Key Organics

Chemistry | Innovation | Quality

Key Organics Fragment Services

BIONET

Fragment Libraries

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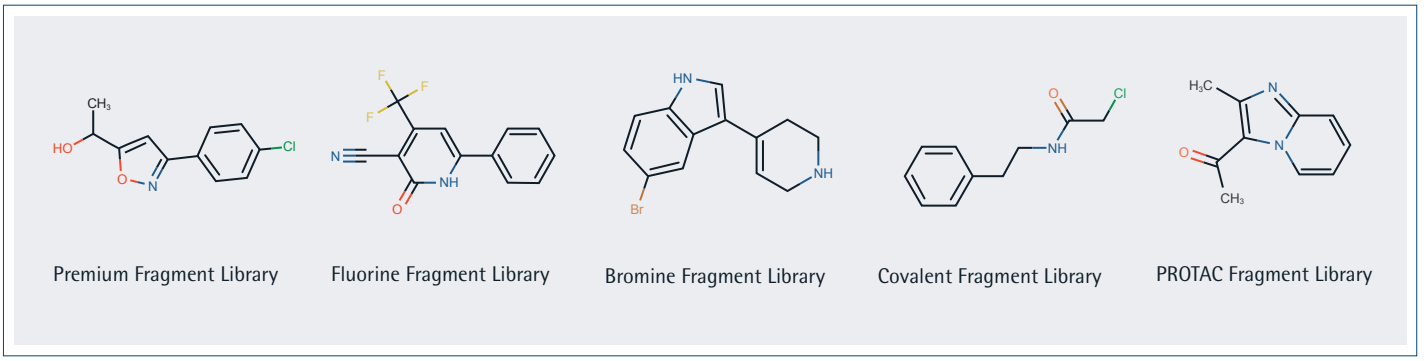
Your Partner for Fragment-Based Drug Discovery (FBDD)

Use of a fragment-based lead generation strategy in a discovery program is now a well-established option for modern biotech and pharmaceutical companies. Multiple drugs have received regulatory approval which has their origins from a fragment-based approach, and there are many more compounds in industry drug pipelines at various stages of preclinical and clinical development. Key Organics has a long history of providing support to teams working on Fragment-Based Drug Design (FBDD) programs, ranging from provision of the original fragment libraries used in screening, through the fragment growth and lead optimisation process, all the way to scale-up and beyond.

BIONET Fragments and Libraries

Key Organics offers more than 44,000 fragments that can be individually selected, allowing researchers to build bespoke fragment sets of size and composition best suited to their research needs and Key Organics can also assist in the selection of diverse subsets. This collection of fragments provides compounds for use in fragment-based screening and drug discovery using high-throughput X-ray crystallography, NMR, SPR and high concentration bioassay methodologies. Key Organics also have the following collection of highly curated Fragment libraries:



Fragment Screening

NMX Research and Solutions has established a Fragment Based Discovery Platform, which combines Key Organics BIONET and NMX proprietary fragment collections with high-throughput biophysical screening technologies, to rapidly identify and characterize fragment hits. Applicable fragment libraries are screened against your target by 1H and/or 19F NMR and are ranked according to consensus binding between different NMR experiments. During follow-up singleton confirmation studies, binding scores are generated and are used to rank-order the hits by binding affinity.

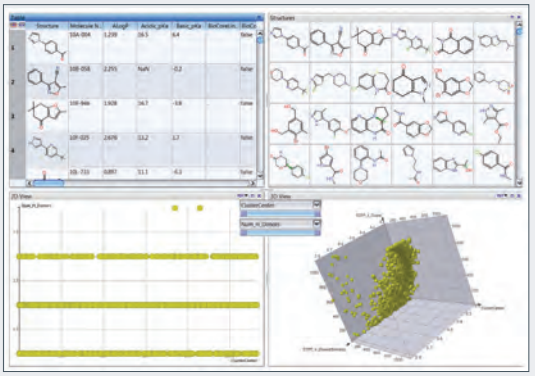
Fragment hits and SAR by catalogue

Key Organics can certainly help regarding following up on any hits, whether that is via SAR by catalogue, where we can search BIONET and commercial space for analogues of compounds of interest or via custom or contract synthesis. For those analogues available through other vendors, we can offer a compound management service to provide the following services:

- Compound Procurement
- Compound Weighing
- Compound Dissolution
- Automated Reformatting & Plating
- Compound Shipping & Logistics to in-house & partner testing laboratories
- Quality Control

Computational Chemistry

Key Organics can filter compound libraries using a range of software tools. These filtering tools can be applied to generate diverse sets of building blocks of a particular functional class for a customer's proposed library synthesis and also to generate filtered, diverse libraries of screening compounds for new lead generation or SAR by catalogue. We can also enumerate virtual libraries using this approach which can be a powerful tool in designing bespoke sets of compounds for Hit to Lead SAR exploration.



