FINAL AGENDA

23rd Annual Discovery on TARGET

September 22-25, 2025

BOSTON, MA | SHERATON BOSTON + VIRTUAL

The Industry's Preeminent Event on Novel Drug Targets and Technologies

Register by July 11 and Save up to $550

MONDAY
September 22

- Covalent Chemistries & Induced Proximity
- Strategies for Targeting Kinases
- Emerging Immune Modulation Strategies
- 3D Models & NAMs in Drug Development
- Synthetic Biology for Drug Discovery & Development

TUESDAY — WEDNESDAY
September 23 — September 24

- Degraders and Molecular Glues – Part 1
- Emerging Drug Targets: Identification & Validation
- Small Molecules for Cancer Targets
- Antibodies Against Membrane Protein Targets
- RNA & DNA Targeting Small Molecule Drugs
- AI/ML-Enabled Drug Discovery – Part 1
- Targeting MASH & Obesity NEW
- TS: Know Your GPCR Molecule: Four Most Common Causes of Drug Candidate Failure

WEDNESDAY — THURSDAY
September 24 — September 25

- Degraders and Molecular Glues – Part 2
- Lead Generation Strategies
- Emerging Cancer Targets for Multispecifics, ADCs, and Biologics
- GPCR-Based Drug Discovery
- Targeting Transcription Factors
- AI/ML-Enabled Drug Discovery – Part 2
- TS: Drug Exposure at the Target: The Role of ADME and Pharmacokinetics

Plenary Keynote Program

The Radicalization of Drug Discovery

Gregory L. Verdine, PhD
President & CEO, LifeMine Therapeutics

GLP-1 Unveiled: Key Takeaways for Next-Generation Drug Discovery

Lotte Bjerre Knudsen, PhD
Chief Scientific Advisor, Head of IDEA (Innovation & Data Experimentation Advancement), Novo Nordisk AS

Organized by Cambridge HEALTHTECH Institute

#BostonDOT | DiscoveryOnTARGET.com

Premier Sponsors: X-CHEM PHARMACEUTICALS

1,100+ Attendees | **110+** Research Posters | **22** Countries Represented | **73%** Pharma & Biotech

About the Event

23rd Annual

In its 23rd year, Discovery on Target is the premier event highlighting "hot" drug targets and emerging modalities, technologies, and strategies for pursuing those targets. The numerous conferences, symposia, courses, and training seminars offer key insights for the successful discovery and development of novel therapeutics, from small molecules to biologics to chimeras and conjugates. The 4 day event covers innovations in target identification and lead generation, which includes cancer therapies, protein degradation, induced proximity, AI/machine learning, membrane proteins, translational models, synthetic biology, and other relevant topics. New this year is an increased coverage of GLP-1, MASH and obesity, ADCs, and bispecifics and small molecules targeting DNA.

This event offers a unique opportunity to engage in meaningful conversations and foster connections with a global audience of 1100+ drug discovery experts. Concurrent sessions with over 220 presentations, 100+ posters, panels, breakout discussions, and 1-1 networking events enable you to customize your on-site experience and engage with problem-solvers and solutions providers who can be future collaborators. Join our growing DOT community to be at the forefront of new ideas and trends in drug discovery. We look forward to welcoming you in Boston!

EVENT AT-A-GLANCE

#BostonDOT

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- Strategies for Targeting Kinases
- Emerging Immune Modulation Strategies
- 3D Models & NAMs in Drug Development
- Synthetic Biology for Drug Discovery & Development

IN-PERSON ONLY

MONDAY
Dinner Short Courses

SC1: Protein Degraders from a Beyond-Rule-of-Five and an ADME Perspective

SC2: Chemical Biology for Covalent Discovery, Phenotypic Screening, and Target Deconvolution

SC3: DNA-Encoded Libraries

SC4: Developing Physiologically Relevant 3D Models

SC5: Best Practices for Targeting GPCRs, Ion Channels, and Transporters

SC6: Recombinant Protein Production to Support Target Identification and Lead Development

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- Targeting MASH & Obesity NEW

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- GPCR-Based Drug Discovery
- Targeting Transcription Factors
- AI/ML-Enabled Drug Discovery – Part 2

IN-PERSON ONLY

- Drug Exposure at the Target: The Role of ADME and Pharmacokinetics

All Access Package includes access to two short courses and all symposia. Separate registration required for other packages.

IN-PERSON ONLY

WEDNESDAY
Dinner Short Courses

SC7: Fragment-Based Drug Design: Advancing Tools and Technologies

SC8: Biophysical Approaches for GPCRs

SC9: Affinity Selection Mass Spectrometry (ASMS): An Introduction

SC10: Next Gen ADCs & Advanced Linkers and Conjugates: Mastering Design, Linker Optimization and Stability

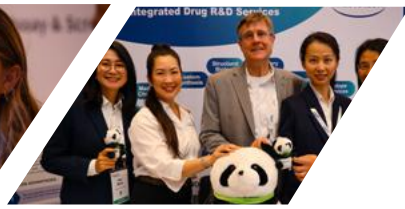
SC11: AI Toolkit for Drug Discovery: LLMs, AI Agents & Prompt Engineering

SC12: Advanced Pharmacology for Drug Discovery: Traps, Tips and Tricks

- Pre-Conference Symposium*
- Conference
- Training Seminar
- Short Courses

Become a Sponsor or Exhibitor

SPONSORSHIP PROGRAMS



CHI's comprehensive sponsorship packages allow you to achieve your objectives before, during, and long after the event. Maximize exposure to hard-to-reach decision-makers through the following sponsorship opportunities:

Podium Presentations - Available within Main Agenda!

Showcase your solutions to a guaranteed, targeted audience through a 15- or 30-minute presentation during a specific conference program. Package includes exhibit space, on-site branding, and access to cooperative marketing efforts by CHI.

One-on-One Meetings

Work with us to identify your target prospects and we will schedule meetings for you. Think of us as your inside sales team with all your hottest leads in close reach. Opportunities sold on a very limited basis.

Invitation-Only Dinner/Hospitality Suite

Sponsors will select their top prospects from the conference preregistration list for an evening of networking at the hotel or at a choice local venue. CHI will extend invitations, conduct follow-up, and confirm attendees. The evening will be customized to meet with your specific objectives.

Corporate Support Exhibit Package

Includes 8'x10' exhibit space. Contact us for more information.

Additional sponsorship & branding opportunities include:

- Meter Boards
- Lanyards
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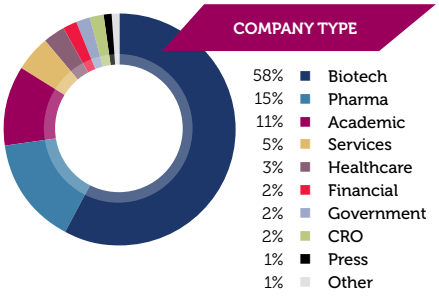
- Tote Bag Exclusive Sponsorship
- Water Bottles
- Conference Track Notebooks
- Tote Bag Insert
- And more!

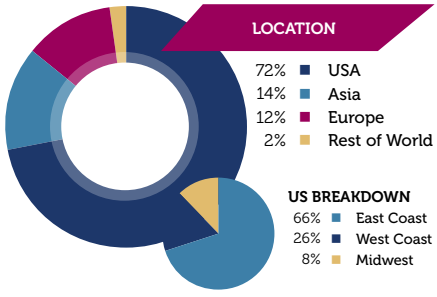
For more information regarding exhibit and sponsorship, please contact:

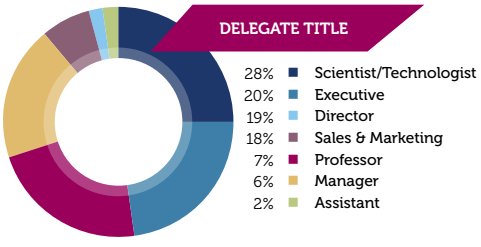
Kristin Skahan
Senior Business Development Manager
781-972-5431
kskahan@healthtech.com

2024 ATTENDEE DEMOGRAPHICS

Discovery on TARGET







Thank You to Our Sponsors

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X-CHEM PHARMACEUTICALS

Corporate Sponsors:

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Supporting Sponsor:

examol

Plenary Keynote Program

Join colleagues from around the world for the Discovery on Target Plenary Keynote Programs. Our plenary keynote presentations will bridge both halves of the event. It's the only time our entire DOT community of drug discovery professionals assembles together to learn about big-picture perspectives, innovative technologies, and thought-provoking trends from luminaries in the field. Later in the day we'll hear about the latest trends in drug discovery from our Plenary Venture Capital Panel. This will be followed by a Collaborations Discussion where we talk about various topics that impact life sciences and how we can address it together to make a difference.

WEDNESDAY, SEPTEMBER 24

11:05 The Radicalization of Drug Discovery

Gregory L. Verdine, PhD, President & CEO, LifeMine Therapeutics

The field of drug discovery stands at a watershed moment of scientific, medical, and commercial opportunity. Realization of this opportunity will require radical innovations that fundamentally expand the functional capabilities of therapeutic interventions and management of the attendant risks. This talk will focus on the discovery, development, and deployment of radically new therapeutic modalities, inspired by nature, that thrust the field forward in non-obvious, impactful, and exciting new directions.

Gregory L. Verdine is Erving Professor of Chemistry and Harvard College Professor, emeritus, at Harvard University and Harvard Medical School; Co-founder, President and Chief Executive Officer of LifeMine Therapeutics (with co-founders Rick Klausner and WeiQing Zhou); Co-founder (with Hal Barron) and Executive Chairman of VidaVinci; and Venture Partner at Andreessen Horowitz. Verdine is an award-winning university educator, pioneering life scientist and innovator, new modality drug discovery entrepreneur, venture capitalist and successful zero-to-one biotech company-builder. He is a Fellow of the Royal Society of Chemistry and the American Association for the Advancement of Science; he has received a Presidential Investigator Award, the Nobel Laureate Signature Award, the AARC Award for Excellence in Chemistry in Cancer Research and an honorary PhD degree from Clarkson University and MS degree from Harvard University. Verdine received Bachelor of Science and doctoral degrees in chemistry from St. Joseph's University and Columbia University, respectively.

11:40 GLP-1 Unveiled: Key Takeaways for Next-Generation Drug Discovery

Lotte Bjerre Knudsen, PhD, Chief Scientific Advisor, Head of IDEA (Innovation&Data Experimentation Advancement), Novo Nordisk AS

This talk will explore the evolution of GLP-1 as a significant component in diabetes and obesity treatment, as well as its direct impact on multiple co-morbidities. It will highlight the role of industry innovation and scientific persistence in overcoming challenges posed by its short half-life, ultimately leading to the successful development of GLP-1 therapies. Key lessons from this journey will inform future drug discovery strategies, emphasizing that today's drug discovery must be based on human data.

Lotte Bjerre Knudsen is a Danish national, born in 1964 in a small town near Copenhagen. She holds a degree in biotechnology from the Technical University of Denmark, and a Doctoral degree in Scientific Medicine from the University of Copenhagen, Denmark. Lotte has been with Novo Nordisk since her university graduation in 1989 and has since then held several positions within the company and is today Chief Scientific Advisor in Research & Early Development and heads up IDEA (Innovation and Data Experimentation Advancement). She has deep experience across the entire value chain of drug discovery and development and has published extensively. Lotte is an inventor on many patents, all fully owned by Novo Nordisk. She has been part of representing Novo Nordisk in five FDA Advisory committees. Lotte has received numerous awards. Most recently, she was the recipient the Paul Langerhans Award from the German Diabetes Association and a co-recipient of the American Association for the Advancement of Science Mani Bhaumik Breakthrough of the Year Award, the Lasker Foundation Lasker-DeBakey Clinical Award and the Breakthrough Prize in Life Sciences.

VENTURE CAPITALIST INSIGHTS

4:15 pm PANEL DISCUSSION: Venture Capitalist Insights into Trends in Drug Discovery

PANEL MODERATOR: Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation

PANELISTS:

Olga Danilchanka, PhD, Principal, MRL Ventures Fund

Jamie Kasuboski, PhD, Partner, Luma Group

Chris De Savi, PhD, CSO Partner, Curie Bio

Devin Quinlan, PhD, Principal, Investment, MPM BioImpact Inc.

Topics to be discussed:

- Key drivers of innovation in drug discovery
- Overcoming hurdles in translating discoveries from the lab to the clinic
- Impact of AI/machine learning, emerging drug modalities, pursuit of challenging drug targets
- Navigating the current regulatory and funding environment
- Perspectives on upcoming challenges and opportunities in drug development

COLLABORATIVE CONVERSATION

5:15 pm Connecting the DOTs to Spark Change!

Join us for an hour of inspiring, informal discussions on how to forge connections and create impactful ecosystems that will help you think, act, and thrive. We have invited pharma, biotech, and academic leaders to share their stories and experiences and to discuss key learnings. There will be time for open discussion and networking. This session will not be recorded for on-demand viewing.

Topics for discussion will include, but certainly not be limited to:

How to Create Opportunities for Scientists to Connect and Collaborate

Saudat Fadeyi, PhD, MBA, Head, Business Development & Strategy, Samyang Biopharm USA, Inc.

How to Educate Scientists to Seek Out Networks and Funding Resources

Sean Ekins, PhD, Founder & CEO, Collaborations Pharmaceuticals

How to Motivate Industry and Academia to Work Together and Forge Partnerships

Shruthi Bharadwaj, PhD, Program Leader, MIT

How to Address Hidden Barriers and Biases

Raquel Mura, DPharm, Founder, RGM Life Sciences Consulting; former VP & Head R&D, Sanofi

How to Uncover Gaps and Systemic Predispositions, Rethinking Clinical Trial Design Conventions

Nisha Perez, PhD, VP Preclinical Development & Clinical Pharmacology, ROME Therapeutics

Chris De Savi, PhD, CSO Partner, Curie Bio

Short Courses*

*All Access Pricing or separate registration required

SHORT COURSES WILL BE OFFERED IN-PERSON ONLY.

