Advanced Small Molecule Drug Design and Synthesis Training Course

Professional Development Training Course Outline

Category	Biotechnology and Pharmaceutical Development	**Duration**	10 Days
Base Fee	$4,000 USD	**Delivery Mode**	Online / On-site Hybrid

Course Introduction

The landscape of Small Molecule Drug Discovery is undergoing a profound and rapid transformation, driven by the integration of cutting-edge computational power and innovative synthetic methodologies. Despite the rise of biologics, small molecules remain the workhorse of the pharmaceutical industry, offering advantages in oral bioavailability, cell permeability, and cost-effective manufacturing. Advanced Small Molecule Drug Design and Synthesis Training Course is designed to equip medicinal and synthetic chemists with next-generation skills in Targeted Protein Degradation (TPD), Artificial Intelligence (AI) in Drug Design, and state-of-the-art Structure-Activity Relationship (SAR) optimization tactics. Participants will transition from traditional "hit-to-lead" strategies to mastery of complex, multi-parametric optimization (MPO) principles, ensuring they can tackle undruggable targets and accelerate the development of first-in-class therapeutic agents, ultimately reducing the high attrition rate in clinical development.

The core of modern medicinal chemistry lies in the iterative design-make-test-analyze (DMTA) cycle, now augmented by Computer-Aided Drug Design (CADD) and high-throughput automation. This training provides a deep dive into advanced topics, from Molecular Dynamics (MD) Simulations to Green Chemistry practices for scalable synthesis. We bridge the gap between theoretical chemoinformatics and practical organic synthesis, focusing on current challenges like designing molecules that adhere to the Beyond Rule of Five space for complex targets, and minimizing ADME/DMPK and off-target toxicity issues. By emphasizing real-world case studies of recently approved drugs like vorasidenib (Voranigo) and resmetirom (Rezdiffra), the course ensures the application of leading-edge techniques to immediate R&D needs.

Programme Curriculum

Advanced Small Molecule Drug Design and Synthesis Training Course

Introduction

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Course Duration

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Course Objectives

1. Master the principles and practical application of Targeted Protein Degradation (TPD), focusing on the design and synthesis of PROTACs and Molecular Glues.
2. Apply advanced Artificial Intelligence and Machine Learning techniques for de novo molecular design and predictive ADME/Tox modeling.
3. Execute Fragment-Based Drug Design and DEL screening campaigns for novel hit generation.
4. Utilize Structure-Based Drug Design, including molecular docking and Molecular Dynamics simulations, for precision ligand-target interaction analysis.
5. Develop robust strategies for multi-parametric optimization of lead compounds to achieve an optimal balance of potency, selectivity, and druggability.
6. Analyze and interpret complex Structure-Activity Relationship and Structure-Property Relationship (SPR) data to guide lead optimization.
7. Synthesize drug candidates using state-of-the-art synthetic methodology, including flow chemistry, C-H activation, and photoredox catalysis.
8. Design compounds that comply with Beyond Rule of Five principles for difficult targets, maintaining favorable physicochemical properties.
9. Implement Green Chemistry and Process Chemistry principles to ensure scalable, cost-effective, and sustainable API manufacturing.
10. Navigate the specialized Drug Metabolism and Pharmacokinetics strategies required for macrocycles and other non-traditional small molecules.
11. Evaluate and mitigate potential off-target toxicity and drug-drug interactions (DDI) using both in silico and in vitro assays.

12. Integrate chemogenomics and computational chemistry tools to explore chemical space and identify novel scaffolds.
13. Gain an understanding of the Regulatory Affairs and Chemistry, Manufacturing, and Controls requirements for small molecule IND and NDA submissions.

Target Audience

1. Senior Medicinal Chemists and Synthetic Chemists.
2. R&D Scientists in Pharmaceutical and Biotechnology.
3. Computational Chemists and Chemoinformaticians.
4. Process Development Chemists.
5. Post-doctoral Researchers and Advanced Ph.D. Students.
6. Pharmacologists and DMPK Scientists.
7. Team Leaders and Project Managers.
8. Regulatory Affairs specialists and CMC.

