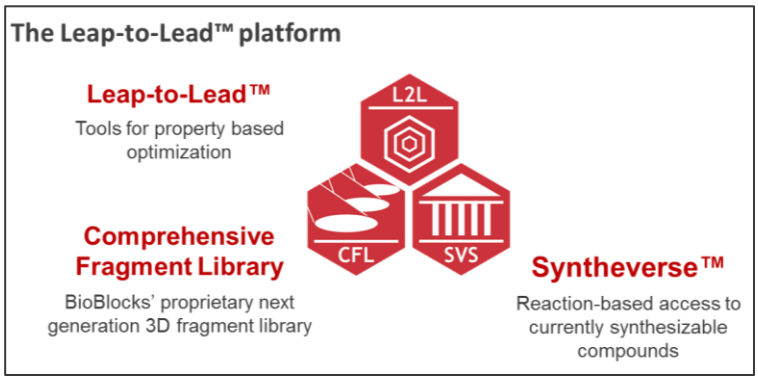
Leap-to-Lead™: New Solutions for Drug Discovery

BioBlocks is excited to announce the launch of **Leap-to-Lead™** platform partnerships, a source of novel, viable, high quality leads. During our 16 successful years creating multiple quality commercializable leads, we identified significant challenges in the current drug discovery process. We developed the Leap-to-Lead™ platform to respond to these challenges by opening up new chemical space that can be effectively navigated to create new chemical matter. We are now seeking partnerships to utilize Leap-to-Lead™ to generate proprietary, high-quality leads for IND-enabling studies for our collaborators.

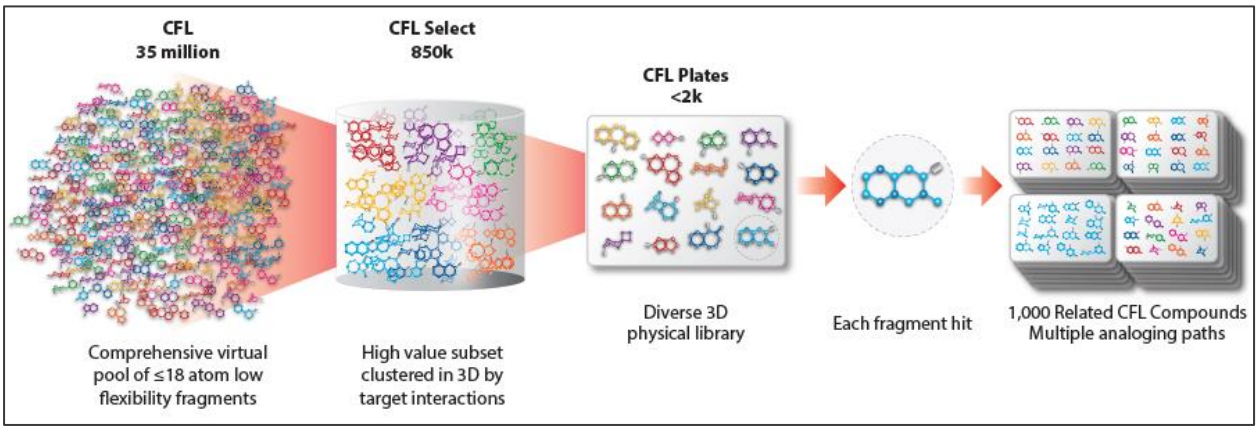
Leap-to-Lead™ Platform in Brief

The Leap-to-Lead™ platform is designed to be a high value enhancement of standard drug discovery process. Using computer enhanced discovery methods we have been able to find novel, low molecular weight lead compounds that have excellent potential to become clinical candidates. This process allows us to radically improve lead generation and optimization for our partners.