MONDAY, SEPTEMBER 22 5:00-7:30 PM

SC1: Protein Degraders from a Beyond-Rule-of-Five and an ADME Perspective

Instructors:

Prasoon Chaturvedi, PhD, Vice President & Head, DMPK, C4 Therapeutics, Inc.

Stefanus Steyn, PhD, Research Fellow, Pharmacokinetics Dynamics & Metabolism, Pfizer

This course focuses on proteolysis targeting chimeras (PROTACs) and will cover topics relevant to developing them as oral therapeutics. The course will include an in-depth look at their physicochemical properties and how these influence solubility and permeability. It will examine ADME topics focusing on *in vitro* assays for stability, polarity, transporters, drug-drug interactions (DDIs), Cytochrome P450 (CYP450) inhibition, and more. Topics will include looking at what is known about how PROTACs are metabolized *in vivo* and strategies to deliver them with adequate PK/PD.

SC2: Chemical Biology for Covalent Discovery, Phenotypic Screening, and Target Deconvolution

Instructors:

Paul Brennan, PhD, Professor, Nuffield Department of Medicine, University of Oxford

Brent Martin, PhD, Vice President, Chemical Biology, Odyssey Therapeutics

Angelo Andres, Senior Scientist, Chemical Biology, AstraZeneca

This course is designed to provide an overview and best practices in the use of chemical biology probes and assays that have been developed for applications in early drug discovery. Next-generation chemoproteomic technologies such as proximity labeling proteomics (BioID, MicroMap, and MultiMap) and their application to drug discovery will be discussed. Chemists and biologists working in lead generation, assay development, phenotypic screening, target discovery and deconvolution, target engagement and mechanism-of-action (MoA) studies will all benefit from attending this course. The instructors will share their knowledge and expertise around the use of various technologies and chemistries, and there will be time for open discussion and exchange of ideas.

SC3: DNA-Encoded Libraries

Instructors:

Svetlana Belyanskaya, PhD, Co-Founder, DEL Source; Former Vice President, Biology, Anagenex

Ghotas Evindar, PhD, Co-Founder & President, DEL Source; Former DEL Platform Senior Manager and Group Leader, GSK

This course provides an overview of DNA-Encoded Library (DEL) screening platforms, discusses common selection strategies for identifying novel hits from DEL campaigns, and delves into parameters for building a library collection. The instructors will also cover strategic considerations in using DEL selection data to accelerate hit-to-lead steps in drug discovery.

SC4: Developing Physiologically Relevant 3D Models

Instructors:

Madhu Lal Nag, PhD, CSO, InSphero

Nathan P. Coussens, PhD, Scientific Director, Molecular Pharmacology Laboratory, Frederick National Laboratory for Cancer Research

With the passing of the FDA Modernization Act 2.0, there is a greater interest in the drug discovery community to develop and use physiologically relevant *in vitro* models for drug candidate testing and IND filings. This course will help attendees understand what it takes to design and develop relevant 3D organoid/spheroid models through the various stages of assay development, automation compatibility and data analysis. The utility of these models in answering specific biological questions and the importance of developing a robust, scalable 3D model–based assay for preclinical decision-making will also be demonstrated through case studies.

SC5: Best Practices for Targeting GPCRs, Ion Channels, and Transporters

Instructor:

Ross Chambers, PhD, Vice President, Antibody Discovery, Integral Molecular, Inc.

Complex membrane proteins are important therapeutic targets and together represent the majority of protein classes addressed by therapeutic drugs. Significant opportunities exist for targeting complex membrane proteins with antibodies, but it has been challenging to discover therapeutic antibodies against them. This course will examine emerging technologies and strategies for enabling the isolation of specific and functional antibodies against GPCRs, ion channels, and transporters, and highlight progress via case studies.

SC6: Recombinant Protein Production to Support Target Identification and Lead Development

Instructors:

Richard Altman, MS, Field Application Scientist, Life Science Solutions, Thermo Fisher Scientific

Dominic Esposito, PhD, Director, Protein Sciences, Frederick National Laboratory

High-quality recombinant proteins are an essential tool for the successful discovery and development of novel therapeutics. Often these protein targets are difficult to produce with success dependent predominantly on the biological and biochemical properties of an individual protein. For this reason, failures in protein production using more standard traditional bacterial approaches have become prevalent. This course will focus on both the insect and mammalian expression systems, which have demonstrated the ability to express complex proteins for a wide variety of applications. We will discuss the concepts, uses, and optimization of these systems along with sharing experimental troubleshooting lessons learned. The course combines instruction and case studies in an interactive environment.

WEDNESDAY, SEPTEMBER 24 6:00-8:30 PM

SC7: Fragment-Based Drug Design: Advancing Tools and Technologies

Instructors:

Ben J. Davis, PhD, Research Fellow, Biology, Vernalis R&D Ltd.

Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation

This course aims to introduce the fundamentals of Fragment-Based Lead Discovery (FBLD) to attendees. The first section will focus on the concepts of using fragments for hit generation. Special emphasis will be placed on practical pitfalls and the many ways to advance fragments to leads and drugs. The second part of the course will discuss the variety of fragment screening methods and when they are best applied. The composition of fragment libraries will also be discussed in detail. The attendees should come away from this course with a solid understanding of what FBLD is and how to apply it.

SC8: Biophysical Approaches for GPCRs

Instructor:

Matthew T. Eddy, PhD, Assistant Professor, Chemistry, University of Florida, Gainesville

This short course will review biophysical methodologies used to investigate the structure–function relationships of G protein-coupled receptors (GPCRs). Through selected examples, we will highlight how these techniques contribute to GPCR structure determination and support drug discovery efforts. Topics will include nuclear magnetic resonance (solution and solid-state), fluorescence spectroscopy and imaging, surface plasmon resonance, and mass spectrometry-based approaches.

Short Courses*

*All Access Pricing or separate registration required

SHORT COURSES WILL BE OFFERED IN-PERSON ONLY.

SC9: Affinity Selection Mass Spectrometry (ASMS): An Introduction

Instructor:

Hans-Peter N. Biemann, PhD, Distinguished Scientist, Integrated Drug Discovery, Sanofi

This course will provide an overview of ASMS as a biophysical assay technique. The focus will be on the main applications of ASMS: (1) for highthroughput screening and (2) ASMS for compound binding studies. Case studies will be presented as well.

SC10: Next Gen ADCs & Advanced Linkers and Conjugates: Mastering Design, Linker Optimization and Stability

Instructors:

Akbar H Khan, PhD, Associate Director, Oncology R&D, Research and Early Development, AstraZeneca

Amit Nayyar, PhD, General Manager, Cohance

Conjugated modalities such as antibody-drug conjugates (ADCs), oligonucleotide conjugates, and peptide-drug conjugates are revolutionizing precision medicine. However, their success relies on smart linker strategies that ensure stability, controlled payload release, and manufacturability. This intensive 2-hour course will explore the latest innovations in linker chemistry, site-specific conjugation, formulation and delivery considerations, and scalable manufacturing approaches. Participants will gain practical insights into optimizing linker design for enhanced efficacy, reduced toxicity, and regulatory compliance.

SC11: AI Toolkit for Drug Discovery: LLMs, AI Agents & Prompt Engineering

Instructors:

Parthiban Srinivasan, PhD, Professor and Director, Centre for AI in Medicine, Vinayaka Mission's Research Foundation, India

Petrina Kamya, PhD, Global Head of AI Platforms & Vice President, Insilico Medicine; President, Insilico Medicine Canada

Deep generative modeling is rapidly transforming *de novo* drug discovery and streamlining the entire process. This artificial intelligence (AI) Toolkit course explores how the Three Waves of AI—from predictive AI to generative AI and the emerging era of Agentic AI—are transforming pharmaceutical innovation. Participants will learn how AI and machine learning (ML) are re-shaping molecular design, enabling the creation of novel compounds with precision-tailored properties. The course delves into the fundamentals of Large Language Models (LLMs), foundational models, and autonomous AI systems, highlighting their potential role in re-inventing the pharmaceutical landscape. Along the way, we'll dissect three pivotal techniques for biopharma-specific LLMs: prompt engineering, retrieval augmented generation (RAG), and fine-tuning. This course is designed for medicinal chemists, molecular modelers, and project managers seeking to harness the capabilities of modern Generative AI concepts and integrate them into their work.

SC12: Advanced Pharmacology for Drug Discovery: Traps, Tips and Tricks

Instructor:

Fabien Vincent, PhD, Consultant; formerly Pharmacology Lab Head, Pfizer Inc.

Characterizing and understanding the interactions of potential therapeutic agents with their targets is fundamental to drug discovery. After first reviewing the fundamentals of pharmacology, we will conduct an in-depth exploration of pharmacology assays and screening funnels as they apply to the validation of hits and their optimization into clinical candidates. A key aim will be to distill important, but often poorly known, pharmacology and screening information in a concise format.

This course will surface pitfalls and offer mitigations strategies on a range of relevant topics with a goal of providing practical information to help prosecute drug discovery projects more effectively from project inception all the way to clinical trials.

Present a Poster and Save $50

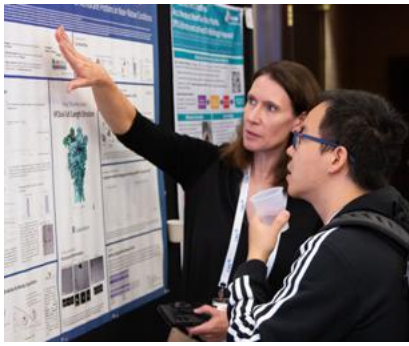
Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure an onsite poster board and/or ensure your poster is included in the conference materials, your full submission must be received, and your registration paid in full by August 15, 2025.

Reasons you should present your research poster at this conference:

- Your research will be seen by our international delegation, representing leaders from top pharmaceutical, biotech, academic and government institutions
- Discuss your research and collaborate with other attendees
- Your poster content will be published in our conference materials
- Receive $50 off your registration

Best of Show Poster Award

Present your poster at Discovery on Target and be automatically entered to win. The winner will be chosen based on the clarity of the short text description, the novelty of data, technology advances and implications of the work presented, visual clarity of the poster presentation, and clear and engaging oral explanation



Training SEMINARS

By Cambridge Healthtech Institute

TUES-WED September 23-24 — **WED-THURS** September 24-25

TRAINING SEMINARS WILL BE OFFERED IN-PERSON ONLY.

Cambridge Healthtech Institute Training Seminars offer real-life case studies, problems encountered and solutions applied, along with extensive coverage of the academic theory and background. Each Training Seminar offers a mix of formal lecture and interactive discussions and activities to maximize the learning experience. These Training Seminars are led by experienced instructors who will focus on content applicable to your current research and provide important guidance for those new to their fields.

TS8A: Know Your GPCR Molecule: Four Most Common Causes of Drug Candidate Failure

Instructor:

Terrence P. Kenakin, PhD, Professor, Pharmacology, University of North Carolina at Chapel Hill

This course discusses the 4 main reasons GPCR candidate molecules often fail in late stage development. I emphasis the correct detection of the pharmacology of the candidate in the disease setting. Topics are: (1) What efficacy is needed to treat the disease? (2) Was the wrong biological target chosen? (3) Was the wrong chemical target chosen? And (4) Know Your Molecule: Were the true efficacies of the candidate molecule adequately known?

TS7B: Drug Exposure at the Target: The Role of ADME and Pharmacokinetics

Instructor:

Erland Stevens, PhD, James G. Martin Professor, Department of Chemistry, Davidson College

This training seminar describes how pharmacokinetics (PK) affects drug exposure at the intended target. The seminar opens with a foundation of clinical PK including the determination of key PK parameters from Cp-time data. Course materials also cover common preclinical ADME assays that allow estimation of a compound's human PK properties. The materials bridge the idea of a compound's PK and its observed pharmacodynamic effects (PD) through coverage of PK/PD modeling. Various drug modalities (e.g., small molecules, antibodies, and peptides) illustrate the concepts of the course.

Join Us in Boston!

Conference Venue and Hotel:
Sheraton Boston
39 Dalton Street
Boston, MA 02199

Discounted Room Rate: $325 s/d
Discounted Room Rate Cut-off Date: August 26, 2025

For additional information please visit DiscoveryOnTarget.com/Travel

*All Access Package includes access to two short courses and all symposia. Separate registration required for other packages.

2nd Annual

Covalent Chemistries & Induced Proximity

Utilizing and Manipulating Protein Binding and Cellular Interactions to Drive New Therapies

MONDAY, SEPTEMBER 22

8:00 am Pre-Conference Symposium Registration Open and Morning Coffee

8:50 Welcome Remarks

EXPLORING INDUCED PROXIMITY

8:55 Chairperson's Remarks
Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation

9:00 An 'Omics Approach for Drug Discovery
Stefan Harry, PhD, ACS Postdoctoral Fellow, Harvard University and Massachusetts General Hospital
We developed DrugMap, a cysteine reactivity atlas across 416 cancer cell lines, uncovering context-specific ligandability driven by redox, conformation, and genetics. This enabled covalent targeting of NFκB1 and SOX10. We further introduced molecular COUPLrs—dual warhead ligands—and CONNECT proteomics, revealing hundreds of inducible protein couplings. A COUPLr targeting EML4-ALK disrupted signaling. Together, these tools map and reprogram protein interactions to access undruggable cancer targets.

10:00 Cereblon: The Gift That Keeps On Giving
Katherine Donovan, PhD, Scientist, Laboratory of Dr. Eric Fischer, Cancer Biology, Dana-Farber Cancer Institute/Harvard Medical School
Small molecules inducing protein degradation via ligase-mediated ubiquitylation are promising in pharmacology. To comprehensively explore the target space of CRBN, we developed a sensitive and high-throughput lysate-based IP-MS pipeline for unbiased identification of molecular glue targets of IMiD-CRBN. Our study offers a broad catalog of CRBN-recruited targets (>290 targets) and introduces a scalable workflow for discovering new drug-induced protein interactions in cell lysates.