Course Modules

Module 1: Strategic Target ID and De Novo Design

- Target validation and the "Druggability" assessment of protein classes.
- AI/ML approaches for hit identification and generative chemistry.
- Applying Chemogenomics to identify novel starting points and privileged scaffolds.
- Case Study: The journey of vorexionib, an AI-designed small molecule inhibitor, from concept to clinic.
- Computational approaches for designing allosteric modulators and orthosteric binders.

Module 2: Fragment-Based Drug Design (FBDD) & DEL

- Principles of FBDD and library design.
- SPR, NMR, X-ray crystallography for fragment validation.
- Fragment linking, growing, and merging strategies for lead compound generation.
- Case Study: Discovery of Vemurafenib, a B-Raf inhibitor, through FBDD.
- Overview of DNA-Encoded Library (DEL) technology and screening logistics.

Module 3: Targeted Protein Degradation (TPD): PROTACs

- Fundamentals of the Ubiquitin-Proteasome System (UPS) and E3 ligases.
- Design and synthesis of the three-part PROTAC molecule.
- Permeability, 'Beyond Rule of Five' properties, and E3-ligase choice.
- Case Study: Design strategies for a successful Oral PROTAC for a cancer target.
- In vitro and in vivo assays for measuring degradation efficiency (DC50?Çï) and cooperativity.

Module 4: Molecular Glues and Emerging Modalities

- The mechanism of molecular glues and their differentiation from PROTACs.
- Strategies for identifying and optimizing a molecular glue lead.
- Design principles for covalent inhibitors and irreversible binding strategies.
- Case Study: The clinical success of thalidomide and its analogs as molecular glues.
- Introduction to macrocyclics and other non-traditional small molecule scaffolds.

Module 5: Advanced CADD and SBDD Techniques

- Sophisticated Molecular Docking protocols and scoring function selection.
- Molecular Dynamics (MD) simulations for understanding conformational changes and binding kinetics.
- Water thermodynamics and its role in predicting ligand binding free energy
- Case Study: Using MD to rationalize the resistance mechanism in the KRASG12C inhibitor Sotorasib.
- QSAR/QSPR models and advanced chemoinformatics for data mining.

Module 6: Physicochemical Properties and DMPK Optimization I

- Understanding the Lipinski's Rule of Five and the Beyond Rule of Five space.
- Strategies for balancing solubility, permeability, and metabolic stability.
- The role of pKa, logD, and molecular flexibility in absorption and distribution.
- Case Study: Optimizing the DMPK profile of Resmetirom for MASH treatment.
- Medicinal chemistry tactics.

Module 7: DMPK Optimization II: Metabolism and Toxicity

- Mechanistic understanding of Cytochrome P450 metabolism and isozyme inhibition.
- Predicting and mitigating drug-drug interactions using in silico and in vitro data.
- Structure-Toxicity Relationship and mitigating off-target toxicity.
- Case Study: Overcoming hepatotoxicity challenges during the development of ALK inhibitors.
- Design for high metabolic stability and overcoming metabolic hotspots.

Module 8: Advanced SAR and MPO Strategies

- Methodologies for Iterative SAR Analysis and data visualization.
- Implementing Multi-Parametric Optimization.
- Design of focused libraries using diversity-oriented synthesis (DOS).
- Case Study: The systematic SAR optimization of the IDH inhibitor Vorasidenib
- Techniques for enhancing selectivity against closely related protein family members.

Module 9: Foundations of Modern Synthetic Chemistry

- Review of essential named reactions.
- Modern methods for complex molecule synthesis.
- Protecting group strategies and total synthesis roadmaps.
- Case Study: Key synthetic steps in the total synthesis of Osimertinib and its complex chiral center.
- Introduction to retrosynthesis planning software and reaction predictability.

