

# FRAGMENT-BASED LEAD GENERATION

## Capabilities Overview

### Screening

- Ligand observe NMR methods: STD, wLOGSY, CPMG

### Library Preparation

- Identity, solubility, purity
- Automated smart pooling

### Follow-up Analysis

- Validation (follow-up singletons)
- Rank-order; cluster

### Target Generation

- Protein generation and purification

### Target Preparation

- Screen design; sample optimization; experimental conditions optimization

### Complimentary Capabilities

- Orthogonal methods (SPR)
- X-Ray Crystallography
- Computational Chemistry
- Chemical elaboration to support optimization
- Biological assay design and support

## Library Screening Options

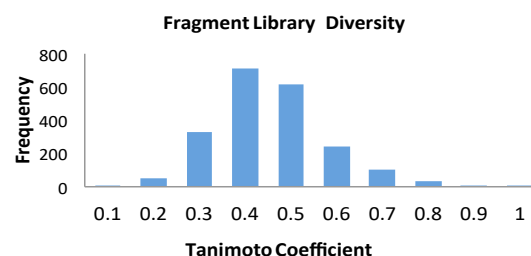
### Fragment Library

#### Commercial and Proprietary

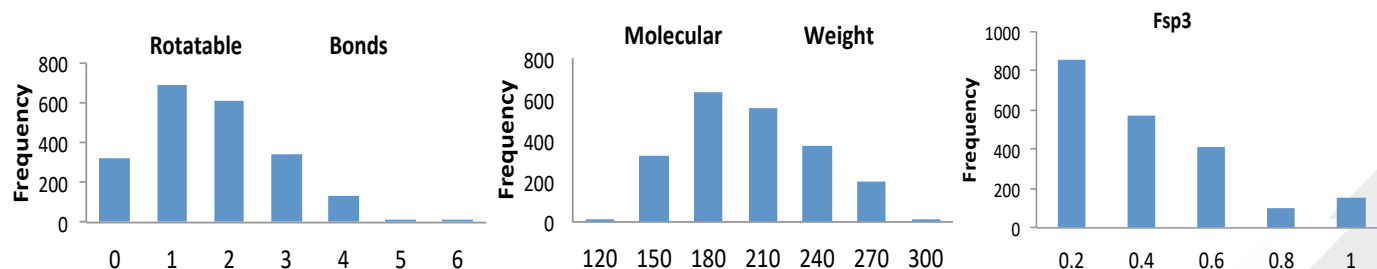
- Fragment sets from internal small molecule collections
- Fragment sets designed from FDA approved drugs
- <sup>19</sup>F- containing fragments
- Covalent fragments
- Commercial fragments

#### External libraries

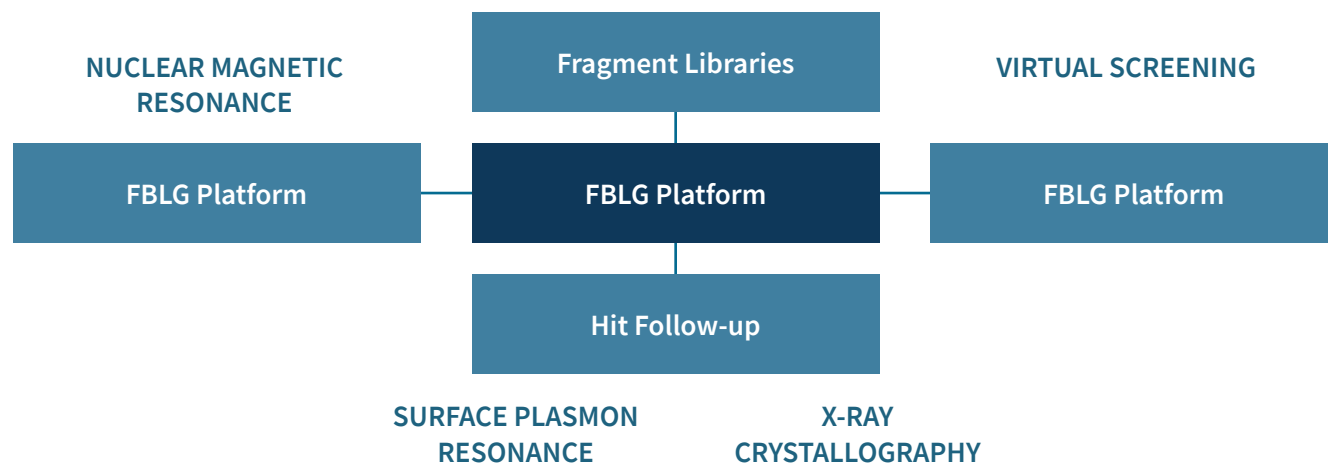
- Client-provided
- Client-selected commercial libraries
- Custom commercial libraries



## Select Fragment Library Properties

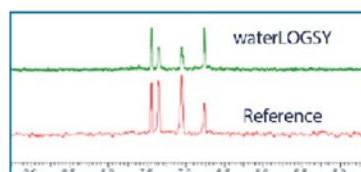
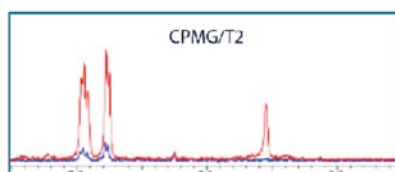
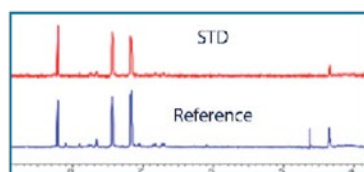


# Cutting Edge Screening Platform



## Versatile Biophysical Screening Methods

Primary Screening via Ligand Observe NMR: STD, wLOGSY and CPMG



### Additional Screening Methods

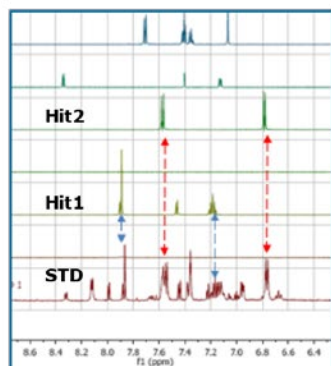
- $^{19}\text{F}$  NMR
- TSA
- SPR

## CASE STUDY:

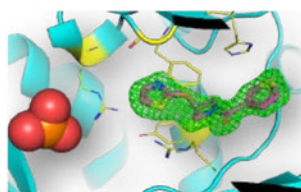
# Fragment-Based Drug Design Of Novel Nampt Scaffolds

NAMPT (nicotinamide phosphoribosyltransferase): An oncology target in the cellular metabolism pathway.

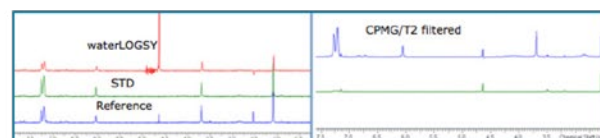
**Primary Screening:** STD NMR of 1000 fragments in 100 pools. Hits were selected based on structural diversity, virtual screening and the strength of the STD signals from the primary screen



**Validation:** X-ray co-crystal structures confirm multiple screening hits as true binders to NAMPT



**Confirmation:** The top hits from the primary screen were screened as singletons and confirmed via STD NMR, waterLOGSY and CPMG experiments



**Orthogonal Methods:** SPR and biochemical assays to confirm binding and functional enzyme inhibition

**Validated Novel Scaffold for NAMPT**