SK life science labs

a subsidiary of SK biopharmaceuticals

MOPED™: A Novel Platform for the Discovery of Molecular Glues

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The 2nd Molecular Glue Drug Development Summit
February 1st, 2024

Molecular glues have advantages as oral therapeutics

A significant unsolved discovery challenge

Molecular glues have favorable properties for safe oral drugs

- Drug like physiochemical space
- Minimal binary biological effects, due to weak binding to one or both of the individual partners
- Selectivity through strong dependence on protein surfaces
- Efficacy not blunted by Hook effect

Glue discovery is an unsolved problem

- Glue discovery is high risk / high reward with most examples being serendipitous
- Steep SAR challenges chemical optimization
- Billions of possible combinations require a novel discovery approach

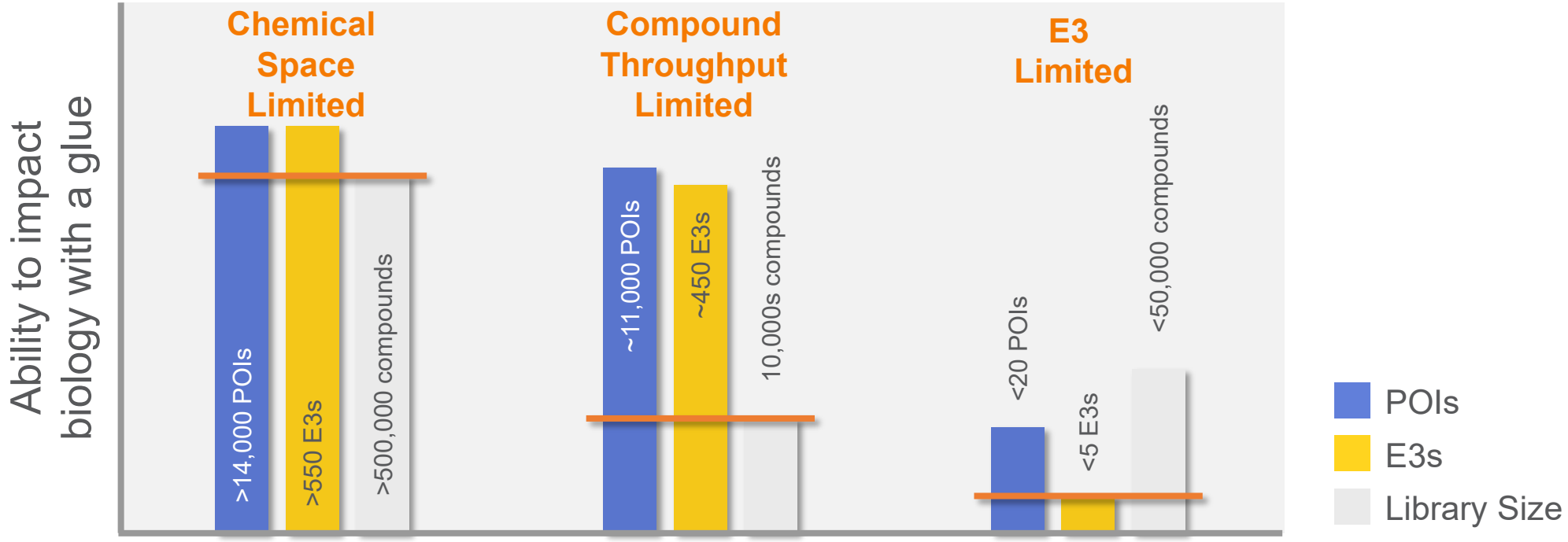
Interest in molecular glue technology highlights the unsolved discovery challenge

Disclosed deals since January 2022

Announcement Date	Licensor	Licensee	Headline	Upfront Payment	Total Biobucks
10/16/2023	Monte Rosa	Roche	Monte Rosa Therapeutics Announces Strategic Collaboration with Roche to Discover Novel Molecular Glue Degraders Targeting Cancer and Neurological Diseases	$50M	>$2B
9/26/2023	A-Alpha Bio	Amgen	A-Alpha Bio Collaborates with Amgen to Identify and Validate Ligase-Target Pairs for Molecular Glue Discovery	Yes; amount undisclosed	Undisclosed
9/20/2023	Orionis	Genentech	Orionis Biosciences Announces Collaboration with Genentech to Discover and Develop Molecular Glue Class Medicines	$47M	>$2B
4/5/2023	Biotheryx	Incyte	Biotheryx Announces Research Collaboration And License Agreement With Incyte For Discovery Of Targeted Protein Degraders For Novel Oncology Targets	$7M	$360M (per target; option for additional)
4/5/2023	Proxygen	Merck	Proxygen Announces Collaboration And License Agreement With MSD For The Discovery And Development Of Novel Molecular Glue Degraders	Yes; amount undisclosed	$2.55B
10/4/2022	Synthex	BMS	Synthex And Bristol Myers Squibb Enter Into A Research Collaboration To Discover And Develop Targeted Protein Degradation (TPD) Therapeutics	Yes (cash and equity investment); amount undisclosed	Over $550M
8/25/2022	A-Alpha Bio	BMS	A-alpha Bio Announces Collaboration With Bristol Myers Squibb To Discover Molecular Glue Targets For Protein Degradation	Yes; amount undisclosed	Undisclosed
6/2/2022	Proxygen	Merck KGaA	Proxygen Announces Strategic Collaboration With Merck To Develop Molecular Glue Degraders	Yes; amount undisclosed	€495M ($554M)
5/10/2022	Evotec	BMS	Evotec And Bristol Myers Squibb Extend And Expand Strategic Partnership In Protein Degradation	$200M	$5B
4/28/2022	Plexium	AbbVie	Abbvie And Plexium Enter Into Multi-target Strategic Collaboration To Develop And Commercialize Targeted Protein Degradation Therapies For Neurological Conditions	Yes; amount undisclosed	Undisclosed
2/3/2022	Plexium	Amgen	Amgen And Plexium Announce Multi-year, Drug Discovery Collaboration To Identify Novel Targeted Protein Degradation Therapies	Undisclosed	Over $500M
1/25/2022	Yeda	Monte Rosa	Monte Rosa Therapeutics And Yeda, The Commercial Arm Of The Weizmann Institute Of Science, Announce License And Research Collaboration To Accelerate Discovery Of Novel Covalent Molecular Glue Degraders	Undisclosed	Undisclosed

SKLSL expands access to targeted biology accessible by TPD

MOPED™ enables target & E3 agnostic glue discovery at scale



MOPED™ is an innovative platform for glue discovery

MOlecular **P**roximity **E**nabled **D**etection (MOPED™)

Emerald

A highly sensitive biochemical workflow to discover glues from defined drug target and pre-selected E3s

Sapphire

An E3 agnostic mass spectroscopy workflow to discover glues against defined drug targets

Molecular Glue Discovery

INCREASE ACCESS TO TARGETS

Targeting structured and unstructured regions

EXPAND E3 OPPORTUNITIES

Known E3s, target matched E3s, and/or E3 agnostic

INCREASE NUMBER OF LEADS

Multiplexing compounds, targets, and/or E3s

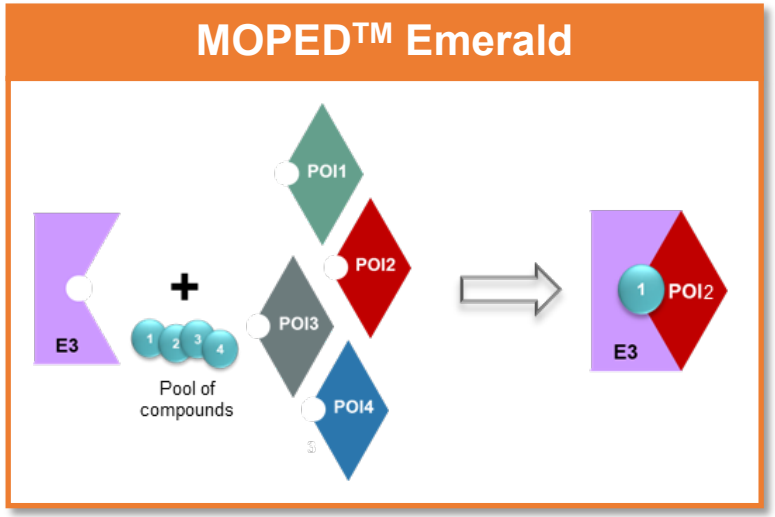
BROADEN BIOLOGICAL IMPACT

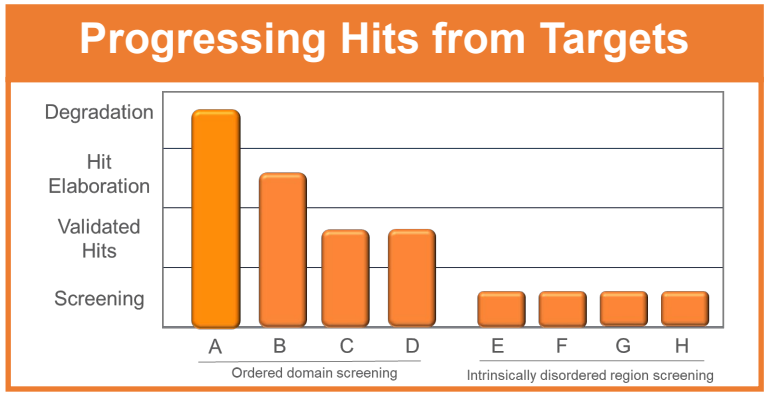
Exploring potential biological functions beyond TPD