Our capabilities include:

- Detecting and filtering Pan Assay Interference compounds (PAINS)
- Detecting and filtering compounds with undesirable, toxic or reactive moieties
- Generating clusters and diverse sets of compounds
- Calculating physiochemical properties

Key Organics Synthetic Chemistry Services

We have worked on thousands of demanding projects for the world's leading Life Science companies. From hit identification to pre-clinical development – we have successfully delivered value through our innovative approach, creativity and product supply.

Hit-to-Lead

We have undertaken numerous projects involving the design and synthesis of novel molecules, either singletons or using our parallel chemistry techniques to prepare focused arrays (typically 10 to 50 compounds at 1 - 50mg scale) with chemical purities of ≥95% (by LC-MS and NMR) for in vitro screening and ADME profiling.

Quality

We have an internal QMS system including verified equipment servicing and calibration, goods in/out SOP/QC and separate storage for different projects/clients.

Compound Storage and Stability Testing

Using our storage space and facilities, Key Organics can store your powder and liquid samples, format them on demand as required and distribute them to your site locations around the world. This service eliminates the need to have an organized compound repository on site while keeping your compounds easily accessible. Our storage conditions range from storage at ambient temperature to a refrigerated environment. We can also perform regular QC checks to monitor compound integrity during storage and provide valuable stability data.

Lead Optimisation

We have extensive experience in collaborative R&D where we move customer projects forward through the milestones of Lead Optimisation. We add value through the analysis of data and provide rational suggestions on future targets using computational tools such as Data Warrior. This is further supported by our expertise in synthesis which can drive target selection. Our approach is focused on enhancing potency, improving physico-chemical properties and metabolic profile with the ability to build a strong IP position. Our project management structure is highly flexible, and we can respond rapidly to project changes. This approach coupled with a high level of productivity allows for a robust and efficient design/make/test cycle to be established.

In later Lead Optimisation, our team has great experience in the synthesis and investigation of more challenging chemistry as the SAR becomes understood more clearly and the need for more "bespoke" compounds becomes clearer as well as establishing early route improvements for pre-candidate compound batches. We also have in depth experience of the synthesis of project support compounds such as deuterium and 13C labels for PK/PD studies and synthesis of competitor compounds to assist in profiling and benchmarking.

TopiVert

> I have been extremely impressed by Key Organics' professionalism and candour during separate multi-gram re-synthesis and route development projects carried out recently. In particular, Key communicated clearly and rapidly with me when any obstacles to project delivery were encountered. Their swift and frank communication gave us time to jointly devise solutions which ensured that objectives were achieved while working to tight deadlines. Key's ability to formulate innovative routes to important organic compounds is also first rate. In this regard, they dramatically improved the availability of one of our crucial intermediates by developing some neat chemistry that relied upon unconventional thinking.

Dr Matthew Fyfe,
Head of Chemistry, TopiVert

Synthetic Chemistry

Our team of highly experienced chemists have extensive synthetic organic chemistry capabilities and expertise that cover the following areas:

- Multi-step complex custom synthesis
- Asymmetric synthesis
- Focused small library synthesis
- Vast hydrogenation/carbonylation expertise
- Heterocyclic chemistry
- Synthesis of literature standards
- Stable labelled compounds
- Pro-drug and linker synthesis
- Manufacturing impurities and metabolites
- Early process development
- Scale up lab to 25 litres