Module 10: C-H Activation and Photoredox Catalysis

- Principles and advantages of Catalytic C-H Activation in drug synthesis.
- Designing C-H activation reactions for late-stage functionalization of complex drugs.
- Fundamentals of Photoredox Catalysis and its application in forming C-C and C-N bonds.
- Case Study: Application of photoredox-mediated cyclization in the synthesis of novel heterocycles.
- Techniques for handling and optimizing reactions with reactive intermediates.

Module 11: Flow Chemistry and Automation

- The shift from batch synthesis to Continuous Flow Chemistry and its benefits.
- Design and setup of flow reactors for hazardous reactions
- Integrating automation and robotics in the Design-Make-Test-Analyze cycle.

- Case Study: Using flow chemistry for the scalable and safer synthesis of a key pharmaceutical intermediate.
- Inline monitoring and real-time process analytics in flow.

Module 12: Green Chemistry and Process Development

- The 12 Principles of Green Chemistry and their application in pharmaceutical R&D.
- Metrics for evaluating reaction efficiency, atom economy, and E-factor.
- Solvent selection, solventless reactions, and biocatalysis for sustainable synthesis.
- Case Study: Re-designing a synthesis route to significantly reduce waste and cost.
- Introduction to Process Chemistry requirements for Good Manufacturing Practice

Module 13: Preclinical Development and CMC

- Salt and polymorph screening to optimize the final drug product's properties.
- Formulation strategies for poorly soluble compounds and complex modalities
- ICH Guidelines for API and drug product development.
- Case Study: Stability and formulation challenges encountered during the development of a CNS-active small molecule.
- Preparing the Chemistry, Manufacturing, and Controls section for an IND application.

Module 14: Biological Assays and Target Engagement

- Advanced in vitro assays.
- Cell-based assays for measuring target engagement and IC50?Çï/EC50?Çï.
- Use of Thermal Shift Assays and Surface Plasmon Resonance (SPR) for binding kinetics.
- Case Study: Interpreting PK/PD data for dose prediction and efficacy.
- Phenotypic screening and target deconvolution strategies.

Module 15: Future Trends and Drug Discovery Project Management

- The role of Agentic AI and Large Language Models in accelerating research.
- Project management principles for multidisciplinary drug discovery teams.
- Strategies for patenting and protecting Intellectual Property
- Case Study: Analyzing the Go/No-Go Decision points in a typical small molecule discovery project.
- The rise of computational epigenetics and molecular editing technologies.

Training Methodology

The course employs a highly interactive and practical **Blended Learning** approach, ensuring deep understanding and skill transfer:

1. Interactive Lectures.
2. Case Study Analysis.
3. Hands-on Workshops.
4. Problem-Solving Exercises.
5. Group Project/Simulation.

Register as a group from 3 participants for a Discount

Send us an email: info@fineskilltrainingcenter.org or call +254769199797

Certification

Upon successful completion of this training, participants will be issued with a globally- recognized certificate.

Tailor-Made Course

We also offer tailor-made courses based on your needs.

Key Notes

a. The participant must be conversant with English.

b. Upon completion of training the participant will be issued with an Authorized Training Certificate

c. Course duration is flexible and the contents can be modified to fit any number of days.

d. The course fee includes facilitation training materials, 2 coffee breaks, buffet lunch and A Certificate upon successful completion of Training.

e. One-year post-training support Consultation and Coaching provided after the course.

f. Payment should be done at least a week before commence of the training, to Fineskill Training Center account, as indicated in the invoice so as to enable us prepare better for you.

Upcoming Scheduled Sessions

Start Date	End Date	Location	Price
23 Nov 2026	04 Dec 2026	Online	$2,000
23 Nov 2026	04 Dec 2026	Physical	$3,000
23 Nov 2026	04 Dec 2026	Physical	$6,000
23 Nov 2026	04 Dec 2026	Physical	$6,000
23 Nov 2026	04 Dec 2026	Physical	$12,000
23 Nov 2026	04 Dec 2026	Physical	$9,000
23 Nov 2026	04 Dec 2026	Physical	$12,000
23 Nov 2026	04 Dec 2026	Physical	$12,000

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