Emerald: Biochemistry designed for molecular glue discovery

Sensitivity to find leads for chemical optimization

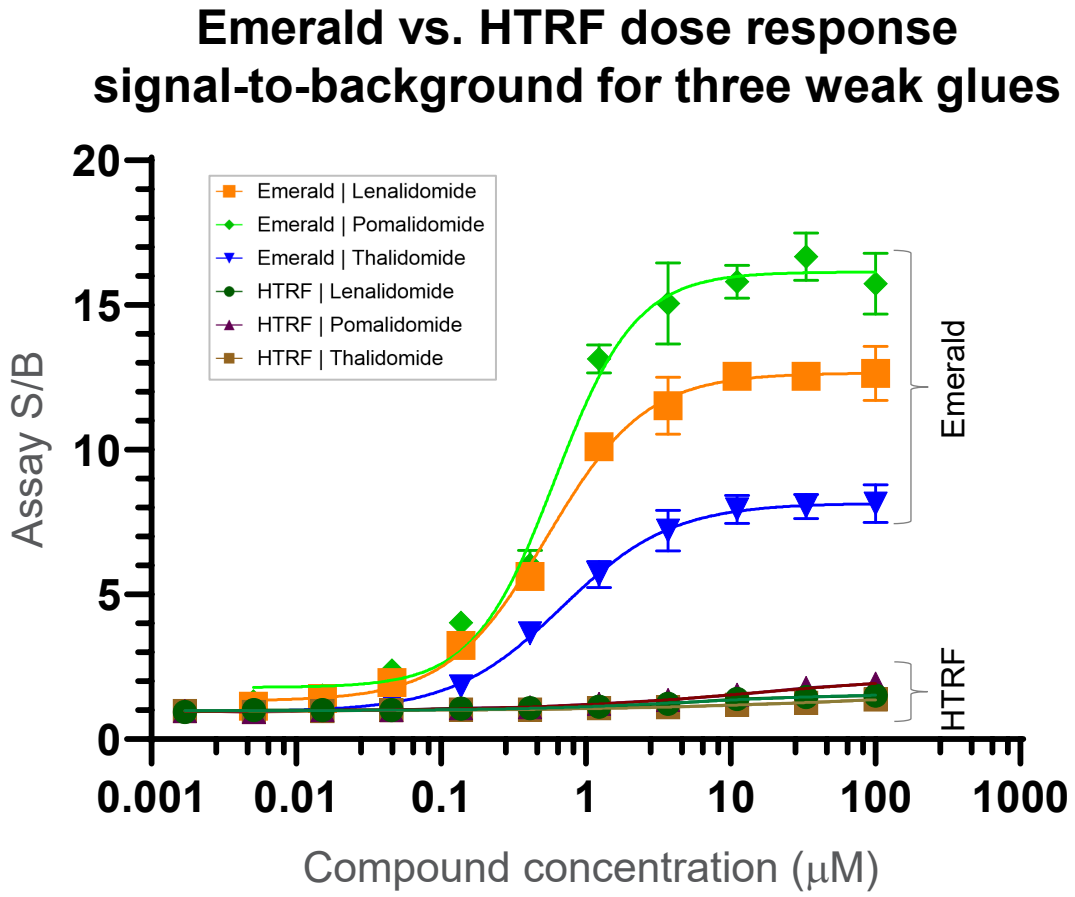
- **Glue screen to measure ternary complex formation**
  - Biochemical assay format with sensitivity to detect <2 nM of ternary complex
  - 10-20 E3s are tested individually and include widely used E3s and target matched E3s
  - Library of E3s expanding throughout 2024
  - Pools of compounds and POIs are tested for efficient 1536-well screening of a >500,000 compound library
- **8 targets in screening through hit follow-up**
- **Oncology target A was screened, yielding molecular glues that demonstrate degradation**
  - Screening start to validated hits in 3 months
  - Validated hits to degradation in 1 month





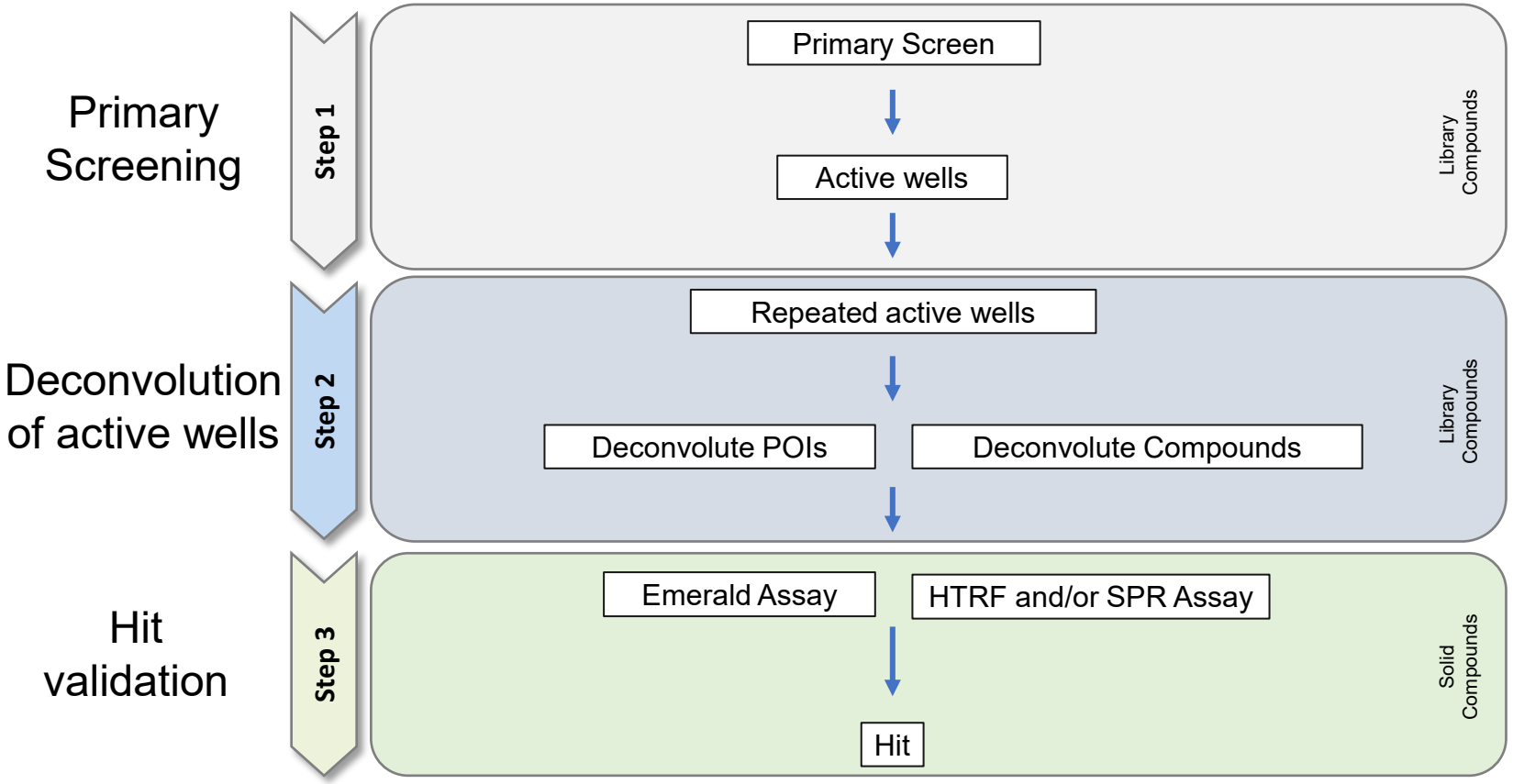
Emerald assay significantly outperforms HTRF for glue screening