10:30 Sponsored Presentation *(Opportunity Available)*

11:00 Enjoy Lunch on Your Own

COVALENT DRUG DISCOVERY

12:30 pm Hydralazine Covalently Inhibits Cysteamine Dioxygenase to Attenuate GPCR Signaling and Glioblastoma Growth
Megan L. Matthews, PhD, Assistant Professor, Chemistry, University of Pennsylvania
Hydralazine (HYZ) has been used clinically for 70 years, but its mechanism of action (MOA) is still unknown. The talk will show how HYZ covalently and irreversibly inhibits a single target and achieves remarkable selectivity across cells and tissues. It connects an old drug to its target, reveals the mechanism of its therapeutic effect, and shows it can be now be repurposed and further optimized to treat neurological brain disorders.

1:00 Discovery and Characterization of Covalent Inhibitors
Hua Xu, PhD, Director, Head of Chemical Biology and Proteomics, AstraZeneca
Covalent modulation of therapeutic targets is an increasingly important modality for drug discovery, particularly after recent success with historically challenging targets like KRAS G12C. In this talk, I'll present the work we have done to discover covalent inhibitors for two different targets, and also describe the chemical biology approaches to understand the selectivity and mechanisms of action of these inhibitors.

1:30 Rewiring Cancer Drivers to Activate Programmed Cell Death
Isabella Graef, MD, CEO, Shenandoah Therapeutics
Sushant Malhotra, Senior Vice President, Drug Discovery
Nearly every cancer is driven by unique cancer drivers. Each cancer cell has inherent self-destruct mechanisms leading to cell death. Despite being genetically validated, many oncogenic drivers are hard to target with drugs. We have created small molecules (TCIPs) that employ chemically induced proximity to trigger potent and specific cell death pathways dependent on the mutated cancer driver. This feature confers upon TCIPs an exquisite specificity in killing cancer cells.

2:00 In-Person Brainstorming Session
This informal session will be led by the speakers, allowing participants to ask questions and exchange ideas around topics related to the symposium. To get the most out of this session, please come prepared to share your ideas and participate in collective problem solving.

2:45 Networking Refreshment Break
Join your colleagues for a cup of coffee or refreshments and make new connections

3:15 Lessons Learned from Developing BTK Molecular Glue Degraders
Jin Wang, PhD, Director, Biochemistry and Molecular Pharmacology, Baylor College of Medicine
In this study, we discovered PS-10, a molecular glue targeting Bruton's tyrosine kinase (BTK). While PS-10 doesn't bind directly to BTK, it does bind to E3 ubiquitin ligase CRBN, forming a ternary complex that leads to efficient BTK degradation. Cryo-EM analysis revealed unique protein interactions and PS-10's mechanism extends to other kinases, demonstrating broader therapeutic potential.

3:45 Going beyond Cysteine for Kinase Covalent Ligand Discovery
Ken Hsu, PhD, Stephen F. and Fay Evans Martin Endowed Associate Professor, Department of Chemistry, The University of Texas at Austin
I will describe sulfonyl-triazoles as an enabling electrophile for developing covalent binders to tyrosine and lysine residues on proteins through sulfur-triazole exchange (SuTEx) chemistry. SuTEx chemistry is highly tunable with respect to protein reactivity and specificity, which can facilitate optimization of potent and selective binders to orthosteric and allosteric sites on kinases. I will conclude my talk by describing efforts to apply SuTEx ligands for modulating kinase function in cells.

4:15 Close of Symposium

5:00 Dinner Short Courses*
*All Access Package or separate registration required. See Short Courses page for details.

7:30 Close of Day

*All Access Package includes access to two short courses and all symposia. Separate registration required for other packages.

16th Annual

Strategies for Targeting Kinases

Novel Chemistries and Techniques for Studying, Modulating, and Degrading Kinases

MONDAY, SEPTEMBER 22

8:00 am Pre-Conference Symposium Registration Open and Morning Coffee

8:50 Welcome Remarks

UNDERSTANDING STRUCTURE-FUNCTION RELATIONSHIPS

8:55 Chairperson's Remarks
Rayees Rahman, PhD, Co-Founder & CEO, Harmonic Discovery

9:00 Enhanced Protein-Ligand Co-Folding for Precise Kinase-SAR Modeling
Rayees Rahman, PhD, Co-Founder & CEO, Harmonic Discovery
Modeling kinase-ligand structure-activity relationships remains challenging due to kinase conformational flexibility and limitations of computational methods like docking. Here, we introduce Terra, a novel protein-ligand co-folding model fine-tuned on kinase conformations and ligand SAR data. Terra achieves correlation coefficients matching or exceeding FEP methods for known and novel kinase targets, with a significantly lower computational cost.

9:30 Applying Quantum Methods to Address Selectivity Challenges in Phosphatases and Beyond
Vid Stojevic, PhD, CoFounder & CEO, Kuano Ltd.
Kinases and Phosphatases present similar challenges due to the conservation and polarity of their active sites, which limits the selectivity and drug-likeness of orthosteric inhibitors. Kuano applies QM/MM to simulate transition states of phosphatases in the PTPN family, guiding the design of novel small molecule inhibitors with enhanced specificity, binding complementarity, and potential for covalency. These 'quantum pharmacophores' along with AI-assisted design workflows offer transferable solutions to kinase inhibitor design.

10:00 Presentation to be Announced

10:30 Sponsored Presentation *(Opportunity Available)*

11:00 Enjoy Lunch on Your Own

12:25 pm Chairperson's Remarks
Ken Hsu, PhD, Stephen F. and Fay Evans Martin Endowed Associate Professor, Department of Chemistry, The University of Texas at Austin

12:30 Development of Brain Penetrant Pantothenate Kinase Activators
Rajendra P Tangallapally, PhD, Senior Scientist, Chemical Biology & Therapeutics, St. Jude Childrens Research Hospital
Pantothenate kinase-associated neurodegeneration (PKAN) is a rare, autosomal recessive disorder. In humans, four isoforms of Pantothenate kinase phosphorylate pantothenate (vitamin B5) is the first and rate-limiting step of Coenzyme A (CoA) biosynthesis. To address CoA deficiency in PKAN patients, we developed first in class small molecule PANK1 and 3 activators using lipophilic efficiency and structure guided design. This approach led to the generation of BBP-671, which advanced into clinical trials.

1:00 Molecular Mechanism of Paradoxical Activation of BRAF by Inhibitors
Nicholas Levinson, PhD, Associate Professor, Department of Pharmacology, University of Minnesota Twin Cities
Raf inhibitors trigger paradoxical activation of BRAF at sub-saturating concentrations. Using biophysical techniques tracking BRAF conformation and oligomerization, we show that paradoxical activation occurs because the first inhibitor molecule to bind to RAF dimers is much more strongly coupled to dimerization than the second inhibitor molecule. NMR experiments show this arises from inherent asymmetry of the BRAF dimer itself. Our results provide new insight into the mechanisms underlying paradoxical activation.

1:30 Modulation of Cancer Specific Interactomes via Chemical Switches and Molecular Glues
Arvin Dar, PhD, Professor, Chemical Biology, Memorial Sloan Kettering Cancer Center
Chemically-induced proximity of bimolecular complexes is a powerful modality to rewire signal transduction networks. Extensively studied in the context of protein degradation, the full potential of chemically-induced proximity for novel targets and pharmacological mechanisms has yet to be realized. I will discuss structure-based strategies to advance chemically-induced proximity in several areas, including as an approach to overcome drug resistance and as a mechanism to achieve ultra-selective modulators of kinase targets.

2:00 In-Person Brainstorming Session
This informal session will be led by the speakers, allowing participants to ask questions and exchange ideas around topics related to the symposium. To get the most out of this session, please come prepared to share your ideas and participate in collective problem solving.

2:45 Networking Refreshment Break
Join your colleagues for a cup of coffee or refreshments and make new connections

3:15 Lessons Learned from Developing BTK Molecular Glue Degraders
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4:15 Close of Symposium

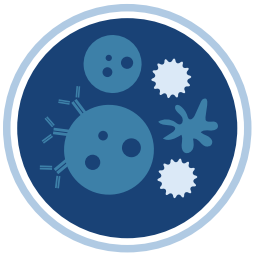
5:00 Dinner Short Courses*
*All Access Package or separate registration required. See Short Courses page for details.

7:30 Close of Day

Pre-Conference Symposia*

MONDAY
September 22

*All Access Package includes access to two short courses and all symposia. Separate registration required for other packages.



4th Annual

Emerging Immune Modulation Strategies

New Methodologies and Modalities for Profiling and Modulating Immune Responses

MONDAY, SEPTEMBER 22

8:00 am Pre-Conference Symposium Registration Open and Morning Coffee

8:50 Welcome Remarks

EXPLORING DIVERSE MODALITIES

8:55 Chairperson's Remarks
Rakesh Dixit, PhD, DABT, CEO & President, Bionavigen Oncology, LLC and CSO, TMAB Therapeutics, Regio Biosciences

9:00 Safety Risks of Immune-Modulation Therapies
Rakesh Dixit, PhD, DABT, CEO & President, Bionavigen Oncology, LLC and CSO, TMAB Therapeutics, Regio Biosciences
Immune modulation holds immense potential in treating a wide range of diseases, but it is not without its risks. Understanding and managing the toxicity associated with these therapies is paramount to maximizing their benefits while ensuring patient safety. The presentation will discuss ongoing research and advances in personalized medicine that are paving the way for more effective and safer immune modulation strategies.

9:30 RNAi Conjugates Targeting Tumor Microenvironment
Shanthi Ganesh, PhD, Senior Scientific Director, Global Nucleic Acid Therapies, Novo Nordisk
We developed RNAi agents to silence PD-L1 in tumor-associated immune cells which mediate immune suppression in the tumor microenvironment (TME) of refractory cancers. Silencing PD-L1 in antigen-presenting cells remodeled the TME, increased cytotoxic T cell infiltration, and mediated single-agent activity in immunotherapy-resistant preclinical tumors. Human active PDL1 RNAi is currently in Phase 1 clinical trials for immunotherapy-refractory cancers (NCT06504368).

10:00 Presentation to be Announced

10:30 Talk Title to be Announced
Phil Leighton, Fellow, Animal Genetics, OmniAb

OmniAb

11:00 Enjoy Lunch on Your Own

12:25 pm Chairperson's Remarks

12:30 Presentation to be Announced

1:00 Presentation to be Announced

1:30 Presentation to be Announced

2:00 In-Person Brainstorming Session
This informal session will be led by the speakers, allowing participants to ask questions and exchange ideas around topics related to the symposium. To get the most out of this session, please come prepared to share your ideas and participate in collective problem solving.

2:45 Networking Refreshment Break
Join your colleagues for a cup of coffee or refreshments and make new connections

3:15 AI Methods to Integrate Multi-Modal Omics, Spatial, and Single-Cell Profiling to Identify Mechanisms and Potential Therapeutic Opportunities
Arvind Rao, PhD, Associate Professor, Department of Computational Medicine and Bioinformatics, University of Michigan
Spatial profiling technologies, coupled with scRNAseq, enable a multi-factorial, multi-modal characterization of the tissue microenvironment. Objective scoring methods inspired by recent advances in statistics and ML can aid the interpretation of these datasets, as well as their integration with companion data like bulk and single-cell genomics. I will discuss analysis paradigms from ML that can be used to integrate and prioritize gene regulatory programs (and therapeutic candidates) underlying oncogenesis.

SYNTHETIC BIOLOGY FOR IMMUNOTHERAPY

3:45 FEATURED PRESENTATION: Targeting Glycans for Cancer Immunotherapy
Jessica Stark, PhD, Assistant Professor of Biological Engineering, Chemical Engineering, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology
Despite the curative potential of cancer immunotherapy, most patients do not benefit from existing treatments. Glyco-immune checkpoints—interactions of cancer glycans with inhibitory glycan-binding receptors called lectins—have emerged as prominent mechanisms of resistance to molecular and cellular immunotherapies. I will describe development of antibody-lectin chimeras: a biologic framework for glyco-immune checkpoint blockades that is now moving toward the clinic.

4:15 Close of Symposium

5:00 Dinner Short Courses*
*All Access Package or separate registration required. See Short Courses page for details.

7:30 Close of Day

"We LOVE CHI conferences like DOT. The warm reception we get from the attendees is always a highlight of our year."

–PhD, Founder & President, NstructuredesignS, LLC

Pre-Conference Symposia*

MONDAY
September 22

*All Access Package includes access to two short courses and all symposia. Separate registration required for other packages.

9th Annual

3D Models & NAMs in Drug Development

Physiologically Relevant Non-Animal Testing Methodologies and Their Emerging Applications

MONDAY, SEPTEMBER 22

8:00 am Pre-Conference Symposium Registration Open and Morning Coffee

8:50 Welcome Remarks

ADVANCES IN USE OF MICROPHYSIOLOGICAL SYSTEMS

8:55 Chairperson's Remarks
James Hickman, PhD, Professor, NanoScience Technology Center, University of Central Florida

9:00 Regulatory Acceptance of Human-on-a-Chip Platforms
James Hickman, PhD, Professor, NanoScience Technology Center, University of Central Florida
A primary limitation in drug discovery is the lack of good model systems and this is especially true for neurodegenerative diseases such as ALS, Myasthenia Gravis, Charcot-Marie-Tooth Disease, and Alzheimer's. Examples will be given of human-on-a-chip systems being developed for these CNS and PNS diseases, one that has enabled a clinical trial (#NCT04658472) that has now proceeded to a two-arm Phase III (NCT06290141 and NCT06290128).