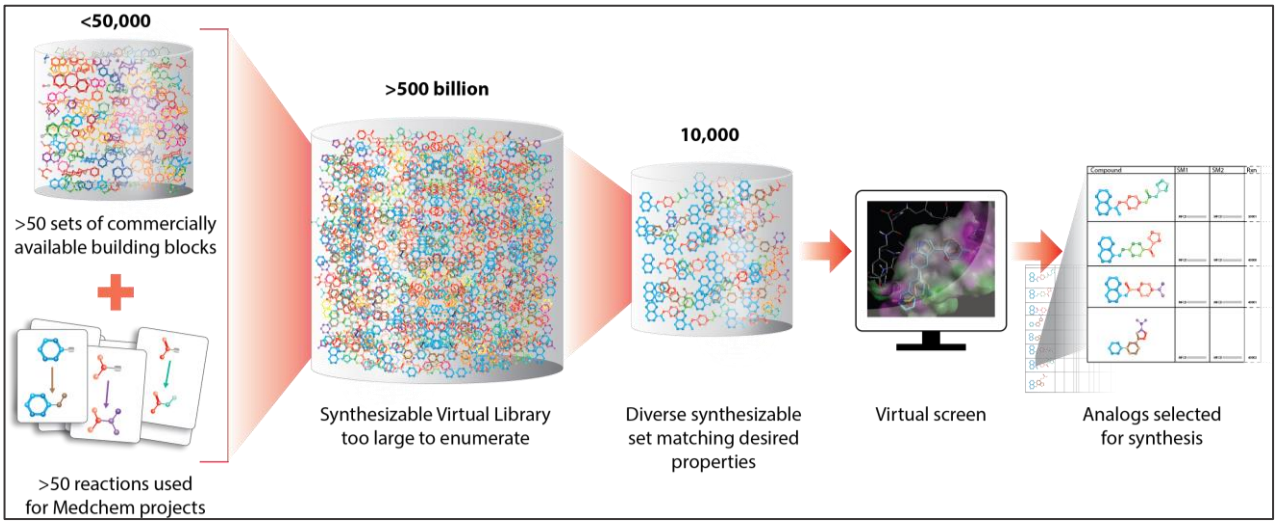
CFL: Medicinally Enriched Fragment Library

Our fragment based lead discovery process is differentiated by the **Comprehensive Fragment Library** (**CFL**), a proprietary collection of over 35 million diverse fragments selected using strict quality and pharmaceutical value criteria. We've carefully curated our library to maximize representation of medically relevant chemical space to prepare **CFL Plates** available for screening by our partners in their assays. Through our proprietary clustering algorithms, we connect hits to novel fragments in the CFL Select Set. The expanded, enhanced hit set from the CFL is carried forward using the **Syntheverse**™ to develop analogs for the next phase of the partnership.



Syntheverse™: Intelligent Lead Creation

The **Syntheverse**™ is an advanced cheminformatic algorithm capable of generating >500 billion compounds of target molecules trained with pre-coded feasible reaction schemes and curated reagent sets, including our proprietary fragments.



The **CFL** screening hits identified are used as inputs by the proprietary Syntheverse™ process to rapidly select analogs from a virtual screen. The resulting analogs are selected for synthesis or purchase if commercially available. BioBlocks' medicinal chemistry expertise is encoded in the Syntheverse™ to provide accurate selections of reaction schemes and immediate synthesis.

Additionally, the Syntheverse™ has powerful capabilities in cases where a lead requires optimization of some set of properties (ie. toxicity, solubility, stability, etc.). The Syntheverse™ can quickly identify groups that can be replaced with improved alternatives and identify the schemes for their synthesis. Starting from CFL screening hits or an existing lead, the iterative Syntheverse™ process can generate novel leads for partners.