- IKZF2 tested against various glutarimide-based CRBN glues



Screening workflow

Screening to hit validation



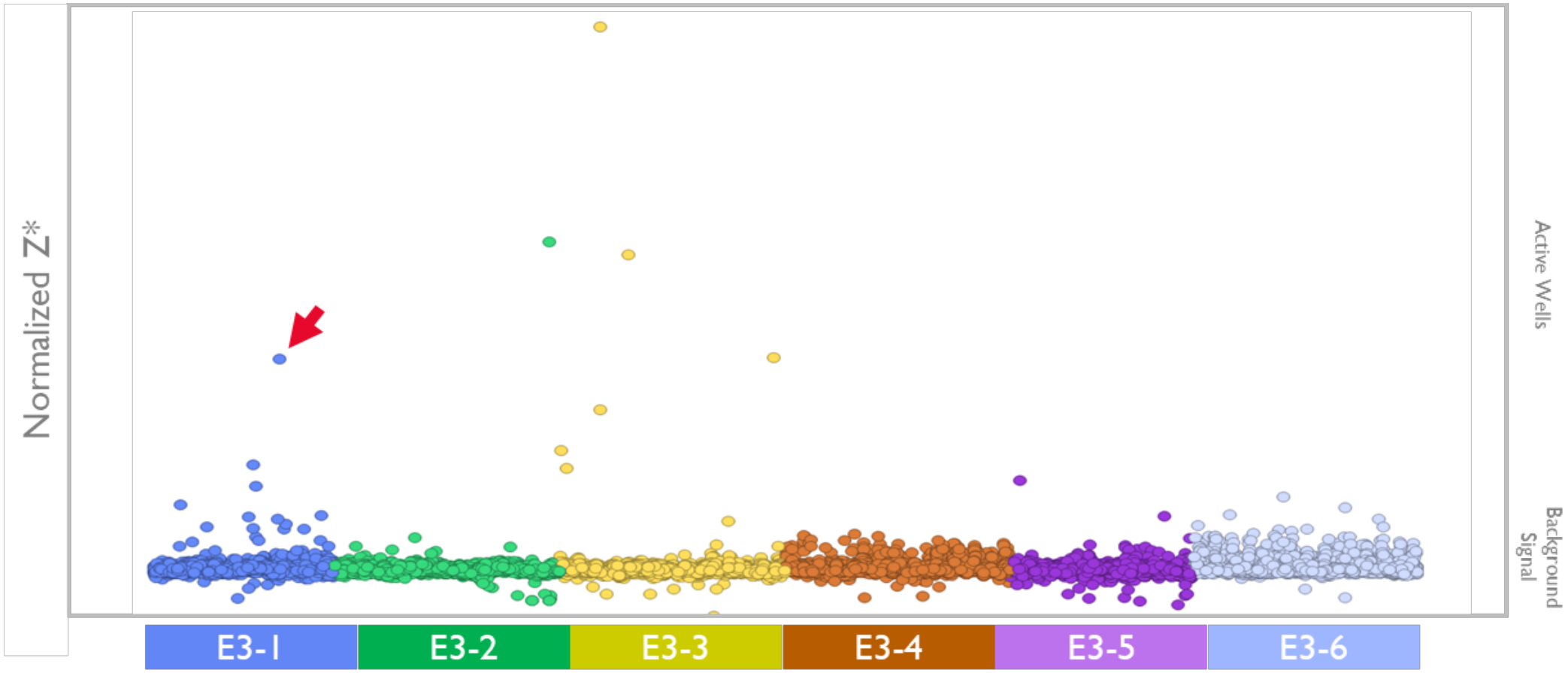
Glue screening for target A

Well established oncology target with known glue degraders

- Target A
  - High value oncology target
  - Multi-domain protein
  - Known glue degraders
- Screen design
  - 460,000 compound Enamine hit locator library
  - 6 E3s
  - 3 of the ordered domains
- Each multiplexed screening well contained a mix of the three domains, one E3, and ~100 compounds

Primary Emerald screen of target A against six E3s

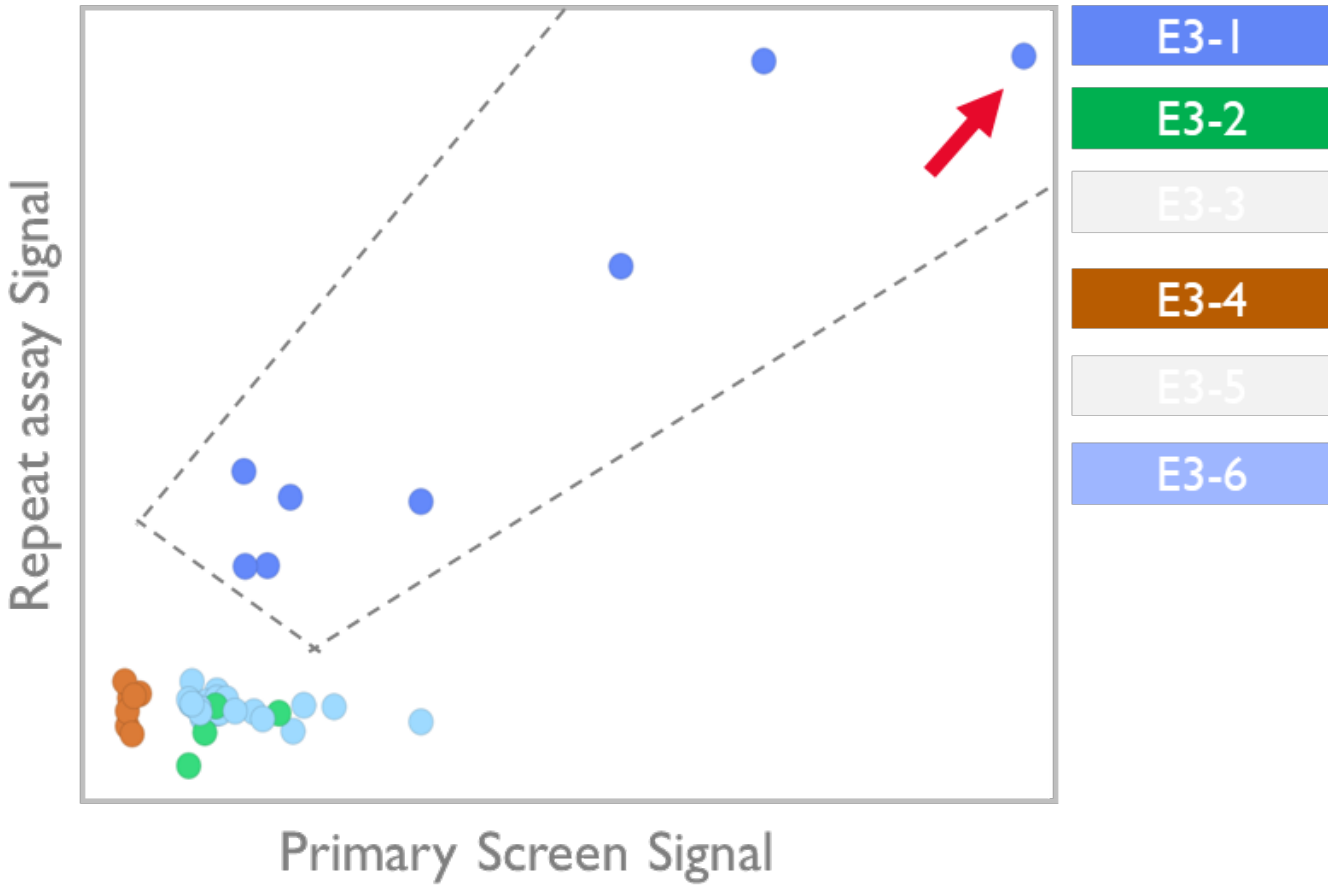
- Diversity library tested against each of 6 E3s identified active wells