9:30 Organ-on-a-chip Modeling: An Ethical and Translational Approach to CMT2S Research
Sandra Smieszek, PhD, Head, Genetics, Vanda Pharmaceuticals Inc.
Animal model reliance is a cornerstone of drug discovery and development. For rare diseases, extensive animal testing is required to create and validate models. This ethical and financial burden curtails rare disease research. We present a neuromuscular junction MPS to study Charcot-Marie-Tooth Disease Type 2S caused by a rare IGHMBP2 variant. This patient-specific *in vitro* model circumvented the need for animal model testing while providing the most representative disease model.

10:00 Balancing Complexity: Development and Implementation of Neuromuscular *In Vitro* Models for Drug Discovery
Jason Ekert, PhD, Head, Neuromuscular Translational Biology, UCB Pharma
This talk discusses the utilization of neuromuscular models for evaluating disorders such as complement-mediated neuromuscular junction damage, myotonic dystrophy, and immune-related responses. The models are used to assess efficacy of various therapeutic modalities with clinically relevant and functional endpoints. The importance of baseline characterization and validation using detailed analysis of healthy and diseased cellular inputs before progressing to complex neuromuscular *in vitro* models will be highlighted.

10:30 Presentation to be Announced

STEMCELL™ TECHNOLOGIES

11:00 Enjoy Lunch on Your Own

INNOVATIVE USE OF ORGANOIDS & *EX VIVO* MODELS

12:25 pm Chairperson's Remarks
Madhu Lal Nag, PhD, CSO, InSphero

12:30 FEATURED PRESENTATION: Programmable Organoids Created Using Automated Multi-step Differentiation, Digital Logic and Neuromorphic Circuits
Ron Weiss, PhD, Professor, Biological Engineering, Massachusetts Institute of Technology
Programmable organoids offer a transformative approach to modeling human biology. We present a synthetic biology platform that integrates automated multi-step differentiation of hiPSCs, synthetic gene circuits implementing multi-input digital logic based on miRNA sensing, and neuromorphic controllers to generate dynamic, responsive organoids. Our genetic circuits enable precise control over cell fate, function, and multicellular maturation, which are applied to the creation of liver and pancreatic organoids.

1:00 De-risking Women's Health Drug Development with Human Organoid Models
Morgan Stanton, PhD, CEO, Opal Therapeutics
Opal Therapeutics is advancing women's health drug discovery with patient-derived endometrial and myometrial organoid models. These 3D cultures replicate the structure and function of human uterine tissue, enabling more accurate study of disorders like endometriosis and fibroids. By capturing patient-specific biology, Opal's platform supports high-throughput drug screening and mechanistic insights with greater clinical relevance than rodent models, offering a promising path to discover and validate therapies for underserved gynecological conditions.

1:30 Donor-to-Donor Variability in Pharmacology: Mole Hill or Mountain?
Fabien Vincent, PhD, Consultant; formerly Pharmacology Lab Head, Pfizer Inc.
A decade ago we started a major transition towards using primary cells, and donor-to-donor variability was a major concern. With now >25 primary cell assays developed for SAR and HTS, sufficient data has been accumulated to conduct a meaningful analysis of these assays in high-throughput pharmacology. Analysis results will be presented along with specific lessons and strategies gathered to facilitate the use of these physiologically relevant assays.

2:00 In-Person Brainstorming Session
This informal session will be led by the speakers, allowing participants to ask questions and exchange ideas around topics related to the symposium. To get the most out of this session, please come prepared to share your ideas and participate in collective problem solving.

2:45 Networking Refreshment Break
Join your colleagues for a cup of coffee or refreshments and make new connections

3:15 Engineering a Chemostatic Microenvironment for Intestinal Cancer Research
Jiaquan Yu, PhD, Research Scientist, Massachusetts Institute of Technology
In our pioneering yet-to-be-published work, we construct a physiologically relevant *ex vivo* colorectal cancer (CRC) interface, unveiling two groundbreaking findings. Firstly, we establish that it is the oxygen gradient—not merely the absolute oxygen levels—that dictates CRC proliferation and architecture. Furthermore, this model facilitates an exploration into how these hypoxic gradients enable novel studies on epithelial-microbiota cocultures and tumor-T cell interactions.

3:45 RosetteArray Platform: High-Throughput Screening of Human Neurodevelopment for Toxicology and Precision Medicine
Randolph Ashton, PhD, Associate Professor, Biomedical Engineering, University of Wisconsin-Madison & Wisconsin Institute for Discovery
The RosetteArray Platform enables quantitative high-throughput screening of human neurodevelopment in standard well plate formats. By combining microarrayed, human pluripotent stem-cell-derived neural organoid culture with AI-based image analysis, the effects of chemical/drug exposures or genetic backgrounds on organoid morphogenesis can be assessed in weeks versus months. Here, we demonstrate the utility of RosetteArray screens for developmental neurotoxicity hazard assessment and modeling Neural Tube Defect and Autism Spectrum Disorder risks.

4:15 Close of Symposium

5:00 Dinner Short Courses*
*All Access Package or separate registration required. See Short Courses page for details.

7:30 Close of Day

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2nd Annual

Synthetic Biology for Drug Discovery & Development

Novel Cellular Engineering and Regulation for Developing Smart Programmable Therapeutics

MONDAY, SEPTEMBER 22

8:00 am Pre-Conference Symposium Registration Open and Morning Coffee

8:50 Welcome Remarks

EXPLORING PROGRAMMABLE CELL CIRCUITS

8:55 Chairperson's Remarks

Akos Nyerges, PhD, Research Associate, Department of Genetics, Harvard Medical School

9:00 Next-Gen Genomically Recoded Organisms for Production of Multi-Functional Programmable Biologics

Farren Isaacs, PhD, Professor, Department of Molecular & Cellular & Developmental Biology, Yale University

9:30 The Dark Proteome of Human Viruses

Shira Weingarten-Gabbay, PhD, Assistant Professor, Department of Microbiology; Head, Laboratory of Systems Virology, Harvard Medical School

My laboratory approaches fundamental questions in virology through the lens of systems biology. We recently discovered thousands of 'hidden' viral proteins across ~700 viral genomes by developing Massively Parallel Ribosome Profiling (MPRP). This new universe of proteins includes immune targets for vaccine design and genomic elements that regulate viral protein expression, offering new insights into the complexity of viral gene regulation.

10:00 FEATURED PRESENTATION: Engineering High-Precision, Dynamic Genetic Control Systems for Cell Fate Programming

Katie Galloway, PhD, W. M. Keck Career Development Professor, Biomedical Engineering and Chemical Engineering, Massachusetts Institute of Technology

To rapidly advance gene and cell-based therapies, synthetic biology aims to harness the power of native biology. Achieving predictable performance in primary cells remains a challenge for accomplishing this vision. Our tools must be deliverable to primary cells and must retain predictable control and performance in these contexts. To address this challenge, we are pioneering the development of compact synthetic circuits that integrate into native pathways and perform in primary cells.

10:30 Sponsored Presentation *(Opportunity Available)*

11:00 Enjoy Lunch on Your Own

SYNTHETIC BIOLOGY-DRIVEN THERAPIES

12:30 pm A Chemical Approach for Developing Novel Biologics

Abhishek Chatterjee, PhD, Professor, Chemistry, Boston College

Site-specific incorporation of noncanonical amino acids (ncAAs) into proteins expressed in living cells by reprogramming the genetic code offers powerful new ways to probe and engineer protein structure and function. In this presentation, I will describe our recent work on expanding the scope of this technology and its application to develop next-generation biotherapeutics such as antibody-drug conjugates and enhanced AAV vectors for gene therapy.

1:00 AI-Assisted Biotechnology for Drug Discovery and Manufacturing of Plant-Inspired Human Therapeutics

Michael Krogh Jensen, PhD, CEO, Biomia

Nature has inspired the development of half of all oral medicines, making natural products a rich source for novel drugs. But nature only makes minute quantities of the world's most critical molecules, and only rarely are they safe and efficient for humans. This presentation will showcase how Biomia uniquely facilitates access, expansion, and exploration of nature-inspired molecules, combining innovative manufacturing and AI-assisted drug discovery of novel, safe, and efficient therapies.

1:30 STX-003: Harnessing the Power of Synthetic Genetic Circuits to Achieve Tumor-Specific IL-12 Expression

Allen Tseng, PhD, Senior Principal Scientist, Strand Therapeutics Inc.

The programmability of mRNA therapeutics makes them amenable to synthetic biology approaches for drugging previously undruggable targets. By utilizing synthetic genetic circuits, we have developed STX-003, an LNP-encapsulated mRNA that expresses IL-12 specifically in tumors. Recombinant IL-12 has potent antitumor effects but is prohibitively toxic. Through the power of synthetic biology, STX-003 leverages the antitumor activity of IL-12 while minimizing its toxicity, improving tolerability while effectively controlling tumors.

2:00 In-Person Brainstorming Session

This informal session will be led by the speakers, allowing participants to ask questions and exchange ideas around topics related to the symposium. To get the most out of this session, please come prepared to share your ideas and participate in collective problem solving.

2:45 Networking Refreshment Break

Join your colleagues for a cup of coffee or refreshments and make new connections

3:15 Decoding the Transcytosome: Using Manifold's *in vivo* Design Engine to Discover New Portals into the Blood-Brain Barrier

Alex Reis, PhD, Principal Scientist, Computation, Manifold Biotechnologies Inc.

Manifold Bio has built a state-of-the-art *in vivo* Multiplexed Protein Screening Platform, powered by a protein-barcoding technology called mCodes. In this work, we screen thousands of nanobody shuttles against 59 unique BBB receptors in mice to identify a novel portal, PX1. In a recent multiplexed NHP study, we tested 38 shuttles to identify ones on par with benchmarks, highlighting the impact *in vivo* screening can have on antibody design.

SYNTHETIC BIOLOGY FOR IMMUNOTHERAPY

3:45 FEATURED PRESENTATION: Targeting Glycans for Cancer Immunotherapy

Jessica Stark, PhD, Assistant Professor of Biological Engineering, Chemical Engineering, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

Despite the curative potential of cancer immunotherapy, most patients do not benefit from existing treatments. Glyco-immune checkpoints—interactions of cancer glycans with inhibitory glycan-binding receptors called lectins—have emerged as prominent mechanisms of resistance to molecular and cellular immunotherapies. I will describe development of antibody-lectin chimeras: a biologic framework for glyco-immune checkpoint blockades that is now moving toward the clinic.

4:15 Close of Symposium

5:00 Dinner Short Courses*

*All Access Package or separate registration required. See Short Courses page for details.

7:30 Close of Day

Cambridge Healthtech Institute's 7th Annual

Degraders & Molecular Glues – Part 1

Design and Optimization of Novel Degraders, Glues, and Conjugates

TUESDAY, SEPTEMBER 23

7:00 am Registration Open and Morning Coffee

7:55 Welcome Remarks

LEVERAGING CHEMICAL BIOLOGY FOR INDUCING PROXIMITY

8:00 Chairperson's Remarks

Ralph Mazitschek, PhD, Assistant Professor, Harvard Medical School; Co-Director of the Chemical Biology Platform, Center for Systems Biology, Massachusetts General Hospital

8:05 FEATURED PRESENTATION: Targeting Post-translational Modifications (PTMs) Through Induced Proximity and Chemical Biology

Edward Tate, PhD, Professor, Chemical Biology, Imperial College London

Our lab works across the field of targeting post-translational modification, from small molecular drug discovery to antibody-degrader conjugates. Here I will introduce our work discovering an exceptionally potent ADC payload with an unprecedented mode of action targeting protein lipidation, and a new approach to unlock proximity-driven pharmacology through Site-specific Ligand-Induced Proximity (SLIP), enabling systematic identification of actionable sites on potential effector proteins, opening new opportunities for future PIP-based drug discovery.

8:50 FEATURED PRESENTATION: Reimagining Druggability Using Chemoproteomic Platforms

Daniel Nomura, PhD, Professor of Chemical Biology and Molecular Therapeutics, Department of Chemistry, University of California, Berkeley

One of the greatest challenges that we face in discovering new disease therapies is that most proteins are considered "undruggable," in that most proteins do not possess known binding pockets or "ligandable hotspots" that small molecules can bind to modulate protein function. Our research group addresses this challenge by advancing and applying chemoproteomic platforms to discover and pharmacologically target unique and novel ligandable hotspots for disease therapy.

9:35 Networking Refreshment Break

Join your colleagues for a cup of coffee or refreshments and make new connections

10:05 A Molecular Glue Degrader of HuR/ELAVL1 to Treat Debilitating Diseases

Yong Cang, PhD, Professor, ShanghaiTech University; Co-Founder & CSO, Degron Therapeutics

Leveraging induced proximity and degradation proteomics, we discovered a novel CRBN-based molecular glue degrader of HuR/ELAVL1, an RNA binding protein abnormally activated in cancer and other diseases. The MGD is moving to the clinics to treat BRAF mutant cancers as a monotherapy, while its efficacy in other disease models, including cancer cachexia, has been validated. The mechanistic studies of HuR degrader in these diseases are going to be discussed.

MECHANISTIC SCREENING & PROFILING

10:35 Rational Molecular Glue Discovery Based on High-Throughput Screening for Novel Ligase-Target Pairs

Abhishek Dogra, Director, Medicinal Chemistry & Induced Proximity, A Alpha Bio Inc.

We describe the application of AlphaSeq, a high-throughput, highly sensitive experimental platform for measuring protein-protein interactions, to elucidate >100 novel interactions between therapeutically relevant targets and diverse set of ligases. We further characterize these PPIs through site-directed mutagenesis to prioritize actionable pairs for rational molecular glue discovery. Finally, we depict the systematic AlphaSeq validation and hit-finding approaches we have employed to identify small molecules that enhance these weak ligase-target interactions.