Process Development & Scale-up Service

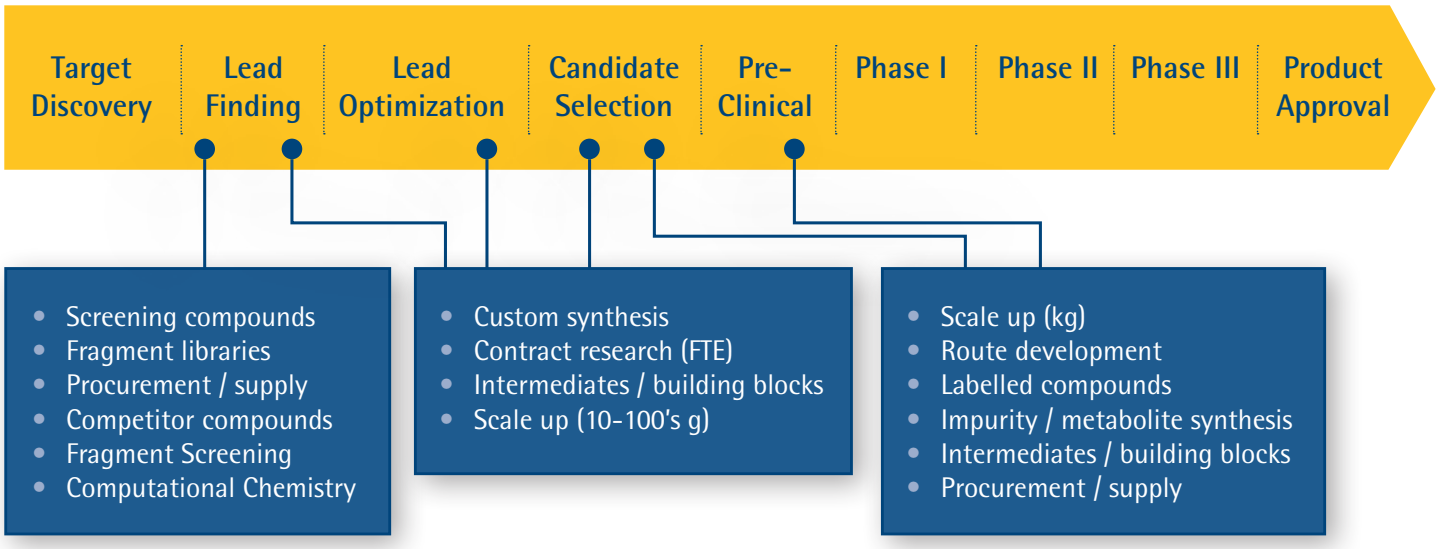
Key Organics has supported many drug discovery programs, from hit validation to preclinical studies. We have particular expertise in the scale-up of synthetic routes to prepare multigram quantities of a lead compound for further studies. As many of our customers work to tight deadlines, we seek to optimise the efficiency of a scale-up route by reducing the number of steps and finding alternatives to chromatographic purification. Our chemists work closely with our in-house analytical team to ensure that final compounds meet or exceed the purity specification required by the customer, we can also provide SDS, BSE/TSE, GMO statements as needed by the client.

We have in house experience of synthesizing various salts of the desired compound to aid salt screening and polymorphism studies.

Our capabilities include:

- Process Chemistry R&D to deliver robust routes
- Scale-up of intermediates and final compounds (Kg scale)
- Synthesis of development quantities of intermediates and of final compounds
- Full reaction profiling
- Production of the necessary documentation to assist the transition into GMP manufacture
- Procurement

Drug Discovery Process Map



Key Organics Facts:

Who are we?

An international CRO based in the UK with over 35 years expertise in synthetic organic chemistry.

Our customers

Our customers range from large Pharma and Agrochemical companies, Medium sized Biotechs and Academic groups - as well as virtual organisations and Start-ups.

Our Services

We offer a wide-range of bespoke chemistry solutions, from the custom synthesis of a single compound to multiple, long-term FTE projects.

Flexibility

We work closely with our customers through the entire process – especially as project milestones often change and resources must be adjusted along the way.

Why work with us?

With established fragment libraries, an extensive BIONET product portfolio and a proven track record in synthetic organic chemistry, Key Organics is able to support your discovery and development chemistry needs. Our project managers and scientists are highly experienced at managing complexity. We utilise ELN, Datawarrior and other software tools to facilitate information exchange.

Quality control

Our Process Development and Scale up Service is supported by Key Organics analytical services. Compounds can be QC checked by any combination of LC-MS, NMR, GC or KF to ensure they meet the required purity and to confirm the correct structure.

Our dedicated team of experienced and highly qualified staff can provide the following services:

- Compound identification and structure elucidation
- Compound purity screening
- Impurity identification and isolation
- Reaction profiling
- Compound purification
- HPLC and GC method development and/or optimisation

Our analytical department is equipped with the following instrumentation:

- NMR: Bruker 400MHz AVIII NMR equipped with a 1H/13C multinuclear probe capable of performing routine 1D experiments plus variable temperature experiments
- LC/LCMS: Agilent 1260 LC multiple wavelength UV/Vis detector, ELSD, 6130 Single Quadrupole MS, Agilent 1260 LC infinity II with IQ MS and Agilent 1100 HPLC
- Gas Chromatography: Agilent 7890 GC, with flame ionisation detector
- DSC 25: TA Instruments

Partners

We work closely and confidentially with various partners who offer complimentary expertise, these include Reach Separations (chiral chromatography) OEA Labs (Elemental analysis, metal analysis) and DNA labs (5 Batch analysis).

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