Target A active well confirmation

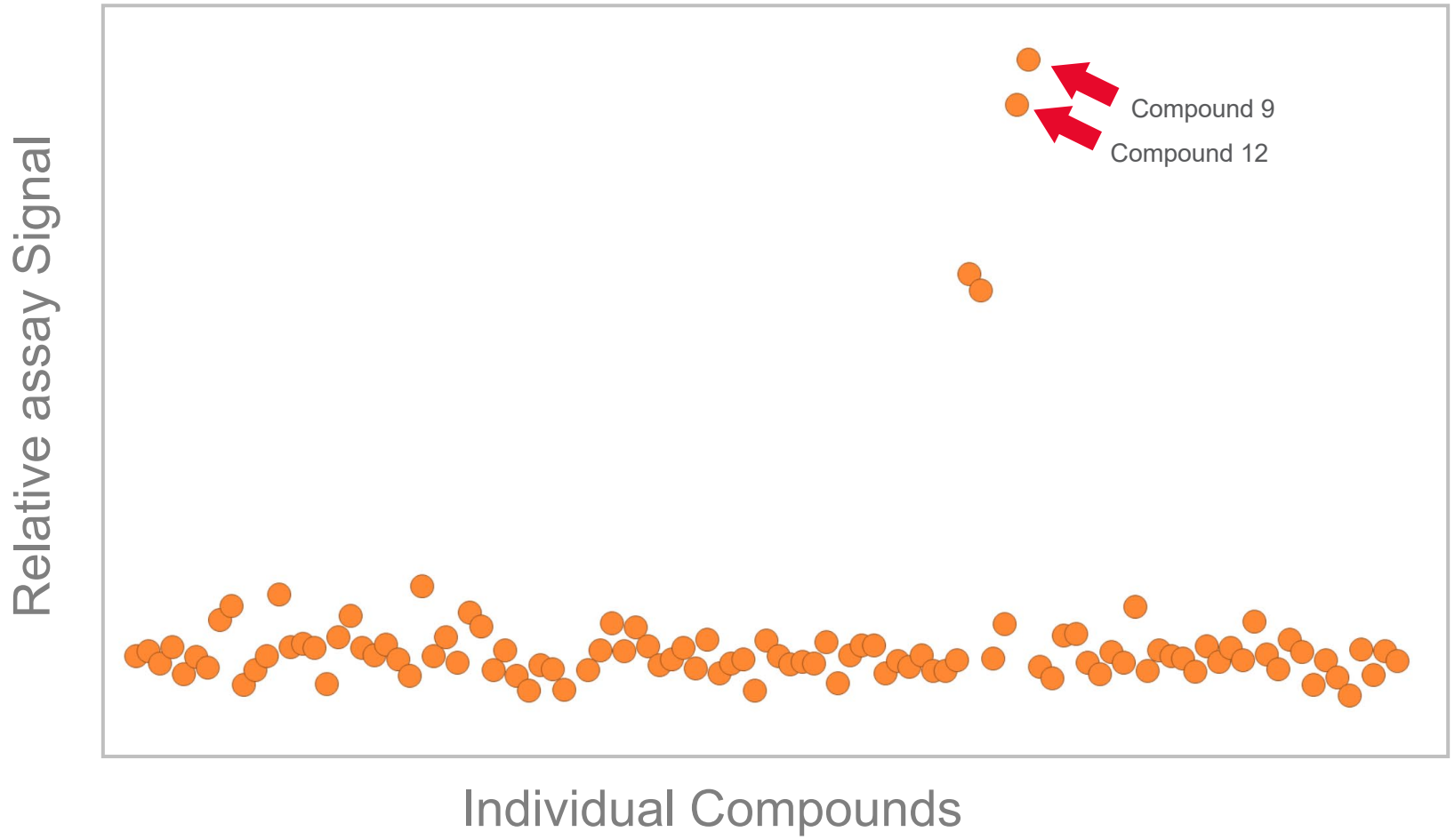
One E3 had active wells that repeat

- Active wells from 4 E3s were retested in triplicate
- Compound pools showing activity across multiple E3s are discarded
- Rate of primary screen confirmation is E3 dependent
- One E3 had wells that confirmed



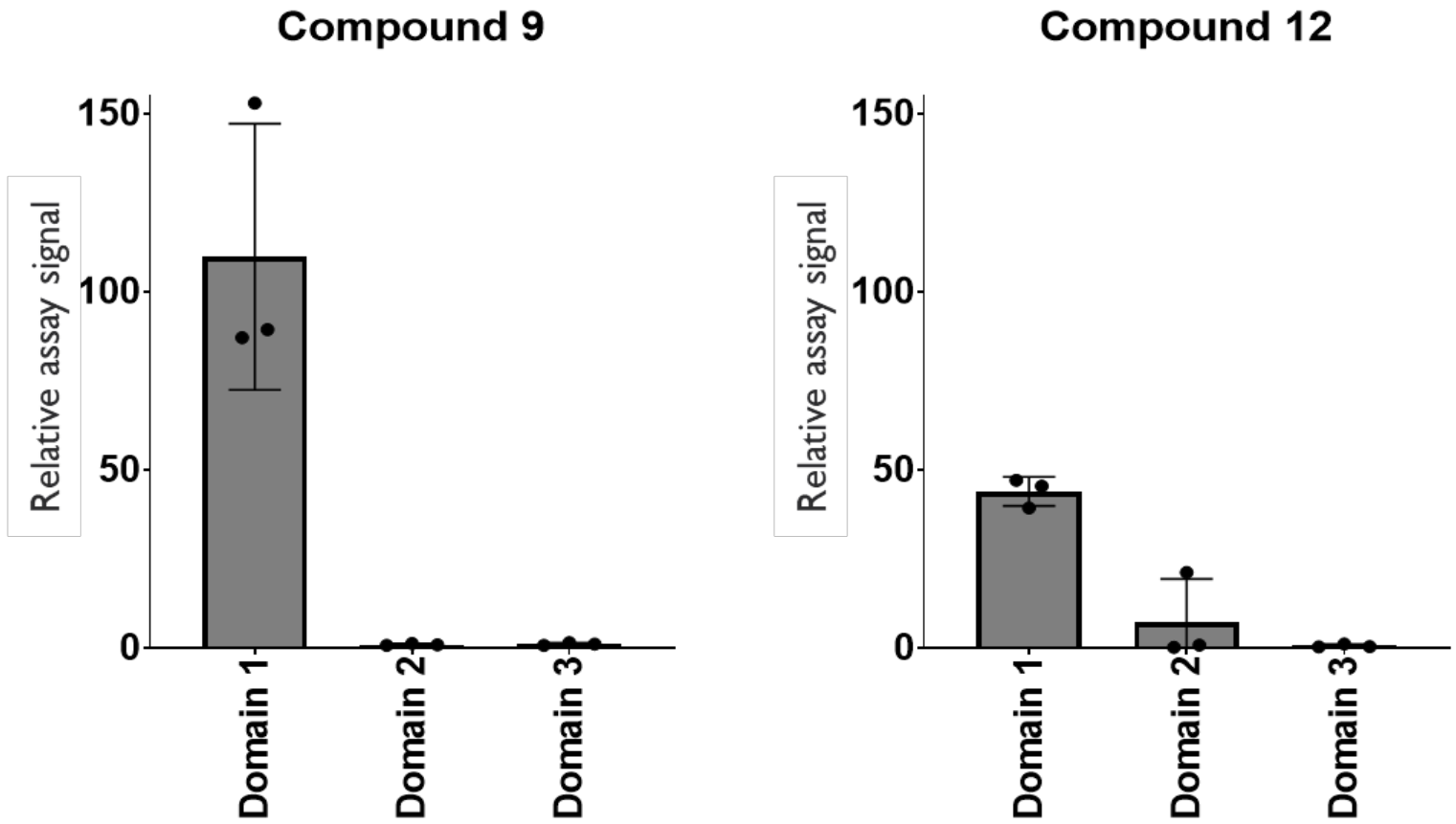
Target A deconvolution of one compound pool

- Pool activity is from four compounds in this individual well



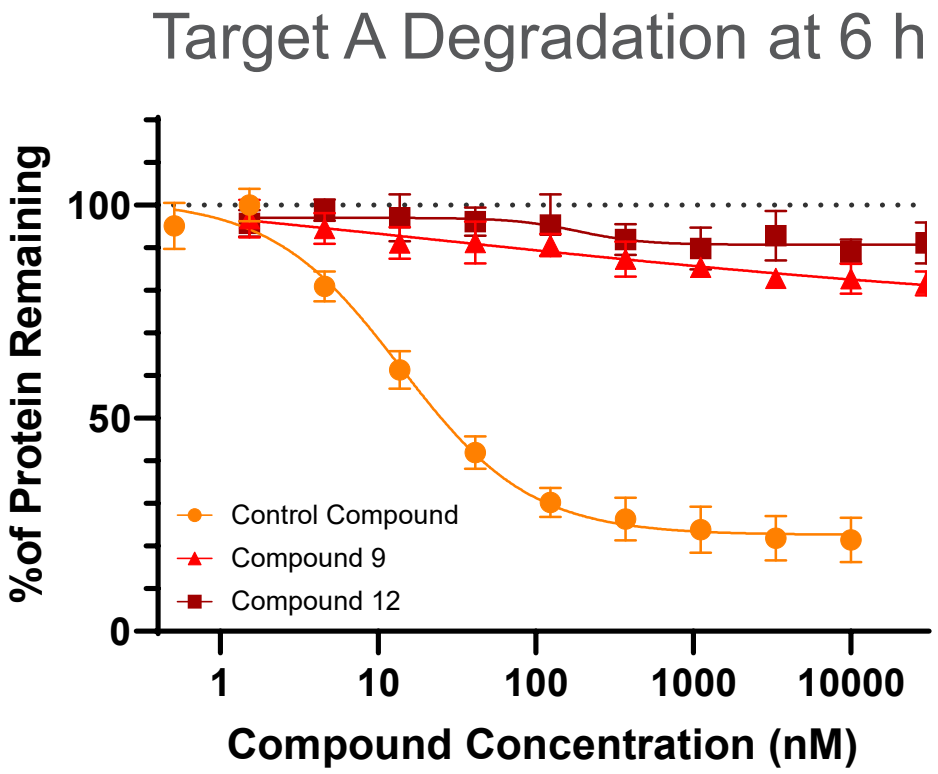
Target A hits are selective to one of the protein domains