11:05 Mechanistic Profiling of Targeted Protein Degraders

Ghaith Hamza, Associate Principal Scientist, Discovery Sciences, AstraZeneca

Immunomodulatory drugs (IMiDs) such as lenalidomide and pomalidomide are clinically approved. Although efficacious, IMiDs have been linked to adverse events. Proteolysis-targeting chimeras (PROTACs) have incorporated IMiD substructures and therefore carry an associated inherent liability. Using *in vitro* assays and proteomics-based readouts, we implemented a robust profiling cascade.

11:35 Sponsored Presentation *(Opportunity Available)*

12:05 pm Transition to Lunch

12:10 Luncheon Presentation to be Announced

X-CHEM
TAKE THE LEAD. DRIVE DISCOVERY.

12:40 Session Break

ORAL DEGRADERS & CANCER

1:15 Chairperson's Remarks

Jin Wang, PhD, Director, Biochemistry and Molecular Pharmacology, Baylor College of Medicine

1:20 Development of Degrader Antibody Conjugates as Double Precision Anti-cancer Therapeutics

Jin Wang, PhD, Director, Biochemistry and Molecular Pharmacology, Baylor College of Medicine

Development of Degrader Antibody Conjugates (DACs) represents a novel therapeutic modality combining antibody specificity with targeted protein degradation. Our DAC has a GSPT1 molecular glue as the payload, enabling selective protein degradation in cancer cells. Different linker chemistries were compared for GSPT1 degradation efficiency and cellular potency. This dual-targeting approach demonstrates potent anti-tumor activity with improved therapeutic window compared to traditional ADCs.

1:50 Mini-PROTACs

Hai Rao, PhD, Professor and Chair, Department of Biochemistry, Southern University of Science and Technology, China

Proteolysis-targeting chimera (PROTAC) that selectively eliminates detrimental proteins represents a promising therapeutic strategy for various diseases. We have developed a set of PROTACs with the short and interchangeable degradation signals that attract several distinct E3 ubiquitin ligases. We demonstrate the utility and efficacy of these mini-PROTACs *in vitro* and *in vivo* against several oncogenic drivers, expanding the repertoire of limited ligands and degradation pathways available for PROTACs.

2:20 Presentation to be Announced

nuclera

2:50 In-Person Breakouts

In-Person Breakouts are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator, or facilitators, who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Breakouts page on the conference website for a complete listing of topics and descriptions.

3:35 Grand Opening Refreshment Break in the Exhibit Hall with Poster Viewing and Best of Show Voting Begins

Degraders & Molecular Glues – Part 1

Design and Optimization of Novel Degraders, Glues, and Conjugates

Don't miss the opportunity to meet the Discovery on Target community, including leading service providers and poster presenters in our first Exhibit Hall break! Grab a cup of coffee or refreshment, vote for awards, and explore booths to fill the Game Card for a chance to win raffle prizes.

ORAL DEGRADERS & CANCER

4:35 Target-Anchored Monovalent Degraders: Case Study on SMARC A

Nicholas F. Endres, PhD, Senior Scientist, Biochemical & Cellular Pharmacology, Genentech, Inc.

Monovalent degraders are molecules that can induce target degradation without containing known ligase binding motifs. As the rules by which these molecules can induce degradation are poorly understood, they are typically found serendipitously. I will describe a systematic drug discovery campaign that led to a potent monovalent degrader of BRM, an important lung cancer target. Furthermore, I will show that this molecule works by covalently recruiting the ligase FBX022.

5:05 Characterization of Selective CBP Degraders for the Treatment of Solid Tumor Indications

Molly Wilson, PhD, Senior Scientist, Foghorn Therapeutics

CREB binding protein (CBP) and E1A binding protein P300 (EP300) are paralog lysine acetyltransferases that function as transcriptional coactivators. Their bidirectional synthetic lethal relationship creates a unique therapeutic opportunity for selectively targeting CBP in EP300-mutant cancers. We demonstrate the potent antiproliferative activity of our selective CBP degraders, both as single agents and in the context of select combination therapies.

5:35 Technology Spotlights *(Sponsorship Opportunity Available)*

6:05 Welcome Reception in the Exhibit Hall with Poster Viewing

Engage with the community, explore the latest innovations, network with service partners and providers, meet the poster presenters, vote for our Best of Show Poster and Best of Show Exhibitor awards in a relaxed, social atmosphere.

7:05 Close of Day

WEDNESDAY, SEPTEMBER 24

7:30 am Registration and Morning Coffee

INNOVATIONS IN TARGETED PROTEIN DEGRADATION

7:55 Chairperson's Remarks

Charu Chaudhry, PhD, Senior Principal Scientist, Molecular Pharmacology, Janssen Pharmaceuticals, Inc.

8:00 PANEL DISCUSSION: Innovations in Protein Degradation in the Biotech Sector

Moderator: Charu Chaudhry, PhD, Senior Principal Scientist, Molecular Pharmacology, Janssen Pharmaceuticals, Inc.

This panel will assemble experts from leading biotechnology companies in the protein degradation field to present brief talks highlighting how they are driving innovation and advancing the science to develop new degrader modalities and pursue challenging targets. The talks will be followed by a panel discussion and will include time for attendees to ask questions.

Panelists:

Bradley DeMarco, PhD, Scientist II, Biochemistry & Biophysics, Monte Rosa Therapeutics

Gwenn Hansen, PhD, CSO, Nurix Therapeutics, Inc.

Kathleen Seyb, PhD, Senior Vice President, Biology & Translational Sciences, Triana Biomedicines Inc.

Kirti Sharma, PhD, Executive Director, Protoemics, Kymera Therapeutics

Nicki Thompson, PhD, CEO, TRIMTECH Therapeutics Ltd.

9:30 Sponsored Presentation *(Opportunity Available)*

9:45 Presentation to be Announced

SpiroChem

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

Start your morning with coffee, connections, and cutting-edge research! Vote for the Best of Show Poster and stay to celebrate the winner! Visit with industry-leading service providers, fill out the Game Card to win a raffle prize and vote for the People's Choice Best of Show Exhibitor.

PLENARY KEYNOTE PROGRAM

10:50 Welcome Remarks from the Discovery on Target Team Lead

11:00 Plenary Keynote Chairperson's Remarks

11:05 PLENARY KEYNOTE: The Radicalization of Drug Discovery

Gregory L. Verdine, PhD, President & CEO, LifeMine Therapeutics

The field of drug discovery stands at a watershed moment of scientific, medical, and commercial opportunity. Realization of this opportunity will require radical innovations that fundamentally expand the functional capabilities of therapeutic interventions and management of the attendant risks. This talk will focus on the discovery, development, and deployment of radically new therapeutic modalities, inspired by nature, that thrust the field forward in non-obvious, impactful, and exciting new directions.

11:40 PLENARY KEYNOTE: GLP-1 Unveiled: Key Takeaways for Next-Generation Drug Discovery

Lotte Bjerre Knudsen, PhD, Chief Scientific Advisor, Head of IDEA (Innovation&Data Experimentation Advancement), Novo Nordisk AS

This talk explores the evolution of GLP-1 as a significant component in diabetes and obesity treatment, and its direct impact on multiple co-morbidities. It highlights the role of industry innovation and scientific persistence in overcoming challenges posed by its short half-life, ultimately leading to the successful development of GLP-1 therapies. Key lessons will inform future drug discovery strategies, emphasizing that today's drug discovery must be based on human data.

12:15 pm Close of Degraders and Molecular Glues- Part 1 Conference

Cambridge Healthtech Institute's 22nd Annual

Emerging Drug Targets: Identification & Validation

Strategies for Transforming Undruggable Targets to Yet-to-be-Drugged Targets

TUESDAY, SEPTEMBER 23

7:00 am Registration Open and Morning Coffee

7:55 Welcome Remarks

LEVERAGING CHEMICAL BIOLOGY FOR INDUCING PROXIMITY

8:00 Chairperson's Remarks

Ralph Mazitschek, PhD, Assistant Professor, Harvard Medical School; Co-Director of the Chemical Biology Platform, Center for Systems Biology, Massachusetts General Hospital

8:05 FEATURED PRESENTATION: Targeting Post-translational Modifications (PTMs) Through Induced Proximity and Chemical Biology

Edward Tate, PhD, Professor, Chemical Biology, Imperial College London

Our lab works across the field of targeting post-translational modification, from small molecular drug discovery to antibody-degrader conjugates. Here I will introduce our work discovering an exceptionally potent ADC payload with an unprecedented mode of action targeting protein lipidation, and a new approach to unlock proximity-driven pharmacology through Site-specific Ligand-Induced Proximity (SLIP), enabling systematic identification of actionable sites on potential effector proteins, opening new opportunities for future PIP-based drug discovery.

8:50 FEATURED PRESENTATION: Reimagining Druggability Using Chemoproteomic Platforms

Daniel Nomura, PhD, Professor of Chemical Biology and Molecular Therapeutics, Department of Chemistry, University of California, Berkeley

One of the greatest challenges that we face in discovering new disease therapies is that most proteins are considered "undruggable," in that most proteins do not possess known binding pockets or "ligandable hotspots" that small molecules can bind to modulate protein function. Our research group addresses this challenge by advancing and applying chemoproteomic platforms to discover and pharmacologically target unique and novel ligandable hotspots for disease therapy.

9:35 Networking Refreshment Break

Join your colleagues for a cup of coffee or refreshments and make new connections

ASSAYS FOR TARGET DECONVOLUTION

10:05 FEATURED PRESENTATION: Pooled TMT-ABPP: Covalent Cysteine Profiling by Combining Sample Multiplexing and Electrophilic Compound Pooling for 100x Increases in Throughput

Steve Gygi, PhD, Professor, Department of Cell Biology, Harvard Medical School

Electrophilic libraries often contain thousands of members, resulting in hundreds of TMT plexes to profile entire libraries. In this talk, I will i) highlight how TMT multiplexing and sample pooling can be combined, ii) address issues with increased DMSO concentrations, iii) discuss strategies for deconvolution, and iv) provide an example of "2D pooling" where deconvolution is built into the sample design.

10:50 FEATURED PRESENTATION: Mice, or Microfluidics? Humanizing Drug Development for Gynecology Diseases

Linda Griffith, PhD, Professor, Biological Engineering & Teaching Innovation, Massachusetts Institute of Technology

Gynecology remains one of the least-funded areas of human health. The NIH has launched "Complement-ARIE" to bolster mergers of systems biology and microphysiological systems for regulatory purposes. Examples of engineering living patient avatars will provide specific technical insights for integrating clinical and molecular/cellular phenotyping and designing *in vitro* models for validating targets and mechanism of action, especially for chronic inflammatory diseases like endometriosis.

11:35 Sponsored Presentation *(Opportunity Available)*

12:05 pm Transition to Lunch

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:40 Session Break

DECIPHERING COMPLEX CELLULAR BIOLOGY

1:15 Chairperson's Remarks

Abigail Mariga, PhD, Senior Principal Scientist, Neuroscience Discovery Biology, Bristol Myers Squibb Co.

1:20 Deconvoluting the Biology of Novel CELMoD Targets Using the Cell Seq Functional Genomics Platform

Abigail Mariga, PhD, Senior Principal Scientist, Neuroscience Discovery Biology, Bristol Myers Squibb Co.

The presentation focuses on integrating multiple technology platforms to identify novel targets for neurodegeneration. This includes conducting *in vitro* screens for CELMoD targets, utilizing the Cell Seq functional genomics platform to link targets to their functions, and validating these targets in iPSC-derived cell models.

1:50 FEATURED PRESENTATION: Harnessing the Transformative Science of Condensates to Redefine Therapeutic Possibilities for Complex Diseases

Ann Boija, PhD, Senior Vice President, Head of Research, Dewpoint Therapeutics

The recognition that condensate dysfunction underlies a broad spectrum of diseases has opened new opportunities to modulate high-value targets. We have leveraged emerging insights into condensate biology to build a comprehensive drug-discovery platform that expands the mechanistic and target space of small-molecule therapeutics. Our condensate-modifying compounds (c-mods) enable selective modulation of undruggable targets, such as MYC and ß-catenin, and demonstrate robust disease-modifying activity *in vitro* and *in vivo*.

2:20 Sponsored Presentation *(Opportunity Available)*

2:50 In-Person Breakouts

In-Person Breakouts are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator, or facilitators, who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Breakouts page on the conference website for a complete listing of topics and descriptions.

3:35 Grand Opening Refreshment Break in the Exhibit Hall with Poster Viewing and Best of Show Voting Begins

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Cambridge Healthtech Institute's 22nd Annual

Emerging Drug Targets: Identification & Validation

Strategies for Transforming Undruggable Targets to Yet-to-be-Drugged Targets

AI/ML FOR TARGET DISCOVERY

4:35 Characterizing Cellular Heterogeneity in Liquid To Identify Novel Targets

Praveen Anand, PhD, Data & Analytics Lead, Data Science and Analytics, UCB Pharma

In this study, we employed scRNA-seq to uncover the complex phenotypic landscape of early T-cell precursor acute lymphoblastic leukemia (ETP-ALL). The computational analyses of gene programs revealed intricate interplay between oncogenic states and immune evasion programs that drives the complex phenotypic landscape in ETP-ALL. The cellular states and transitions identified not only improves our comprehension of disease pathogenesis but also aids in the identification of potential therapeutic targets.

5:05 Leveraging Multiomics Data to Identify and Prosecute Targets Implicated in Women's Health

Petrina Kamya, PhD, Global Head of AI Platforms & Vice President, Insilico Medicine; President, Insilico Medicine Canada

Endometriosis and alternative sources of non-hormonal contraception are neglected and challenging issues associated with women's health. Today, I will discuss how we leverage multiomics data and AI to identify novel targets implicated in endometriosis and how we contribute to the challenge of designing novel non-hormonal contraceptives using AI.