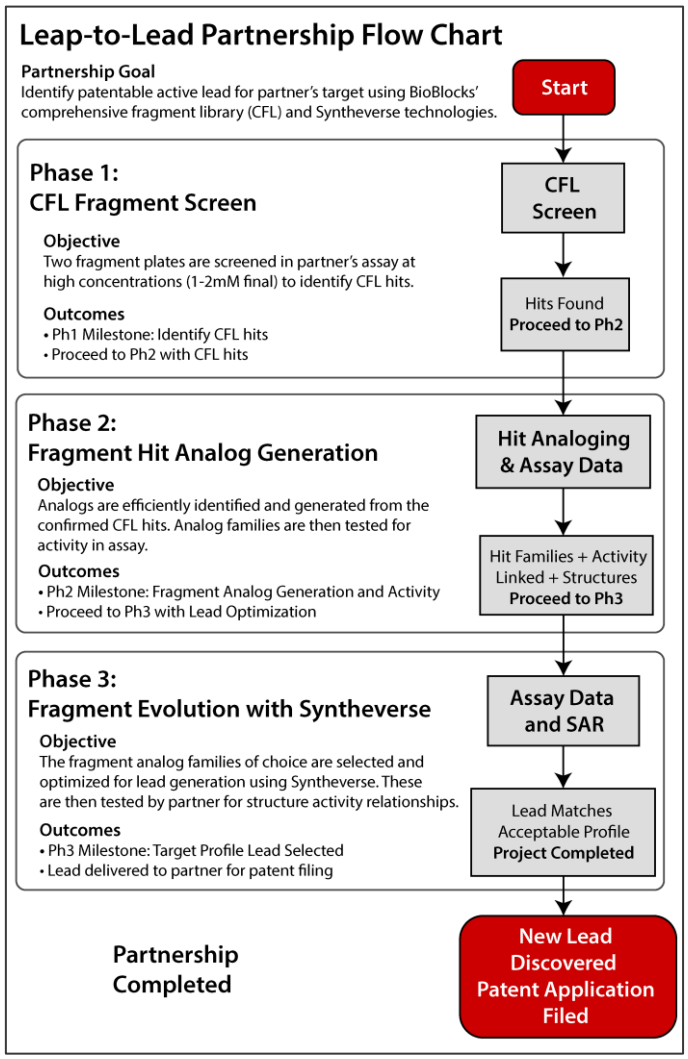
Leap-to-Lead™ Process Overview

A FBLD **Leap-to-Lead™** project consists of three phases, with the main goal of delivering a novel pre-clinical lead that enables the partner to file a new patent. Each phase is iterative, with clear milestones and expectations from both parties at each phase.

1. A typical partnership begins with the **CFL Fragment Screen** (Phase 1) to identify fragment hits using the partner's assay.
2. BioBlocks will use Phase 1 information to generate **Fragment Analogs** (Phase 2), both commercially available and synthetic, in two rounds for a partner's assay.
3. The Leap-to-Lead™ process then continues to **Fragment Evolution** (Phase 3), where fragment leads from Phase 2 will be optimized to leads using a combination of BioBlocks' Syntheverse™ technology and the partner's physical assays.

This process will entail sustained synthesis of analogs generated by the Syntheverse™ by BioBlocks, and testing by the partner over several rounds.

Efficient Lead Generation in Partnership Phases



In **Phase 1**, a partner will receive the current screening plates from BioBlocks: the physical set of fragments from the **CFL**, representative of larger virtual clusters in the BioBlocks repertoire. Customized CFL plates are available from BioBlocks for shipment to partners. Each plate well contains a single fragment at 200 mM concentration in DMSO; to be diluted to 1-2 mM (≤1% DMSO) in the partner's assay of choice.

We anticipate Phase 1 to take 1-2 months, less if the partner's assay(s) of choice are well-established and validated for the target. CFL hits are identified by the assay, and the project proceeds to Phase 2.

In **Phase 2**, BioBlocks will use information on the hits identified from Phase 1 to generate fragment analogs in robust hit sets. The analoging stage will generate families of similarly structured hits, which will be tested in the partner's assays. We ensure that synthesis is kept to a minimum efficient set to avoid unnecessary synthesis time and cost. Hits from this Phase will be analyzed for activity patterns, a strong indicator of early fragment success. A family of similar analogs showing a range of activities indicates a valuable starting point for hit-to-lead. Choosing from the CFL active families, the partner approves a selection of specific families to proceed to Phase 3.

We anticipate Phase 2 to take 2-4 months, depending on the proportion of commercial to synthetic compounds and timely feedback from the partner's assay(s). This proportion, based on the need for novelty in early compounds, will be determined for each specific project by BioBlocks and the partner.

In **Phase 3**, fragments leads from Phase 2 will be optimized to leads using a combination of BioBlocks' **Syntheverse**™ technology and the partner's physical assays. This process will entail sustained synthesis of analogs generated by the Syntheverse™ and testing by the partner for improved activity over optimization rounds. Bearing in mind the costs and time of both BioBlocks and the partner, clear goals will be jointly set for the profile of a successful lead.