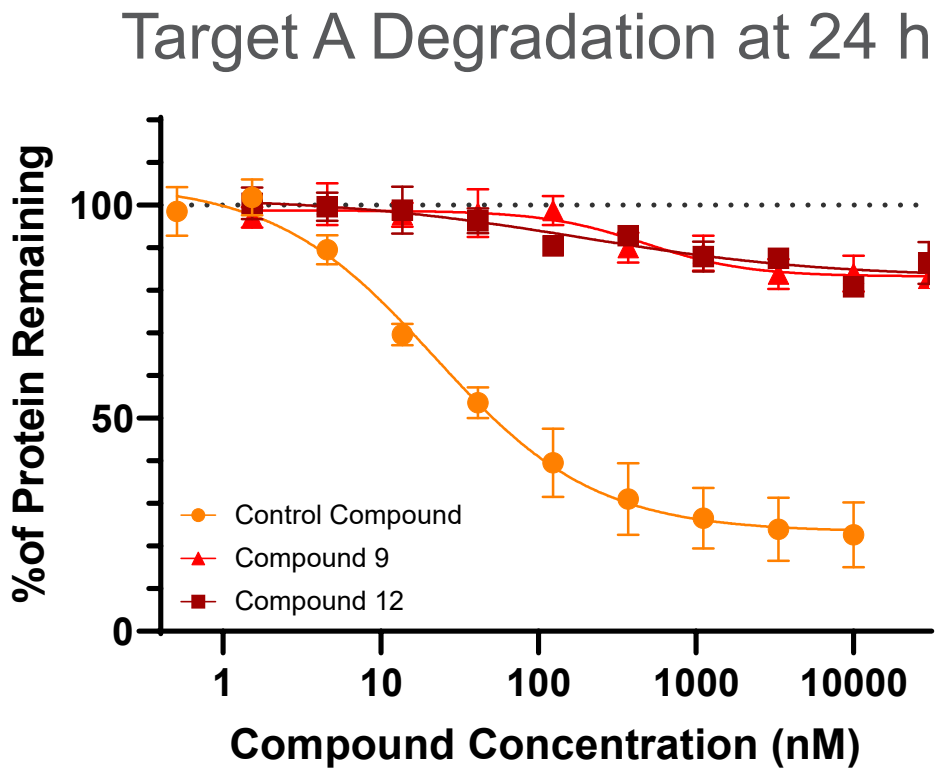
- Compounds 9 and 12 leverage one E3 and a single protein domain



Target A hits are weak degraders

Two compounds from the screening library show degradation of target A in a HiBiT assay





Glue screening for target B

Challenging oncology target of interest across pharma

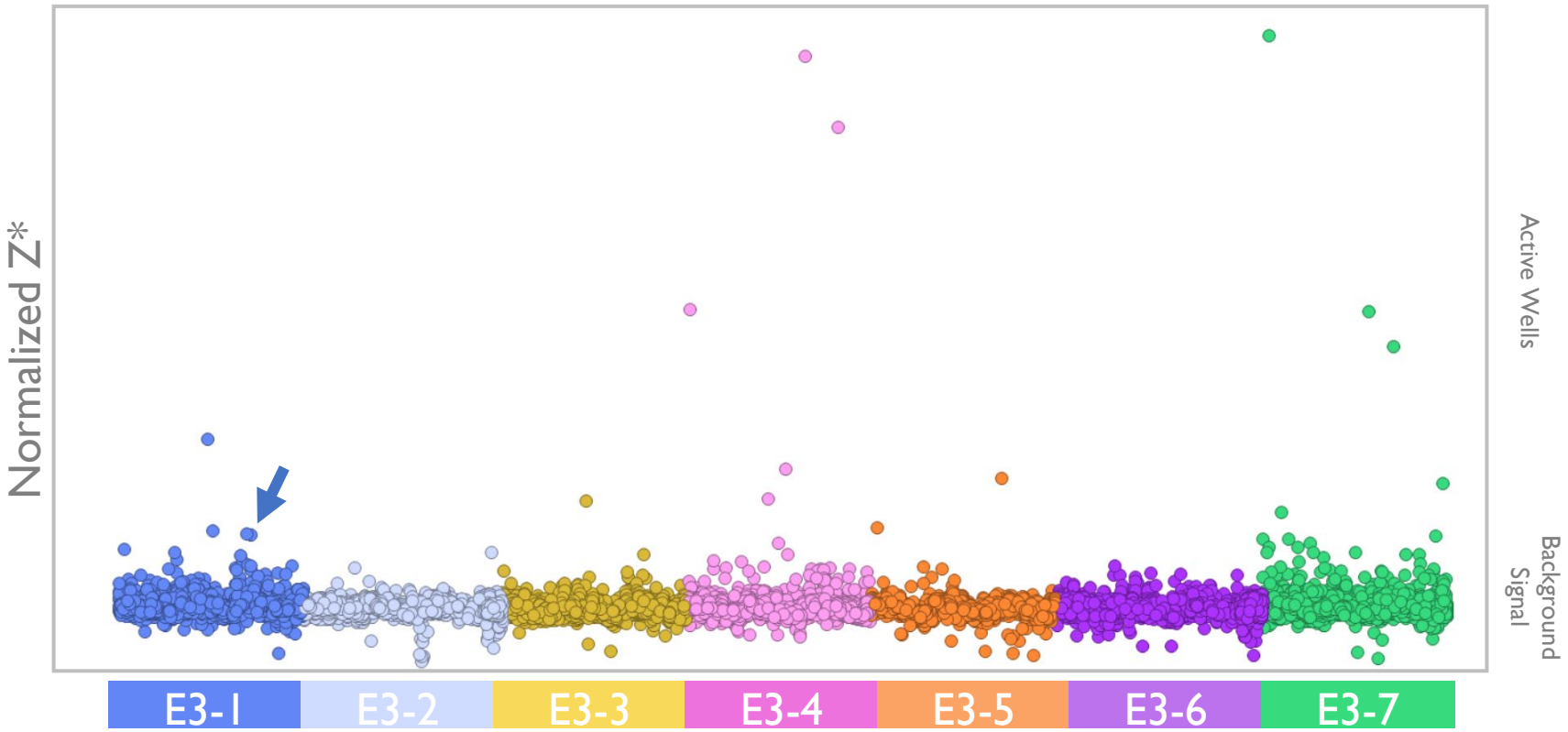
- Target B
  - High value oncology target
  - Multi-domain protein
  - Challenging to identify potent inhibitors

- Screen design
  - 460,000 compound Enamine hit locator library
  - 7 E3s
  - 3 of the ordered domains

- Each multiplexed screening well contained a mix of the three domains, one E3, and ~100 compounds

Primary Emerald screen of target B against seven E3s

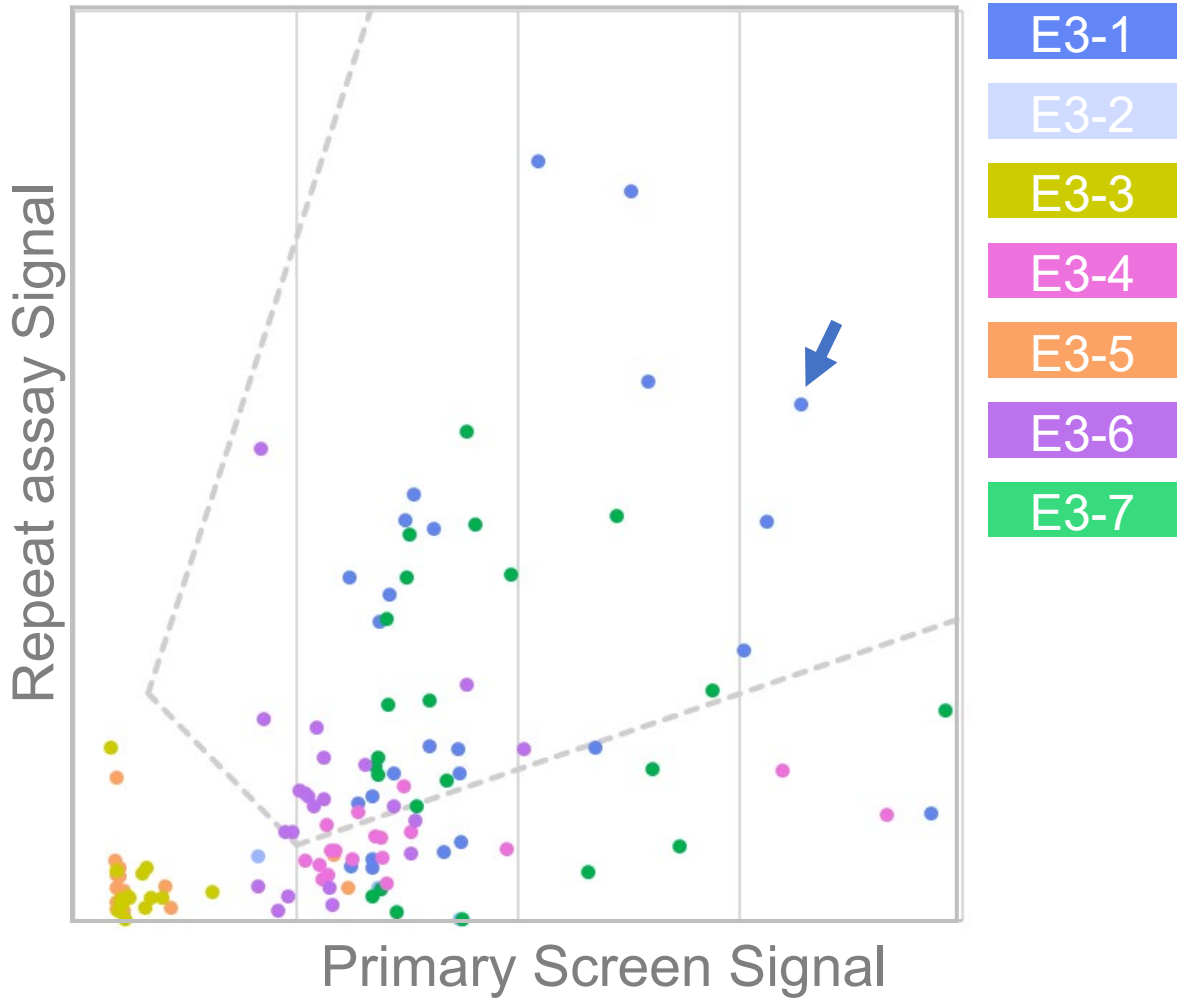
- Diversity library tested against each of 7 E3s identified active wells



