X-CHEM
TAKE THE LEAD. DRIVE DISCOVERY.

Covalent Ligand Discovery

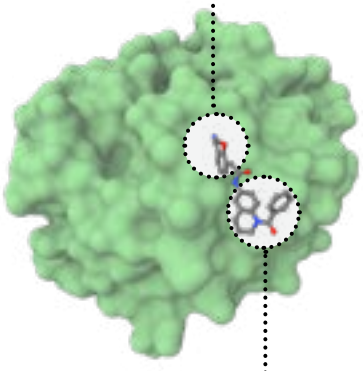
X-CHEM'S COVALENT LIGAND DISCOVERY UNLOCKS:

- Leads for previously intractable targets
- Novel mechanisms of action
- Enhanced selectivity & efficacy
- Targeting of disease-relevant mutants
- Optimized property profiles

A Laser-focused Covalent Targeting Strategy

With recent FDA approvals of covalent drugs (e.g. Zanubrutinib, Ritlecitinib), covalent targeting is improving patient outcomes. By forming irreversible bonds with protein targets, covalent inhibitors offer enhanced potency, prolonged half-life, and the potential to address therapeutically relevant mutations or difficult-to-target proteins.

X-Chem's Versatile Covalent Drug Discovery Apprach



"Electrophile-first" Approach

- Identify electrophilic compounds *via* covalent DEL screening
- Enhance potency, specificity, and rapid onset

"Ligand-first" Approach

- Identify reversible compounds via non-covalent DEL screening or starting with a known ligand
- Incorporate electrophiles using structural data
- Optimize scaffold and reactive warhead to improve potency, specificity and rapid onset

Our Unique Advantages

- Broad target applicability
- Tailored strategy based on project needs
- Faster path to optimized leads
- Toxicity and off-target mitigation

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SUITABLE FOR:

- Kinases
- Transcription factors
- Proteases
- GTPases
- E3 ligases
- Proteins with C, K, H, S, T in or near the binding pocket

Explore our published work:

X-Chem's Covalent Drug Discovery Toolkits

World's First and Evolving Covalent DELs (*Electrophile-based approach*)
DEL technology is the only method capable of creating and screening ultra-large collections of electrophilic compounds designed to form covalent bonds with targets. Our covalent libraries feature billions of proprietary, drug-like molecules equipped with diverse, clinically validated electrophilic warheads, including those found in FDA-approved drugs.

Machine-learning Driven Design *(Ligand-based approach)*
X-Chem's computational tools harness machine learning trained on DEL selection data to streamline hit identification and SAR-by-catalog expansion. These AI-powered models rapidly explore chemical space, efficiently predicting and optimizing binders to accelerate discovery timelines and improve success rates. Non-covalent inhibitors found using this approach can then be engineered to become covalent inhibitors.

Warhead Reactivity & Safety Profiling *(Applicable for both approaches)*
Our advanced GSH reactivity assays differentiate between specific and non-specific covalent compounds, providing a more accurate assessment of potential off-target toxicity. By analyzing kinetic parameters for irreversible binders, we ensure our covalent warheads strike the right balance between efficacy and safety.

ADMET Optimization *(Applicable for both approaches)*
Leveraging in vitro and in silico strategies, partners can expect that the pharmacokinetic profiles of the covalent engagers are optimized. We carefully balance ADME with the specific requirements of covalent binding, enabling sustained target engagement while maintaining optimal drug-like properties.

X-Chem is the partner you need to unlock exponential possibilities in your covalent drug discovery.

Find Your Next Covalent Drug Molecule With X-Chem

ABOUT X-CHEM

X-Chem, Inc. is the leader in small molecule discovery science, providing pharmaceutical and biotech companies a complete, seamless solution for screening, hit validation and lead optimization. As pioneers of DNA-encoded chemical library (DEL) technology, the company leverages its market-leading DEL platform to discover novel small molecule leads against challenging, high-value therapeutic targets. In-house lead optimization services enable clients to progress their compounds directly for even higher quality outputs. Our expertise in medicinal chemistry, custom synthesis and scale-up process chemistry enables us to support all aspects of drug discovery, supporting lead optimization through candidate identification.

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