5:35 FEATURED PRESENTATION: Simulating Biologically Relevant Protein Motions in Challenging Disease Targets

Woody Sherman, PhD, CIO, Psivant Therapeutics

Understanding protein dynamics is critical for drug discovery against challenging targets. We describe an integrated platform that combines all-atom physics-based simulations with biophysical data, including HDX-MS and crystallography, to model biologically relevant protein motions and thermodynamics. We use this approach to enable mechanism-driven design strategies to advance our therapeutic pipeline of novel orally bioavailable molecules against clinically validated inflammation and immunology targets.

6:05 Welcome Reception in the Exhibit Hall with Poster Viewing

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7:05 Close of Day

WEDNESDAY, SEPTEMBER 24

7:30 am Registration and Morning Coffee

NOVEL PLATFORMS FOR SCREENING TARGETS

7:55 Chairperson's Remarks

Joshua P. Plotnik, PhD, Principal Research Scientist, Oncology Discovery Research, AbbVie, Inc.

8:00 Novel Synthetic Lethal Targets within the mRNA Quality-Control Pathway

Joshua P. Plotnik, PhD, Principal Research Scientist, Oncology Discovery Research, AbbVie, Inc.

PELO–HBS1L and SKI complex synthetic lethality alters the normal cell cycle and drives the unfolded protein response through the activation of IRE1, as well as robust tumor growth inhibition. Our results indicate that PELO and HBS1L represent novel therapeutic targets whose dependence converges upon SKI complex destabilization, a common phenotypic biomarker in diverse genetic contexts representing a significant population of patients with cancer.

8:30 A Comprehensive Platform for Identification of Novel Synthetic Lethal Targets and Drug Combinations Using Patient-Derived Cells

Krzysztof Brzozka, PhD, CSO, Ryvu Therapeutics

Our study identifies and validates synthetic lethal (SL) interactions in colorectal cancer (CRC), focusing on actionable vulnerabilities linked to APC and KRAS mutations. By integrating engineered primary cancer models, patient-derived xenografts, and transcriptomic profiling, we discovered novel SL targets that offer a promise for personalized CRC therapies. These findings bridge preclinical and clinical research, paving the way for safer and more effective treatment options tailored to CRC's unique mutational landscape.

9:00 Harnessing Cellular Metabolite Screening for RNA-Targeting Small-Molecule Drug Discovery

Benjamin Brigham, PhD, Senior Scientist, Biophysics, Atavistik Bio

Small-molecule targeting of RNAs has become a leading drug discovery approach. However, identifying RNA binders that produce functional effects remains a significant challenge. Endogenous cellular metabolites provide an untapped source of inspiration for small-molecule leads. Atavistik Bio has leveraged the AMPS (Atavistik Metabolite Proprietary Screening) platform to screen metabolites against RNA. We will present the AMPS platform, our hit identification workflows, and a case study of the SERPINA1 5'UTR.

9:30 Presentation to be Announced Clarivate

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

Start your morning with coffee, connections, and cutting-edge research! Vote for the Best of Show Poster and stay to celebrate the winner! Visit with industry-leading service providers, fill out the Game Card to win a raffle prize and vote for the People's Choice Best of Show Exhibitor.

PLENARY KEYNOTE PROGRAM

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11:00 Plenary Keynote Chairperson's Remarks

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12:15 pm Close of Emerging Drug Targets: Identification & Validation Conference

Cambridge Healthtech Institute's 7th Annual

Small Molecules for Cancer Targets

Discovering Orally-BioAvailable, Targeted-Oncology Therapeutics

TUESDAY, SEPTEMBER 23

7:00 am Registration Open and Morning Coffee

7:55 Welcome Remarks

TARGETING WRN HELICASE

8:00 Chairperson's Remarks
Heike Wobst, PhD, Director, Pharmacology, Jnana Therapeutics

8:05 Targeting Allosteric Sites of WRN Helicase
Mihir Mandal, PhD, Principal Scientist, Medicinal Chemistry, Merck

8:35 Discovery of MOMA-341, a Chemically Distinct, Potent, and Selective Covalent Inhibitor of Werner Syndrome Helicase (WRN)
Momar Toure, PhD, Director, Medicinal Chemistry, MOMA Therapeutics
MOMA-341 is a distinct, potent and selective clinical stage covalent inhibitor of WRN. Covalent series optimization was based on refinement of covalent warhead trajectory, compound rigidity, and improvement of binding affinity to drive high kinact/KI. Further refinement of potency and ADME properties, guided by *in vivo* target occupancy prediction, led to the discovery of MOMA-341, which demonstrates robust tumor regression in mouse xenograft models and is in clinical development.

9:35 Networking Refreshment Break
Join your colleagues for a cup of coffee or refreshments and make new connections

PROGRESS AGAINST PRIZED CANCER TARGETS

10:05 FEATURED PRESENTATION: Drugging the p53 Y220C Mutant with a Covalent Activator
Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation
Loss-of-function mutations of the TP53 gene are the most common genetic defects across all human cancers. The p53 Y220C mutation, which occurs in ~1% of cancers, leads to destabilization, aggregation, and loss of p53 protein function. Frontier Medicines has used multiple approaches to discover FMC-220, a potential first-in-class covalent activator of p53 Y220C, which is highly potent and selective in restoring p53 tumor suppressor function.

10:35 A First-in-Class RAS-PI3Ka Interaction Inhibitor in Clinical Trials
Dominic Esposito, PhD, Director, Protein Sciences, Frederick National Laboratory
BBO-10203 is a first-in-class novel PI3K/RAS breaker compound which is currently in clinical trials for treatment of mutant KRAS or PIK3CA cancers as well as HER2-amplified breast cancers. This unique molecule which is capable of disrupting the interaction of this critical protein-protein interaction has the potential to revolutionize treatment of a variety of severe cancers without the side effects of hyperglycemia observed in current PI3K inhibitors used as standard-of-care.

11:05 Discovery of AMG 410, an H/N-RAS Sparing pan-KRAS Inhibitor with Dual GTP(on)/GDP(off)-state Activity for the Treatment of Diverse KRAS-mutant Tumors
Wei Zhao, PhD, Senior Principal Scientist, Medicinal Chemistry, Amgen Inc
KRAS is one of the most frequently mutated oncogenes in human cancers. Our medicinal chemistry effort guided by experiences in the development of sotorasib (KRAS G12Ci) and structure/property-based design principles led to the identification of AMG 410, an orally bioavailable, reversible pan-KRAS inhibitor. AMG 410 is highly selective against both HRAS and NRAS, and is a dual GTP(on)- and GDP(off)-state inhibitor. AMG 410 showed good preclinical efficacy and tolerability.

11:35 Sponsored Presentation *(Opportunity Available)*

12:05 pm Transition to Lunch

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:40 Session Break

SMALL MOLECULES AND THE TUMOR MICRO-ENVIRONMENT

1:15 Chairperson's Remarks
William N. Pappano, PhD, Research Fellow, AbbVie, Inc.

1:20 Discovery of ABBV-973, a Potent, Pan-Allele Small-Molecule STING Agonist for Intravenous Administration for Cancer Immunotherapy
Kenneth Bromberg, PhD, Senior Principal Research Scientist, AbbVie Inc.
STimulator of INterferon Genes (STING) is an innate immune sensor that is critical for driving anti-tumor immune responses. We implemented a fragment-based screening approach to discover ABBV-973, a potent pan-allele STING agonist for cancer immunotherapy. The profile of ABBV-973 enables robust anti-tumor activity while mitigating T cell toxicity. Furthermore, we developed multiple strategies to further minimize cytokine release syndrome-like toxicity, a key challenge for translating STING agonists clinically.

1:50 Using Stapled Peptide Helicons as Protein Degraders
Markus Haeberlein, PhD, Executive VP Discovery Science, Parabilis Medicines

2:20 Sponsored Presentation *(Opportunity Available)*

2:50 In-Person Breakouts
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ORAL DEGRADERS & CANCER

4:35 Target-Anchored Monovalent Degraders: Case Study on SMARC A
Nicholas F. Endres, PhD, Senior Scientist, Biochemical & Cellular Pharmacology, Genentech, Inc.
Monovalent degraders are molecules that can induce target degradation without containing known ligase binding motifs. As the rules by which these molecules can induce degradation are poorly understood, they are typically found serendipitously. I will describe a systematic drug discovery campaign that led to a potent monovalent degrader of BRM, an important lung cancer target. Furthermore, I will show that this molecule works by covalently recruiting the ligase FBX022.

5:05 Characterization of Selective CBP Degraders for the Treatment of Solid Tumor Indications
Molly Wilson, PhD, Senior Scientist, Foghorn Therapeutics
CREB binding protein (CBP) and E1A binding protein P300 (EP300) are paralog lysine acetyltransferases that function as transcriptional coactivators. Their bidirectional synthetic lethal relationship creates a unique therapeutic opportunity for selectively

targeting CBP in EP300-mutant cancers. We demonstrate the potent antiproliferative activity of our selective CBP degraders, both as single agents and in the context of select combination therapies.

5:35 Technology Spotlights *(Sponsorship Opportunity Available)*

6:05 Welcome Reception in the Exhibit Hall with Poster Viewing
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7:05 Close of Day

WEDNESDAY, SEPTEMBER 24

7:30 am Registration and Morning Coffee

TACKLING CHALLENGING CANCER TARGETS WITH SMALL MOLECULES

7:55 Chairperson's Remarks
Gottfried Schroeder, PhD, Associate Principal Scientist, Quantitative Biosciences, Merck & Co., Inc.

8:00 Discovery of the Potential First-in-Class MALT1 Protease Inhibitor ABBV-525 for the Treatment of B Cell Lymphomas
William N. Pappano, PhD, Research Fellow, AbbVie, Inc.
The MALT1 paracaspase is constitutively activated in various B cell malignancies by chronic stimulation of the B cell receptor or through gain-of-function mutations in upstream components of the NF-kB pathway. ABBV-525 allosterically inhibits MALT1 and has potent preclinical activity as a monotherapy or bolsters combination therapeutics in models of non-Hodgkin's lymphoma. ABBV-525 is an investigational drug currently in Phase I clinical studies for the treatment of B cell malignancies.

8:30 FORX-428: A Novel, Potent PARG Inhibitor Demonstrating Strong Anti-Tumor Activity in Preclinical Cancer Models
Luca Iacovino, PhD, Senior Scientist, Biophysics, FoRx Therapeutics
FORX-428 is a potent and orally bioavailable inhibitor of poly(ADP-ribose) glycohydrolase (PARG), a key enzyme in the DNA damage response. Inhibition of PARG by FORX-428 leads to PAR chain accumulation, inducing replication stress and tumor cell death. The compound exhibits strong, reversible binding to PARG, selective cytotoxicity across different cancer cell lines, and robust anti-tumor efficacy in xenograft models, demonstrating best-in-class potential among PARG and PARP inhibitors.

9:00 An MTA-Cooperative PRMT5 Inhibitor with Potent Oral *in vivo* Efficacy
Mikkel Vestergaard, PhD, Principal Scientist, Medicinal Chemistry, Amgen Research Copenhagen
MTAP-deleted cancers accumulate MTA, which partially inhibits PRMT5 and creates vulnerability. We identified AM-9959, from DEL screening of the PRMT5:MEP50+MTA complex, forming an inhibitory ternary complex and subsequent optimization to AM-9747, leadking to a selective inhibitor of PRMT5 dimethylation in MTAP-deleted cells. AM-9747 was well tolerated and effectively inhibited arginine dimethylation and tumor growth in MTAP-deleted tumors, without affecting MTAP-WT tumors. Further optimization led to the clinical trial candidate AMG193.

9:30 Sponsored Presentation *(Opportunity Available)*

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12:15 pm Close of Small Molecules for Cancer Targets Conference

Cambridge Healthtech Institute's 13th Annual

Antibodies Against Membrane Protein Targets

New Strategies and Technologies to Accelerate the Discovery and Development of Biotherapeutics against Complex GPCR, Ion Channel, and Transporter Targets

TUESDAY, SEPTEMBER 23

7:00 am Registration Open and Morning Coffee

7:55 Welcome Remarks

EMERGING MODALITIES FOR MEMBRANE PROTEIN TARGETS

8:00 Chairperson's Remarks
André A. R. Teixeira, PhD, Senior Director, Antibody Platform, Institution for Protein Innovation

8:05 Design and Development of Multispecifics and Novel Conjugations for GPCR Targets
Ross Cheloha, PhD, Investigator, Chemical Biology of Signaling Section, Laboratory of Bioorganic Chemistry, National Institutes of Health
G protein-coupled receptors (GPCRs) are key drug targets, but ligand promiscuity complicates mechanistic studies. We hypothesized that linking GPCR ligands to antibodies could improve specificity and performance. We linked small-molecule GPCR agonists to nanobodies. Such conjugates showed high receptor specificity, potency, and pronounced signaling bias. This approach also facilitates selective targeting of receptor assemblies, offering a path towards logic-gated ligand function.

8:35 Plug-and-Play Platform to Create Biparatopic Antibodies against Membrane Protein Targets
André A. R. Teixeira, PhD, Senior Director, Antibody Platform, Institution for Protein Innovation
The Institute for Protein Innovation (IPI) has created a platform to generate biparatopic antibodies against membrane proteins, bypassing traditional binning and structural studies. This end-to-end system integrates antigen engineering, yeast display, and next-generation sequencing to develop high-quality binders. We have already produced biparatopics against 11 distinct targets, demonstrating the platform's effectiveness in rapidly generating stable, cooperative binders for challenging membrane proteins.