Target B active well confirmation

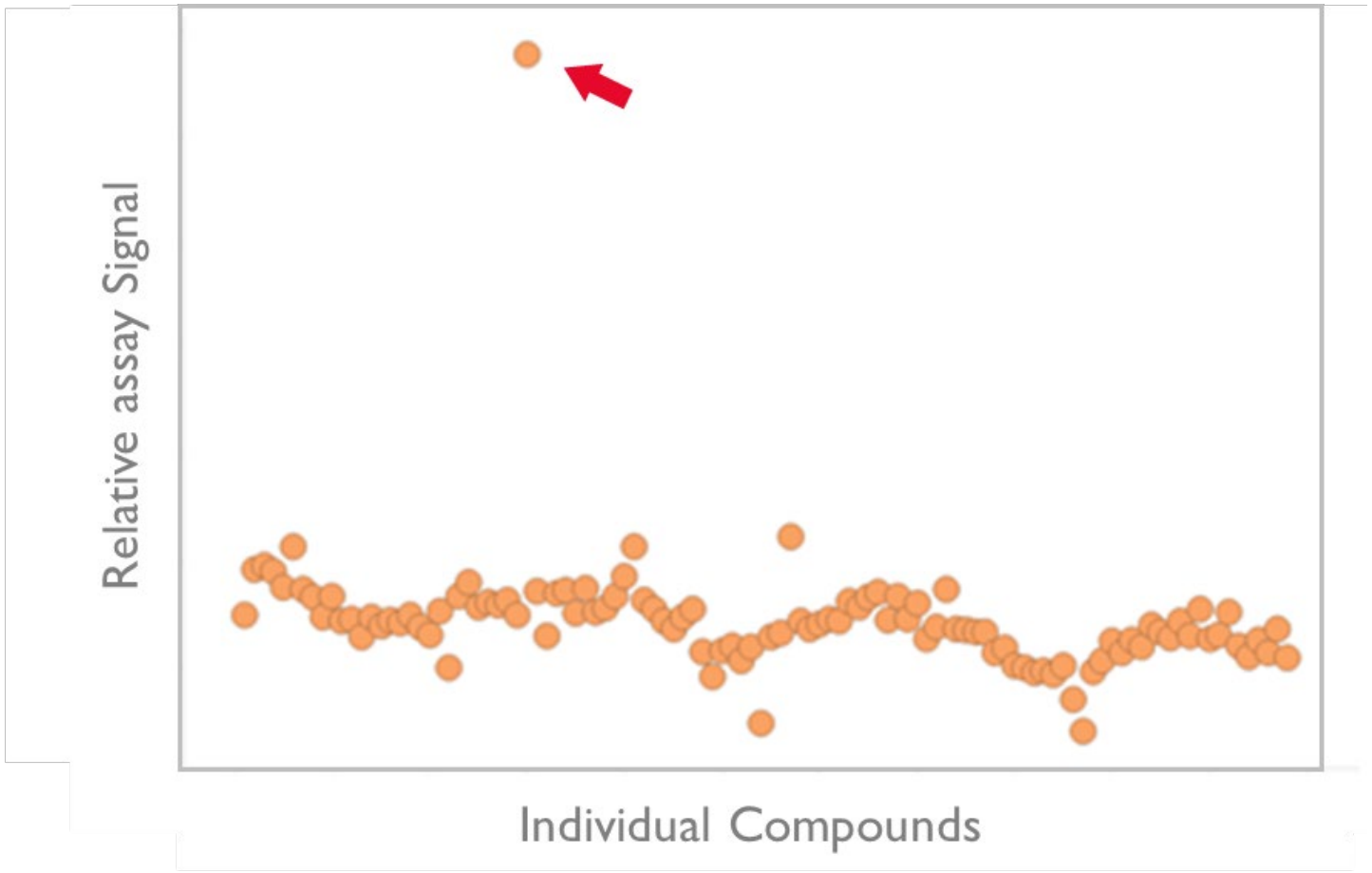
4 E3s had active wells that repeated

- Active wells from 7 E3s were retested in triplicates
- Compound pools showing activity across multiple E3s are discarded
- Rate of primary screen confirmation is E3 dependent
- Four E3s had wells that confirmed



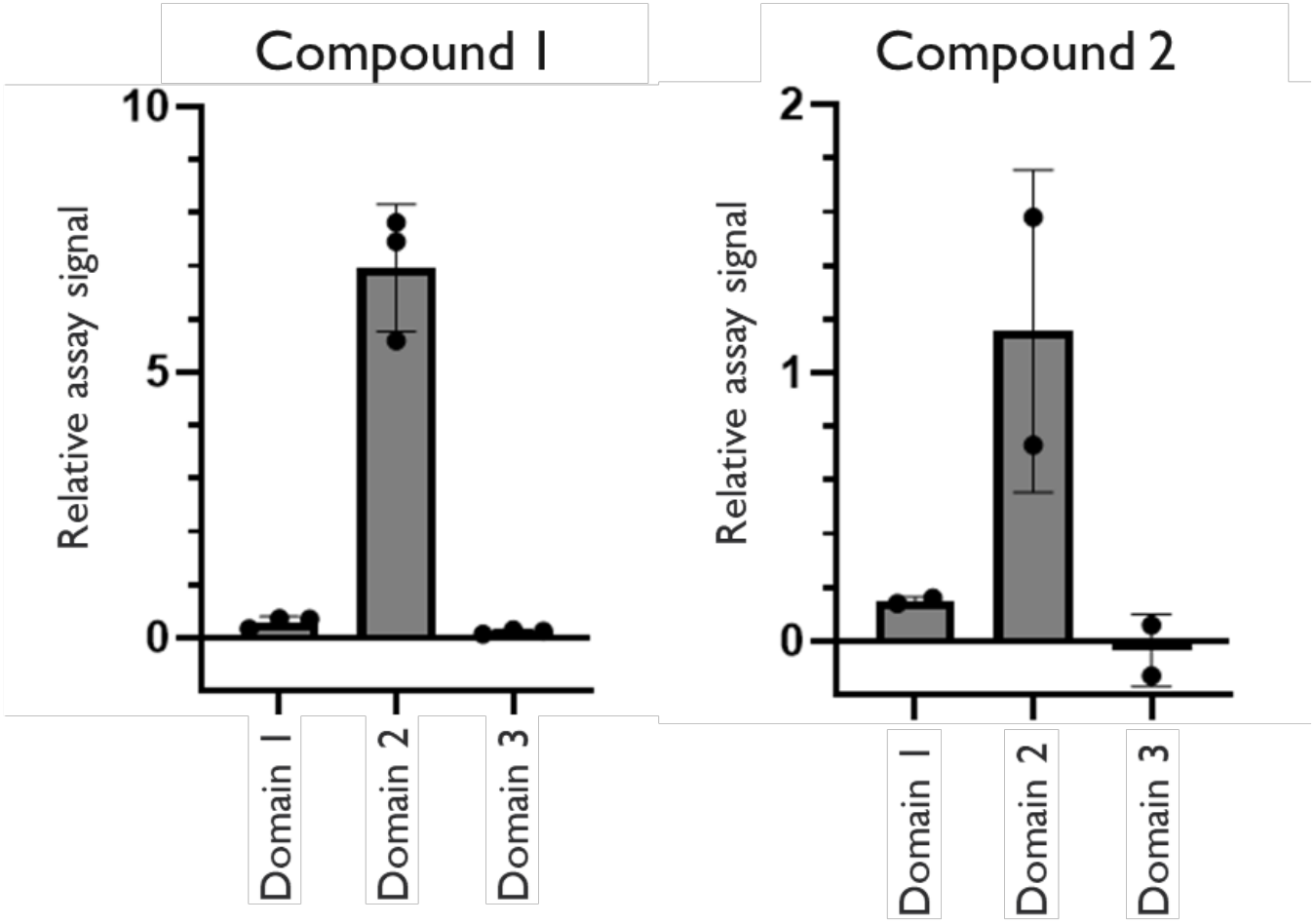
Target B deconvolution of one compound pool