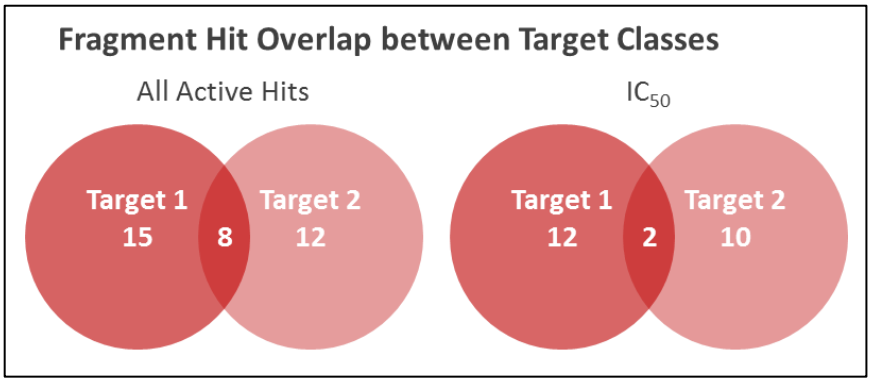
This Phase will likely take 6-12 months or more, depending on the project and the agreement made with the partner. Phase 3 is completed when a lead or leads are generated that fit an acceptable profile for further lead optimization.

Screening Results

To date, the CFL plates have been screened in >8 fragment assays of different formats. Hit rates have ranged between 5 and 15% for targets that are expected to have small-molecule ligands. The results of the first two screens and **analog phases** have been revealed publicly and are summarized below.

Hit Summary, all projects

- Typical FBLD hit rates
- Activities range from 100 µM to 2 mM
- Minimal overlap of potent compounds
- IC_{50}'s vary 10X between target classes for hits in common



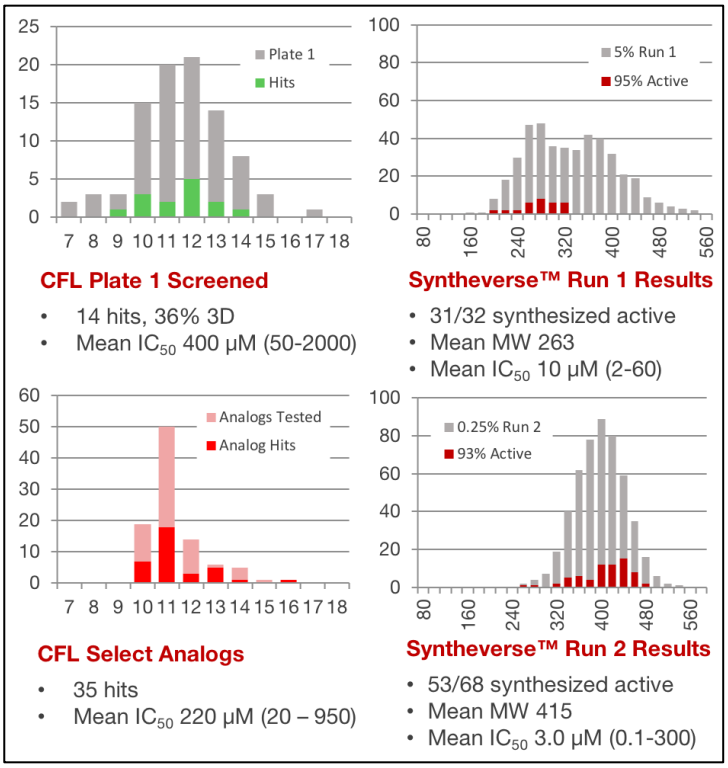
Case Study: Leap-to-Lead™ Technology in Action

Targeting SGK1 for TNBC Indication with Visionary Pharmaceuticals

Visionary and BioBlocks formed a partnership to identify novel inhibitors of SGK1. Using the Leap-to-Lead™ platform we were able to deliver an active lead with novel chemical space leading to a recent patent application.

