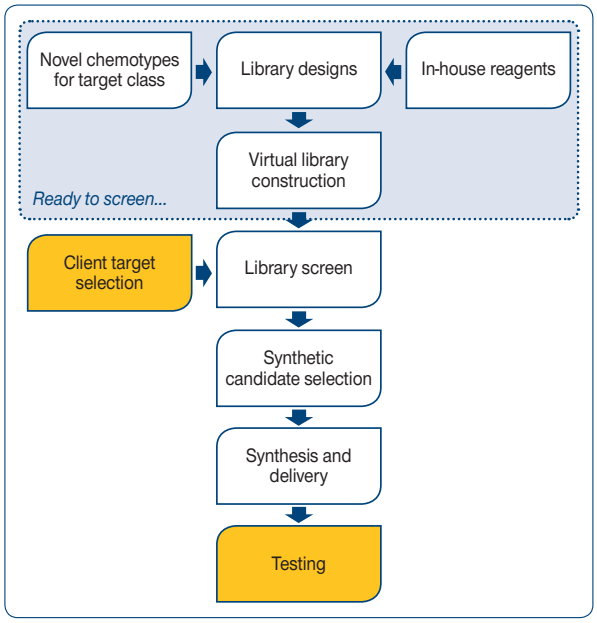
Key Organics
Chemistry | Innovation | Quality

PROSARIX

The Key Finder™ Concept

Key Finder™ libraries are a new product and service for use in drug discovery. These 'ready to run' virtual libraries with follow-on synthesis combine a number of advantageous features:

- Novel and large drug-like chemistry space designed for a specific target family;
- Library designs based on in-house reagents and templates, enables rapid synthesis;
- Virtual screen of library against client's requested pharmacology profile;
- Design and synthesis of compounds delivered to client;
- Provides unique service capability for target class - bespoke design and chemistry.



Library design is based on state of the art modelling capabilities:

- Using target structure and related family homology models;
- Designed to be broad enough to be relevant for different receptor subtypes;
- Final novel chemotypes selected based on predicted receptor affinity from a large panel; and
- Many novel chemotypes (~10) in a final target class library.

Key Finder™ provides considerable benefits when compared to conventional hit finding:

- ☑ Integrated design and synthesis workflows from inception
- ☑ Ready-to-run receptor models provide basis for rapid *in silico* screening for desired subtype pharmacology
- ☑ Tractable chemistry routes support rapid delivery of designed compounds:
  - novel drug-like chemistry space
  - enables expedient transition to LO phase
- ☑ Patentable chemotypes enabling IP generation, and
- ☑ Integrated *in silico* design and chemistry team to drive your project provides basis for rapid follow-on LO.

Chemistry Deliverables:

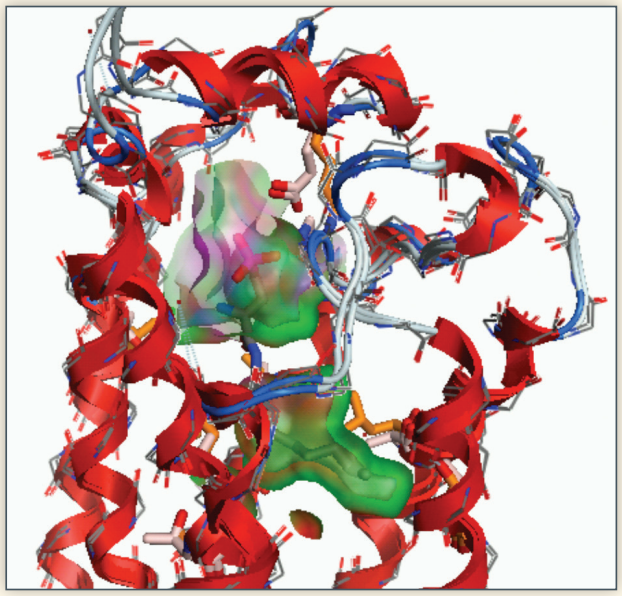
- Typically 20 – 100+ compounds in size (client determined)
- Designed to have drug-like properties
- 1-50 mg of isolated material (for in vitro screening and/or early ADME assessment)
- ≥95% chemical purity by LC-MS and 1H NMR.

Spingosine Phosphate Receptor Key Finder™ Library

S1PR Library

The sphingosine-1-phosphate receptor subfamily comprises five members (S1P1-5).

S1PR agonism has demonstrated therapeutic relevance for inflammatory conditions such as multiple sclerosis and Fingolimod is the first S1PR drug of this class to be approved. Significant research is now focussing on exploring the therapeutic potential of the different S1PR subtypes, with both selective or partially selective agonist and antagonists. S1P receptors are class A GPCRs and recently (2012) a crystal structure of S1P1 bound to an antagonist was solved. This template enables the accurate modelling of antagonist states of S1P2-5 subtypes as well as predictions of the activated receptor conformations.



For the S1PR Key Finder™ library, S1P2-5 receptor models were constructed and some have been validated by the docking performance of known modulators before being used to screen prospective chemotypes as fragments across the subtypes (agonist and antagonist forms). High scoring novel chemotypes have then been decorated using virtual library schemes with Key Organics' in-house reagents.

S1PR Library Description

The S1PR Key Finder™ library consists of:

- >800K enumerated compounds
- 10 different chemotypes

Compounds have been filtered according to the following property space:

- MW range <500
- PSA <140Å^2
- 100% drug-like by Lipinski criteria
- 68% lead-like by Oprea criteria

About us

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Key Finder™ libraries have been developed by Key Organics in partnership with Prosarix Ltd. Key Organics are a leading provider of chemistry services based in Camelford, UK. Prosarix are a specialist provider of computational chemistry services based in Cambridge, UK, with considerable experience in delivering hit finding and lead optimisation capabilities to a wide range of targets/indications. Prosarix and Key Organics have worked together on a number of projects and have now formed a partnership to provide a cutting edge service to support Key Finder™ library screening and implementation.

What we offer

A rapid *in silico* screen of the Key Finder™ libraries for the desired customer target profile leading to the identification of and synthesis of a focused library of hit candidates. Patentable chemotypes enabling IP generation. Libraries, or particular chemotypes within the library are accessible on a non-exclusive or exclusive basis. Follow on Lead Optimisation support is available through Prosarix and Key Organics.

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