- Pool activity is from one compound in this individual well



Target B hits are selective to one of the protein domains

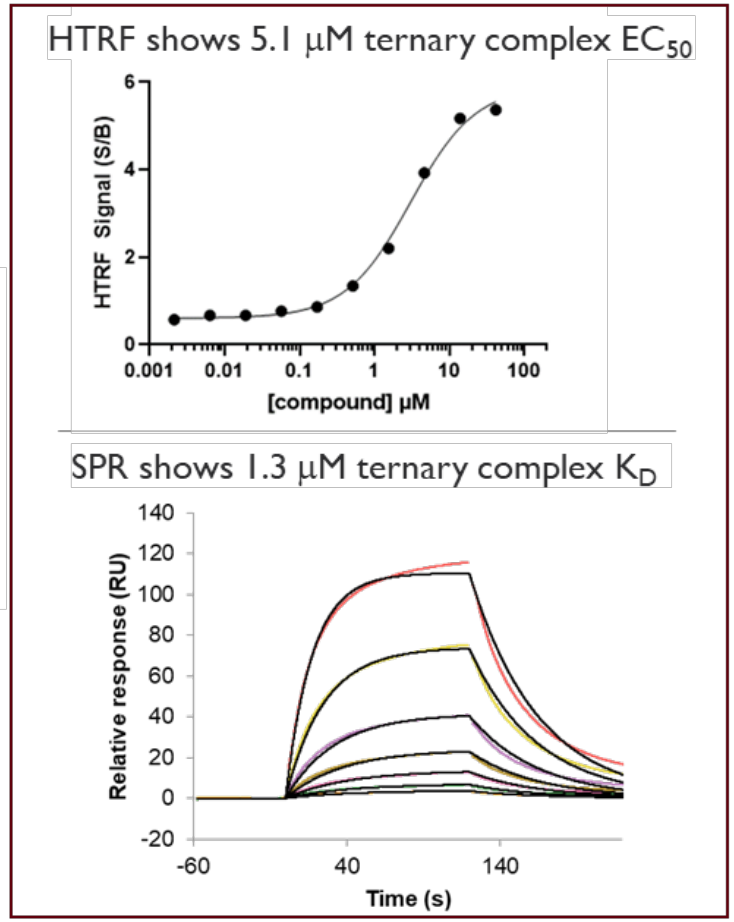
- Compounds 1 and 2 leverage one E3 and a single protein domain