Collaboration Workflow

- **CFL** plates screened in SGK1 assay
- Hits identified from CFL screen
- Analogs selected by standard process improved activity
- One hit family selected for hit-to-lead phase
- Efficient hit-to-lead accomplished with only 2 **Syntheverse**™ runs
- Cell active compounds with improved properties discovered



Collaboration Milestones

- Developed a **Lead Series** that has improved properties compared to literature leads
- Developed **novel IP** - patent application filed
- Advanced partnership to **Lead Optimization**
- **Partnered** with a public biotech to explore alternative indications

Read more on our poster from **MEDI_2017**

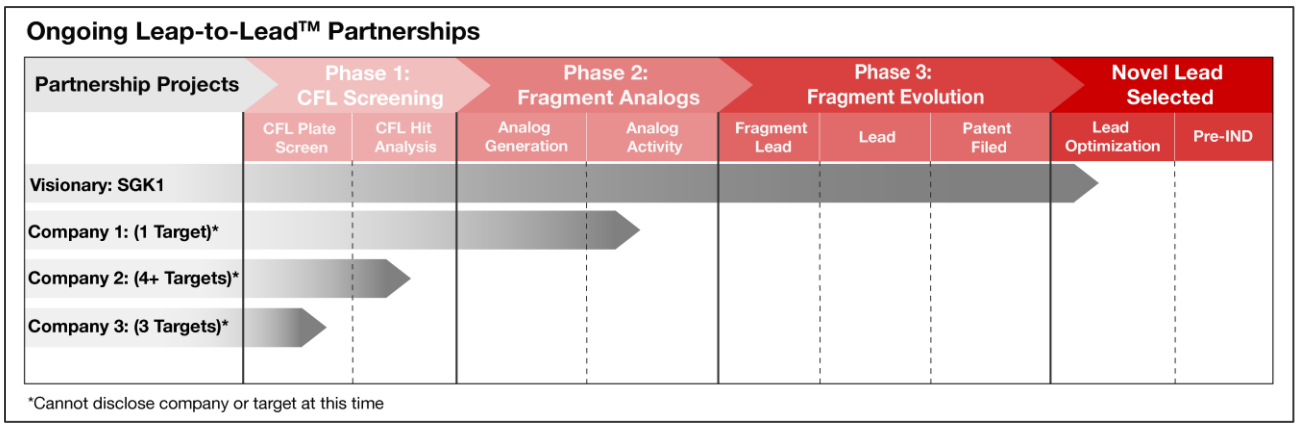
BioBlocks
A CHEMISTRY PARTNER IN DRUG DISCOVERY

Partnering Benefits

Leap-to-Lead partnerships create strategic value by providing novel quality leads cost efficiently for partners' valuable targets.

- Efficiently generate patentable preclinical leads
- Improve your compounds at any stage using chemical evolution processes
    - Initial screening, lead optimization, pre-clinical, and beyond
- Gain better activity and IP options via advanced cheminformatics algorithms
- Rescue patent position of known leads using novel scaffolds
    - Access a large virtual set (>500B) of synthesizable structures

Novel IP is critical to succeeding in the therapeutic market. Since opening its doors in San Diego, BioBlocks' scientists have inventorship in **patents issued** and assigned to 6 different companies and contributions to patents with many other companies pending. Leap-to-Lead™ partnerships aim to generate patentable preclinical leads, positioning our partners to advance leads into clinical trials, and ultimately to market, and achieve critical commercialization and business milestones. . We are seeking partnerships with research-driven drug discovery/development entities at all stages to utilize **Leap-to-Lead**™.



With your target expertise and our advanced platform, we can lower the challenging hurdles of drug discovery. Together we create de-risked assets with market value for your organization.

About Us

BioBlocks is a medicinal chemistry company specialized in preclinical lead discovery. Over the past 16 years, we have developed numerous preclinical assets for our partners. BioBlocks focuses on creating proprietary, high-quality leads by combining its expertise in medicinal chemistry with its cutting-edge **Leap-to-Lead**™ platform. For more information on how to partner with BioBlocks, please send an email to **ppallai@bioblocks.com** or follow us on **LinkedIn**.