9:05 Protein Degraders for Membrane Protein Targets
Jing Li, PhD, Principal Scientist, Genentech
This talk explores the emerging application of targeted protein degradation to membrane proteins. Unlike conventional inhibitors that block protein function, these new approaches remove the protein entirely, opening new ways to overcome resistance and targeting previously "undruggable" targets. New advances in technologies for degrading cell surface proteins are discussed in the talk. The presentation illustrates how these tools expand the druggable space and open up new ways to treat diseases

9:35 Networking Refreshment Break
Join your colleagues for a cup of coffee or refreshments and make new connections

10:05 Discovery of T Cell Receptor Mimics Antibodies Highly Specific to pMHC Molecules through Display Technologies
Loukas I Goulatis, PhD, Senior Scientist, Biotherapeutics, Boehringer Ingelheim Pharmaceuticals Inc.
T cell engagers (TcEs) based on T cell receptor mimic (TcRm) antibodies allow for the targeting of non-surface tumor antigens, estimated to comprise around 80-85% of the tumor cell's proteome, grounded on specific interaction of antibodies towards MHC-presented peptides. In this talk, I will discuss the methods we have developed to address the challenge of identification of peptide-MHC specific TcEs employing phage and yeast display for high-throughput discovery of TcRm antibodies.

10:35 FEATURED PRESENTATION: Insights from Current Pipelines of Antibody-Based Therapeutics against GPCR, Ion Channel, and Transporter Targets
Catherine Hutchings, PhD, Independent Consultant
Complex multi-pass transmembrane proteins represent some of the most important drug target classes across a wide range of diseases. This presentation will review the progress made by antibody-based therapeutics in the GPCR, ion channel, and transporter preclinical and clinical pipelines. In addition, an update on the breadth and diversity of target opportunities in this landscape will be provided, with the diversity afforded by next-generation modalities and recent developments highlighted.

11:05 KEYNOTE PRESENTATION: Nanobodies Reveal Mechanistic Diversity in Angiotensin Receptor Ligands
Laura M. Wingler, PhD, Assistant Professor, Pharmacology and Cancer Biology, Duke University School of Medicine
The angiotensin II type 1 receptor (AT1R) plays a critical role in regulating vasoconstriction and is an important therapeutic target for the treatment of hypertension. Here, we describe the development of nanobody (single-domain antibody fragments) ligands of AT1R with various pharmacological profiles. These nanobodies utilize molecular mechanisms distinct from those of small molecule and peptide AT1R ligands. These data underscore the unique therapeutic opportunities that nanobody-based GPCR drugs could offer.

11:35 Talk Title to be Announced
Jan Kubicek, CSO & Co-Founder, Cube Biotech GmbH

Cube Biotech

11:50 Sponsored Presentation *(Opportunity Available)*

12:05 pm Transition to Lunch

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:40 Session Break

DISCOVERY PLATFORMS AND ANTIGEN STRATEGIES

1:15 Chairperson's Remarks
Catherine Hutchings, PhD, Independent Consultant

1:20 Biotherapeutics Discovery in the Digital Era: Tackling Complex Targets and Platform Optimization
Danyal Butt, PhD, Principal Research Scientist, AbbVie, Inc.
The constantly growing demand for novel biotherapeutics drives technology innovation, enabling efficient antibody discovery. Optimization and digitalization of discovery workflows is essential for successful identification of antibodies against challenging targets and the sampling of diverse repertoires. In this talk, automated platform technologies for biotherapeutics discovery workflows are presented highlighting the integration of sequence information, screening data, and informatics for large panels of antibodies, laying the groundwork for AI/ML model development.

1:50 High-Throughput Screening Methods for Antibody Discovery Using Droplet Microfluidics and Cell-Based Assays
Raluca Ostafe, PhD, Director, Molecular Evolution, Purdue University
Antibodies against membrane proteins such as GPCRs and other receptors are critical for therapeutic modulation, yet discovery remains slow. Functional epitopes are often conformational and only accessible in native membrane contexts. By combining droplet microfluidics with cell-based assays, antibodies can be screened directly from primary B cells for both binding and functional activity. This high-throughput approach enables discovery of modulatory antibodies targeting native conformations of complex membrane-associated proteins.

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Antibodies Against Membrane Protein Targets

New Strategies and Technologies to Accelerate the Discovery and Development of Biotherapeutics against Complex GPCR, Ion Channel, and Transporter Targets

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IN-PERSON ONLY BREAKOUT: Antibody Discovery Against GPCRs: Challenges and Lessons Learned
André A. R. Teixeira, PhD, Senior Director, Antibody Platform, Institution for Protein Innovation

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STRATEGIES AND TECHNOLOGIES FOR FUNCTIONAL ASSAYS

4:35 Exploiting the Biochemical Toolbox to Enable GPCR Drug Discovery
Nam Nguyen, PhD, Principal Scientist, Therapeutic Proteins, Regeneron Pharmaceuticals Inc.
G protein-coupled receptors (GPCRs) pose numerous challenges to drug development. Most notably, their poor expression and nonideal biochemical properties present major hurdles for *in vitro* manipulation such as reconstitution into lipid bilayers or formation of GPCR-transducer complexes. In this presentation, I will highlight approaches taken at Regeneron to produce GPCRs to support antibody-discovery campaigns and the use of G proteins as tools to functionally validate purified receptors.

5:05 Expanding the Scope of New Therapeutic Targets and Drug Discovery of Challenging and Orphan GPCRs
Laurent Sabbagh, PhD, Scientific Director, Domain Therapeutics
Orphan GPCRs represent an untapped reservoir of therapeutic potential for developing innovative treatments across different indications. However, drug development for these—100 uncharacterized GPCRs is challenging due to the absence of validated ligands and limited understanding of their signaling, complicating drug-screening assay design. I will discuss different constitutive activity i.e., ligand independent-based applications of our bioSens-All platform to develop high-throughput screening assays for orphan-GPCR drug-discovery efforts.

5:35 Super-Resolution Imaging with Single-Antibody Labeling
Ying S Hu, PhD, Assistant Professor, Chemistry and Biomedical Engineering, University of Illinois Cancer Center
Antibodies targeting membranes have traditionally been evaluated using ensemble-based measurements, which mask molecular heterogeneity and dynamic interactions. In this talk, I will discuss a single-antibody labeling technique that enables precise localization of antibody binding with 10–20 nm resolution, reveals binding kinetics that distinguish specific from non-specific targets, and resolves membrane nanostructures to uncover their functional roles in receptor-mediated signaling.

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7:05 Close of Day

WEDNESDAY, SEPTEMBER 24

7:30 am Registration and Morning Coffee

COMPUTATIONAL DESIGN AND OPTIMIZATION

7:55 Chairperson's Remarks
Danyal Butt, PhD, Principal Research Scientist, AbbVie, Inc.

8:00 Case Studies of *de novo* Design for Biotherapeutics Against Membrane Protein Targets
Diego Del Alamo, PhD, Computational Biologist, GSK
Membrane proteins make common drug targets, but their structures are sometimes difficult to resolve at high resolution. This can be challenging when using cryo-EM to study proteins without any distinctive soluble features or domains. Here, I present examples of drug targets being structurally enabled by applying modern protein design tools for further study by cryo-EM. Promising results, as well as failure points, showcase these workflows in greater detail.

8:30 Design of *de novo* Proteins Targeting Voltage-Gated Potassium Channel Kv1.3
Vladimir Yarov-Yarovoy, PhD, Professor, Physiology and Membrane Biology, University of California, Davis
Human voltage-gated potassium channel, Kv1.3, is a key therapeutic target for autoimmune and neuroinflammatory diseases. We used deep-learning-based RFdiffusion and AlphaFold2 methods to design *de novo* proteins targeting the extracellular Kv1.3 pore region. Functional testing of top designs using whole-cell patch clamp electrophysiology revealed three designs with nanomolar range potency for Kv1.3. These results highlight the potential of *de novo* design for generating high-affinity binders targeting ion channels.

9:00 AI-Based Image Analysis of Label-Free T Cell Mediated Tumor Killing Facilitates Robust Hit Identification
Josefa dela Cruz-Chuh, Scientist 4, Genentech
To identify effective immune engagers, including T cell therapies or T cell-dependent bispecific antibodies, robust screening of T cell-mediated tumor killing co-culture is crucial. Traditional imaging relies on fluorescently labeled cells, risking artifacts and phototoxicity. We introduce an AI/ML-based method utilizing only brightfield images to identify phenotypic changes, eliminating fluorescent markers. This innovative approach applied to T cell-killing assays maintains consistency, enhances efficiency, and allows analysis of diverse tumor cells without complex segmentation.

9:30 Sponsored Presentation *(Opportunity Available)*

10:00 Coffee Break in the Exhibit Hall with Poster Viewing
Start your morning with coffee, connections, and cutting-edge research! Vote for the Best of Show Poster and stay to celebrate the winner! Visit with industry-leading service providers, fill out the Game Card to win a raffle prize and vote for the People's Choice Best of Show Exhibitor.

PLENARY KEYNOTE PROGRAM

10:50 Welcome Remarks from the Discovery on Target Team Lead

11:00 Plenary Keynote Chairperson's Remarks

11:05 PLENARY KEYNOTE: The Radicalization of Drug Discovery
Gregory L. Verdine, PhD, President & CEO, LifeMine Therapeutics
The field of drug discovery stands at a watershed moment of scientific, medical, and commercial opportunity. Realization of this opportunity will require radical innovations that fundamentally expand the functional capabilities of therapeutic interventions and management of the attendant risks. This talk will focus on the discovery, development, and deployment of radically new therapeutic modalities, inspired by nature, that thrust the field forward in non-obvious, impactful, and exciting new directions.

Antibodies Against Membrane Protein Targets

New Strategies and Technologies to Accelerate the Discovery and Development of Biotherapeutics against Complex GPCR, Ion Channel, and Transporter Targets

11:40 **PLENARY KEYNOTE: GLP-1 Unveiled: Key Takeaways for Next-Generation Drug Discovery**

Lotte Bjerre Knudsen, PhD, Chief Scientific Advisor, Head of IDEA (Innovation&Data Experimentation Advancement), Novo Nordisk AS

This talk explores the evolution of GLP-1 as a significant component in diabetes and obesity treatment, and its direct impact on multiple co-morbidities. It highlights the role of industry innovation and scientific persistence in overcoming challenges posed by its short half-life, ultimately leading to the successful development of GLP-1 therapies. Key lessons will inform future drug discovery strategies, emphasizing that today's drug discovery must be based on human data.

12:15 pm **Close of Antibodies Against Membrane Protein Targets Conference**

Cambridge Healthtech Institute's 7th Annual

RNA & DNA Targeting Small Molecule Drugs

Identifying New Pathways, Modalities, and Strategies for Therapeutic Intervention

TUESDAY, SEPTEMBER 23

7:00 am Registration Open and Morning Coffee

7:55 Welcome Remarks

NOVEL RNA SPLICING MODULATORS

8:00 Chairperson's Remarks
Elisabetta Morini, PhD, Instructor, Department of Neurology, Massachusetts General Hospital

8:05 Splicing Modulators as a Therapeutic Strategy for 4R Tauopathies
Elisabetta Morini, PhD, Instructor, Department of Neurology, Massachusetts General Hospital
Tauopathies are neurodegenerative diseases marked by accumulation of 4R Tau isoforms due to mutations in MAPT exon 10 or adjacent introns. We developed splicing modulator compounds (SMCs) that promote exon 10 exclusion, reducing 4R Tau expression and pathology in patient-derived neurons with Tau-P301L or S305N mutations. Lead SMCs also reduced pTau in a Tau-N279K mouse model, supporting their therapeutic potential for treating 4R tauopathies.

8:35 Small Molecule mRNA Splicing Modulators that Prevent Somatic Expansion in Huntington's Disease
Sridhar Narayan, PhD, Vice President, ReviR Therapeutics
Small molecules that modulate mRNA splicing are an ideal modality for treatment of neurodegenerative disorders with high unmet need, due to their brain penetration and oral bioavailability. Here we present an update on our work towards the development of splicing modulators that prevent somatic expansion in Huntington's Disease. We will discuss the preclinical data on the safety and efficacy of our lead molecule and its progress towards clinical development.

9:05 Splice Modulators Target PMS1 to Reduce Somatic Expansion of the Huntington's Disease-Associated CAG Repeat
Zachariah McLean, PhD, Instructor in Neurology, Center for Genomic Medicine, Massachusetts General Hospital
Huntington's disease (HD) is a dominant neurological disorder caused by an expanded CAG repeat in HTT. Lowering mutant huntingtin has been proposed for treating HD, but genetic modifiers implicate somatic CAG repeat expansion as the driver of onset. We find that branaplam and risdiplam, small-molecule splice modulators that lower HTT, also decrease the rate of CAG repeat instability through pseudoexon inclusion in age-at-onset modifier, PMS1.

9:35 Networking Refreshment Break
Join your colleagues for a cup of coffee or refreshments and make new connections

10:05 Successful Application of an RNA-Splicing Modulator Platform to Develop Molecules Targeting Multiple Disease Areas
Thomas Wynn, PhD, Director, Medicinal Chemistry, Rgenta Therapeutics
Rgenta Therapeutics has developed a proprietary, integrative RNA-targeting oral small molecule discovery platform to deliver first-in-class therapies. We are pursuing targets in the oncology and neurological diseases space, exemplified by the oncogenic transcription factor c-MYB and the PMS1 gene. In this presentation, we'll share an overview of our platform and recent progress on selected targets.

10:35 PANEL DISCUSSION: Session Speakers Discuss Advances in Finding New Splicing Sites and Developing New Modulators
Moderator: Elisabetta Morini, PhD, Instructor, Department of Neurology, Massachusetts General Hospital

11:35 The Elongator drew the short straw: discovery of first-in-class anti-cancer inhibitors targeting the ELP3-tRNA interface
Daniele Carettoni, Scientific Officer, Biological Sciences, Axxam SpA
The tRNA epitranscriptome represents a previously unexplored anti-cancer target space. We developed a novel HTS assay to probe the interaction between tRNA and ELP3, the catalytic subunit of the Elongator complex. This led to the discovery of first-in-class small molecules that selectively inhibit ELP3, showing strong efficacy in patient-derived cancer cells and xenograft models with a favorable safety profile.