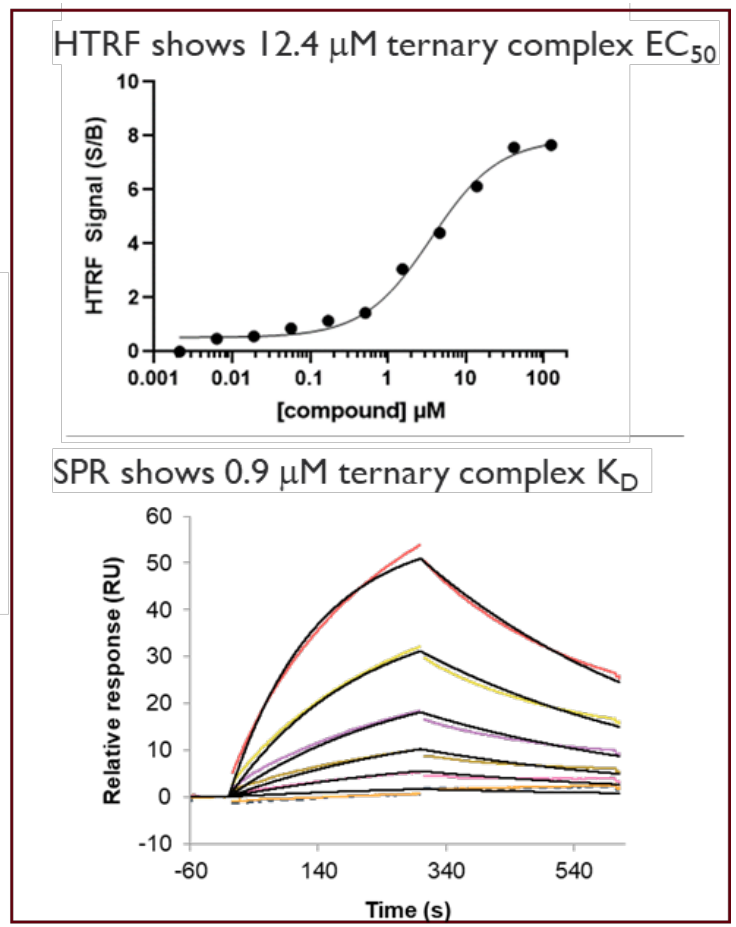
Target B hits form ternary complexes

Compound 1 and compound 2 have distinct ternary complex kinetics

Compound 1

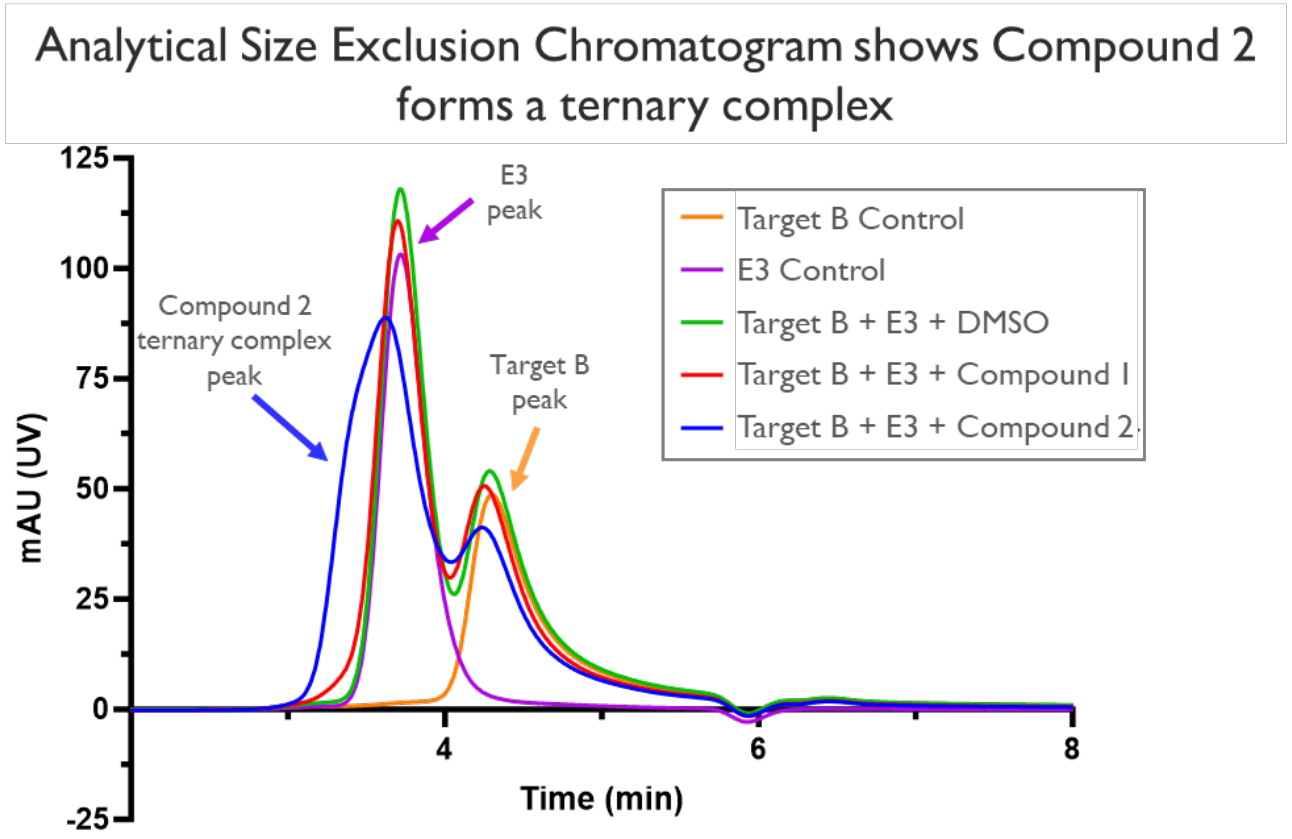


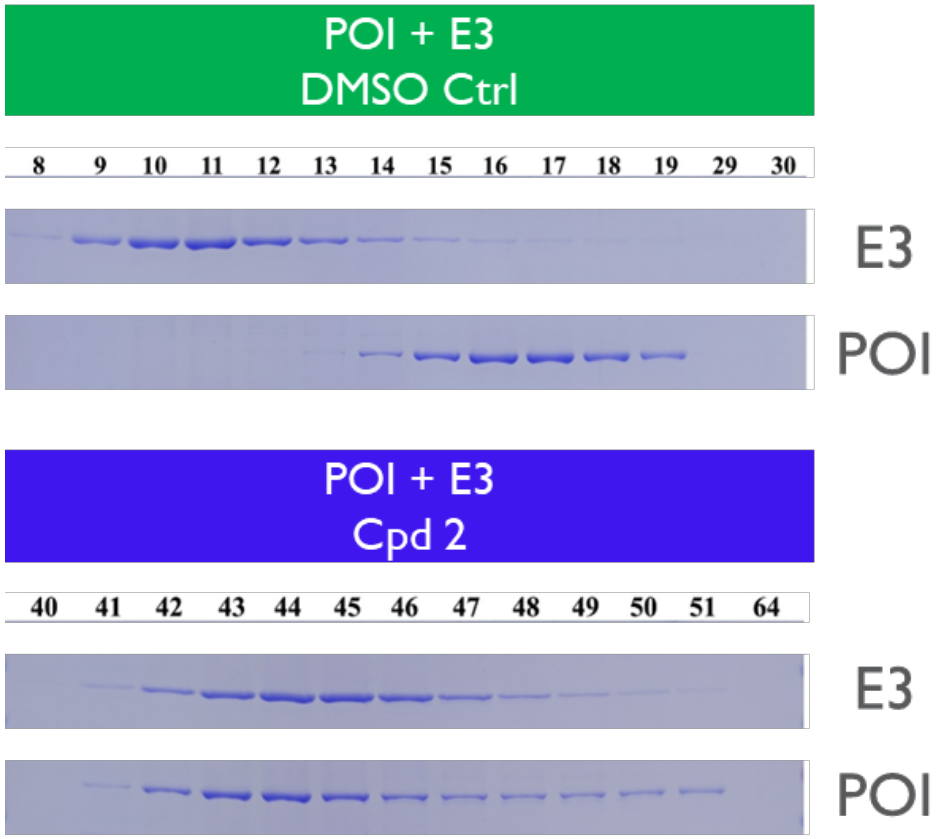
Compound 2



Target B hits form ternary complexes

- Ternary complex formed in the presence of compound 2 as demonstrated by aSEC

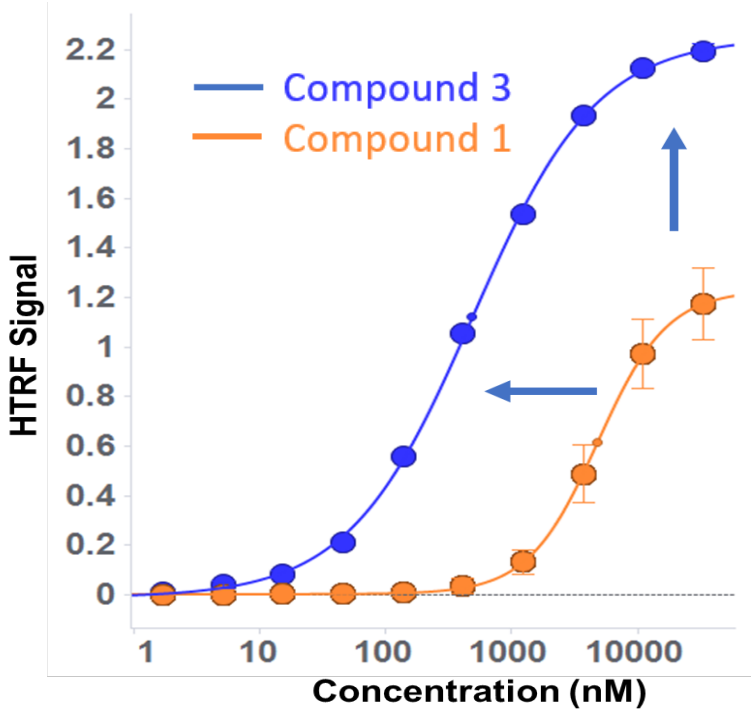




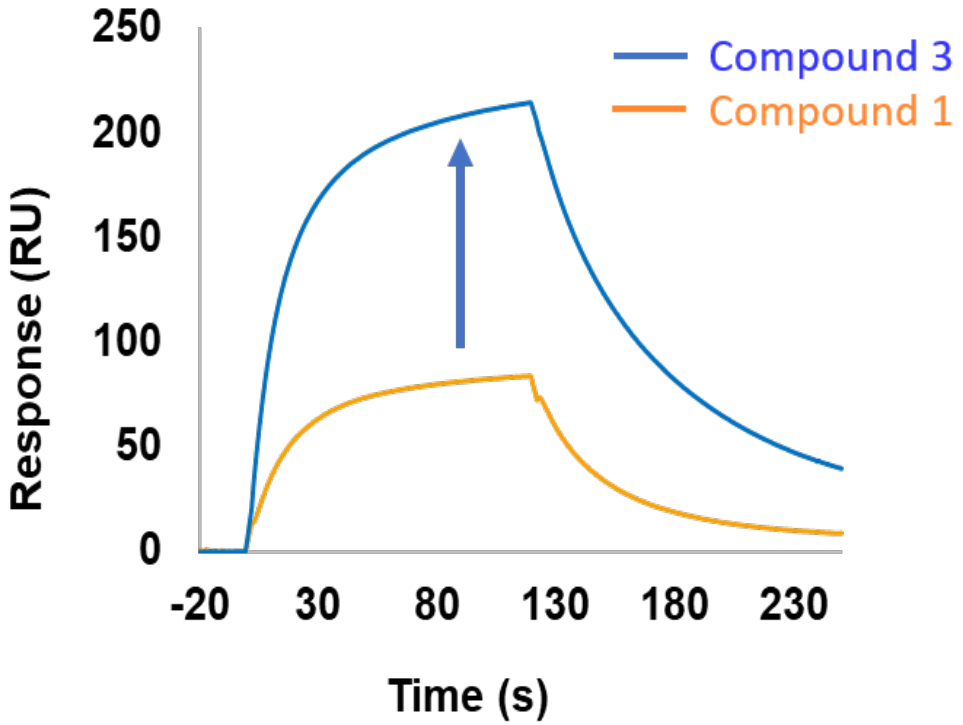
MOPED™ Emerald: Target B hit are progressing

- Compound 3 shows target B HTRF EC50 of 0.5 μM a 10-fold improvement from the original hit and 3-fold increase in AUC in ternary complex

HTRF ternary complex assay

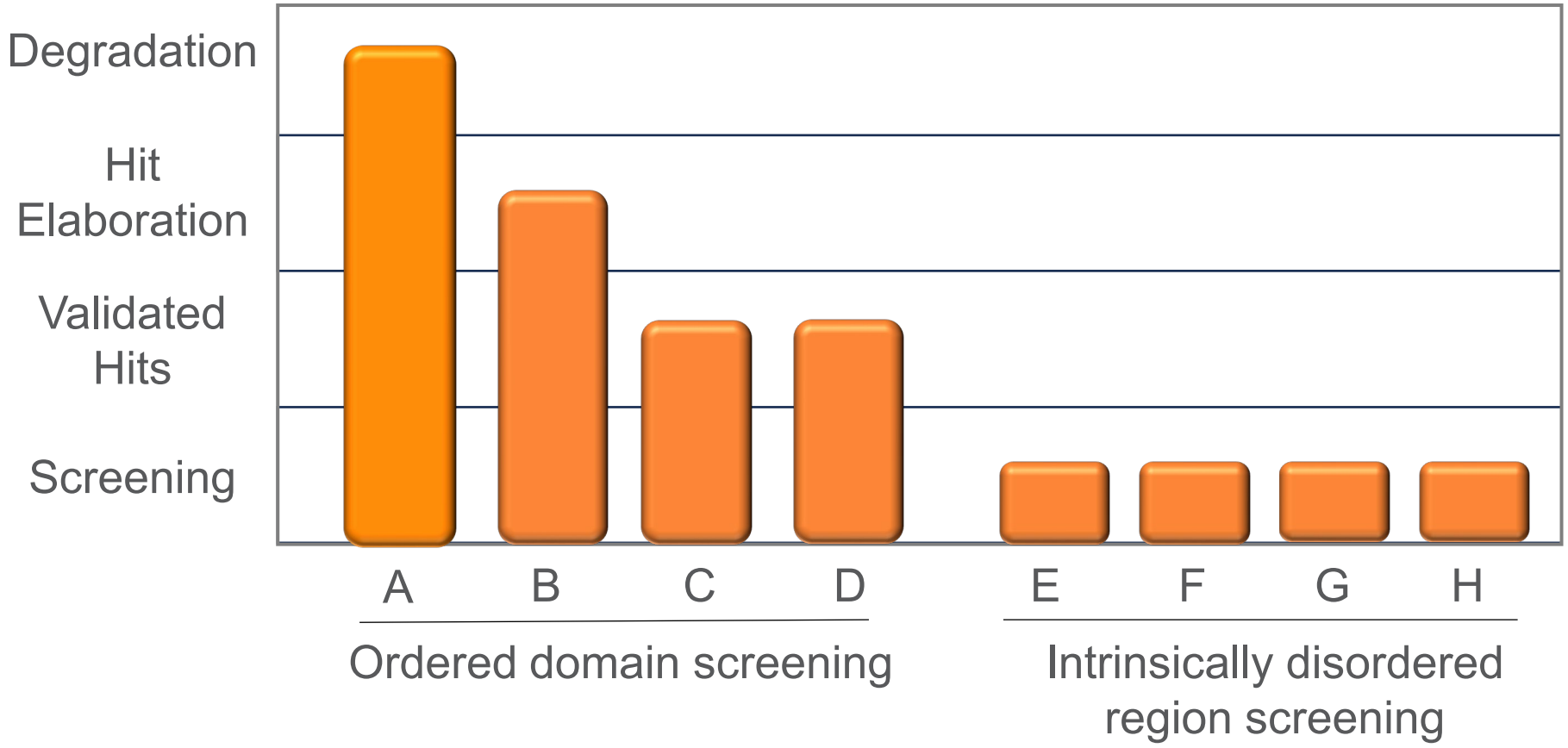


SPR ternary complex assay



MOPED™ Emerald: Summary of 8 unique proteins screened

- Workflow is fully enabled with hits progressing



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Thank You