12:05 pm Transition to Lunch

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:40 Session Break

NOVEL RNA TARGETING STRATEGIES

1:15 Chairperson's Remarks
Nikolai Naryshkin, PhD, CSO, Ribonaut Therapeutics

1:20 FEATURED PRESENTATION: Reprogramming RNA to Target the Undruggable
Dominic J. Reynolds, PhD, CSO, R&D, Remix Therapeutics
Remix Therapeutics developed the REMaster platform to identify small molecules that impact the expression of disease-driving mRNAs through modulation of RNA processing. This led to the discovery of REM-422, a first-in-class degrader of the MYB oncogene. REM-422 is an oral small molecule that induces the degradation of MYB mRNA and protein expression resulting in antitumor activity in MYB-dependent human tumor models and is currently in Phase 1 clinical trials.

1:50 Recent Advances in the Discovery of RNA-targeted Small Molecules
Emily Garcia Sega, PhD, Senior Scientist, Medicinal Chemistry, Arrakis Therapeutics
Our mission at Arrakis is to solve very broadly the problem of how to drug RNA with small molecules. This presentation will provide an update on the platform we have built to achieve that mission and provide early data on specific mRNA targets.

2:20 Sponsored Presentation *(Opportunity Available)*

2:50 In-Person Breakouts
In-Person Breakouts are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator, or facilitators, who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Breakouts page on the conference website for a complete listing of topics and descriptions.

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4:35 Presentation to be Announced

5:05 Presentation to be Announced

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RNA & DNA Targeting Small Molecule Drugs

Identifying New Pathways, Modalities, and Strategies for Therapeutic Intervention

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7:05 Close of Day

WEDNESDAY, SEPTEMBER 24

7:30 am Registration and Morning Coffee

NOVEL PLATFORMS FOR SCREENING TARGETS

7:55 Chairperson's Remarks
Joshua P. Plotnik, PhD, Principal Research Scientist, Oncology Discovery Research, AbbVie, Inc.

8:00 Novel Synthetic Lethal Targets within the mRNA Quality-Control Pathway
Joshua P. Plotnik, PhD, Principal Research Scientist, Oncology Discovery Research, AbbVie, Inc.
PELO–HBS1L and SKI complex synthetic lethality alters the normal cell cycle and drives the unfolded protein response through the activation of IRE1, as well as robust tumor growth inhibition. Our results indicate that PELO and HBS1L represent novel therapeutic targets whose dependence converges upon SKI complex destabilization, a common phenotypic biomarker in diverse genetic contexts representing a significant population of patients with cancer.

8:30 A Comprehensive Platform for Identification of Novel Synthetic Lethal Targets and Drug Combinations Using Patient-Derived Cells
Krzysztof Brzozka, PhD, CSO, Ryvu Therapeutics
Our study identifies and validates synthetic lethal (SL) interactions in colorectal cancer (CRC), focusing on actionable vulnerabilities linked to APC and KRAS mutations. By integrating engineered primary cancer models, patient-derived xenografts, and transcriptomic profiling, we discovered novel SL targets that offer a promise for personalized CRC therapies. These findings bridge preclinical and clinical research, paving the way for safer and more effective treatment options tailored to CRC's unique mutational landscape.

9:00 Harnessing Cellular Metabolite Screening for RNA-Targeting Small-Molecule Drug Discovery
Benjamin Brigham, PhD, Senior Scientist, Biophysics, Atavistik Bio
Small-molecule targeting of RNAs has become a leading drug discovery approach. However, identifying RNA binders that produce functional effects remains a significant challenge. Endogenous cellular metabolites provide an untapped source of inspiration for small-molecule leads. Atavistik Bio has leveraged the AMPS (Atavistik Metabolite Proprietary Screening) platform to screen metabolites against RNA. We will present the AMPS platform, our hit identification workflows, and a case study of the SERPINA1 5'UTR.

9:30 Presentation to be Announced

Clarivate™

10:00 Coffee Break in the Exhibit Hall with Poster Viewing
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12:15 pm Close of RNA & DNA Targeting Small Molecule Drugs Conference

Cambridge Healthtech Institute's 4th Annual

AI/ML-Enabled Drug Discovery - Part 1

Design and Optimization of Novel Drugs and Modalities

TUESDAY, SEPTEMBER 23

7:00 am Registration Open and Morning Coffee

7:55 Welcome Remarks

AI-DRIVEN DRUG DESIGN

8:00 Chairperson's Remarks
Anthony Bradley, D.Phil, Assistant Professor, Department of Chemistry, University of Liverpool

8:05 Generative Design in Drug Discovery: Are We Truly Innovating or Merely Complicating?
Anthony Bradley, D.Phil, Assistant Professor, Department of Chemistry, University of Liverpool
As generative models grow more complex, discerning their actual contributions to drug design becomes challenging. This presentation assesses the impact of these models, focusing on molecule synthesizability and 3D integration. We critically analyze limitations from small datasets and the models' tendency to infer patterns without genuine extrapolative power. Emphasizing need for clarity in evaluation, we propose strategies for meaningful benchmarks to ensure generative models deliver tangible improvements in drug discovery.

8:35 AI/ML-Enabled Growing of Small Molecules from Fragment Seeds within Protein Cavities
Jordi Mestres, PhD, Founder & CSO, Chemotargets
Structure-based generative modelling (SBGM) represents a change of paradigm in drug discovery, from virtually screening ultra-large chemical libraries to virtually growing molecules with desired physicochemical and ADME properties directly inside the protein cavity. In this talk, the SBGM platform developed at Chemotargets to generate novel synthetically feasible drug-like molecules for protein targets will be introduced. Both retrospective fragment-to-drug examples and prospective fragment-growing case studies will be presented.

9:05 Integrating AI/ML with a Unique Chemical Space to Create Efficiency and Optionality in Early Drug Discovery
Hok Hei Tam, PhD, Co-Founder and CTO, Montai Therapeutics; Senior Principal, Flagship Pioneering
Advanced AI/ML modeling makes it possible to efficiently and specifically discover new oral therapeutics for chronic disease. Montai's CONECTA platform integrates proprietary bioassay data and machine-learning models built on repositories of chemistry and multi-factorial biological data on complex disease pathways and drug-like properties. The integration of multi-modal modeling into the candidate selection process efficiently identifies those with the highest probability of becoming successful drugs to address significant unmet needs.

9:35 Networking Refreshment Break
Join your colleagues for a cup of coffee or refreshments and make new connections

10:05 Technology Spotlights *(Sponsorship Opportunity Available)*

10:10 Technology Spotlight by Examol
Speaker to be Announced, Examol

10:35 PANEL DISCUSSION: From GPU to GMP- Bridging AI/ML Tools and Real-World Drug Discovery
Moderator: Anthony Bradley, D.Phil, Assistant Professor, Department of Chemistry, University of Liverpool
Panelists:
Erin Davis, PhD, CTO, Technology, X Chem Inc
Ashwini Ghogare, PhD, Executive Director and Head of AI & Automation for Drug Discovery, MilliporeSigma
Petrina Kamya, PhD, Global Head of AI Platforms & Vice President, Insilico Medicine; President, Insilico Medicine Canada
Jordi Mestres, PhD, Founder & CSO, Chemotargets
Janet Paulsen, PhD, Senior Alliance Manager, Drug Discovery, NVIDIA Corp.
Woody Sherman, PhD, CIO, Psivant Therapeutics
Mike Tarselli, PhD, Specialist Leader, Specialists, Amazon.com

11:35 Supercharge Computational Drug Discovery with AI-Powered Serverless High-Performance Computing (HPC)
Fengbo Ren, Founder & CEO, Fovus
Fovus is an AI-powered, serverless high-performance computing (HPC) platform delivering intelligent, scalable, and cost-efficient supercomputing power at the computational scientists' fingertips. Fovus uses AI to optimize HPC strategies and orchestrates cloud logistics, making cloud HPC a no-brainer and ensuring sustained time-cost optimality for computational drug discovery amid quickly-evolving cloud infrastructure. By accelerating time-to-insights and optimizing cloud costs, Fovus helps biotech clients accelerate Design-Make-Test-Analyze (DMTA) cycles and discover more with less. Join this talk to learn how Fovus can supercharge your computational drug discovery with case studies and GROMACS/AlphaFold 3 benchmarking results. Learn more at fovus.co.

11:50 Sponsored Presentation *(Opportunity Available)*

12:05 pm Transition to Lunch

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:40 Session Break

AI/ML FOR TARGET DISCOVERY

1:15 Chairperson's Remarks
Tudor Oprea, MD, PhD, CEO, Expert Systems, Inc.

1:20 Artificial Intelligence for Target Prioritization and Therapeutic Indication Expansion
Tudor Oprea, MD, PhD, CEO, Expert Systems, Inc.
At Expert Systems, we firmly believe in temporal validation for all AIML models as a means to significantly reduce predictive errors and hallucinations. We will discuss our Target Druggability model, which, trained on data current as of 2017, correctly predicts nearly 80% of novel drug targets (2018-2024). We will also discuss using agentic LLMs that conduct automated reasoning to suggest novel therapeutic indications for existing intellectual property.

1:50 A Framework for Autonomous, Fully Transparent AI-Driven Target Discovery
Douglas Selinger, PhD, CEO & Founder, Plex Research Inc.
The exponential increase in biomedical data offers unprecedented opportunities for drug discovery, yet often overwhelms traditional data analysis methods. Here we introduce a framework for autonomous artificial intelligence (AI)-driven drug discovery that integrates knowledge graphs with large language models (LLMs) and which is capable of planning and executing automated drug discovery programs on a massive scale while providing details of its research strategy, progress, and all supporting data.

2:20 Presentation to be Announced

2:50 In-Person Breakouts

Cambridge Healthtech Institute's 4th Annual

AI/ML-Enabled Drug Discovery - Part 1

Design and Optimization of Novel Drugs and Modalities

In-Person Breakouts are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator, or facilitators, who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Breakouts page on the conference website for a complete listing of topics and descriptions.

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AI/ML FOR TARGET DISCOVERY

4:35 Characterizing Cellular Heterogeneity in Liquid To Identify Novel Targets

Praveen Anand, PhD, Data & Analytics Lead, Data Science and Analytics, UCB Pharma

In this study, we employed scRNA-seq to uncover the complex phenotypic landscape of early T-cell precursor acute lymphoblastic leukemia (ETP-ALL). The computational analyses of gene programs revealed intricate interplay between oncogenic states and immune evasion programs that drives the complex phenotypic landscape in ETP-ALL. The cellular states and transitions identified not only improves our comprehension of disease pathogenesis but also aids in the identification of potential therapeutic targets.

5:05 Leveraging Multiomics Data to Identify and Prosecute Targets Implicated in Women's Health

Petrina Kamya, PhD, Global Head of AI Platforms & Vice President, Insilico Medicine; President, Insilico Medicine Canada

Endometriosis and alternative sources of non-hormonal contraception are neglected and challenging issues associated with women's health. Today, I will discuss how we leverage multiomics data and AI to identify novel targets implicated in endometriosis and how we contribute to the challenge of designing novel non-hormonal contraceptives using AI.

5:35 FEATURED PRESENTATION: Simulating Biologically Relevant Protein Motions in Challenging Disease Targets

Woody Sherman, PhD, CIO, Psivant Therapeutics

Understanding protein dynamics is critical for drug discovery against challenging targets. We describe an integrated platform that combines all-atom physics-based simulations with biophysical data, including HDX-MS and crystallography, to model biologically relevant protein motions and thermodynamics. We use this approach to enable mechanism-driven design strategies to advance our therapeutic pipeline of novel orally bioavailable molecules against clinically validated inflammation and immunology targets.

6:05 Welcome Reception in the Exhibit Hall with Poster Viewing

Engage with the community, explore the latest innovations, network with service partners and providers, meet the poster presenters, vote for our Best of Show Poster and Best of Show Exhibitor awards in a relaxed, social atmosphere.

7:05 Close of Day

WEDNESDAY, SEPTEMBER 24

7:30 am Registration and Morning Coffee

AI/ML FOR PREDICTIVE MODELING

7:55 Chairperson's Remarks

Sean Ekins, PhD, Founder & CEO, Collaborations Pharmaceuticals, Inc.

8:00 Machine Learning and Large-Language Models for Modeling Complex Toxicity Pathways

Sean Ekins, PhD, Founder & CEO, Collaborations Pharmaceuticals, Inc.

Addressing certain toxicities such as drug-induced seizures and steroidogenesis may require complex models to enable predictions. We now describe how we have generated large numbers of machine-learning models for either individual toxicity targets or large language models (ProtBERT, MolBART) to enable predictions for prospective testing.

8:30 A Multimodal Transformer Breaking the Data Wall between Lab and Clinic

David Farina Jr., PhD, Senior Research Scientist, Machine Learning, Iambic Therapeutics Inc.

Enchant is a multimodal transformer designed to break the data wall between lab and clinic by predicting clinical outcomes from preclinical data. Trained on diverse, heterogeneous datasets, it addresses the scarcity of clinical data by leveraging stage discovery data of various modalities. Enchant enables informed decision-making earlier in the drug development pipeline, accelerating and de-risking the path from discovery to the clinic.

9:00 Identification of VHH-Binders from an Immunized-Antibody Repertoire from Computational Methods Alone

Nicholas Woodall, PhD, Scientist, Computational Platform, Visterra Inc.

We used a bioinformatics approach to analyze the immune repertoire of a llama immunized with a target antigen, prioritizing those antibodies inferred to be clonally expanded. We employed AlphaFold2 to dock these antibodies, selecting those predicted to bind an epitope of interest. This *in silico* strategy yielded a 60% hit rate in identifying binders. We found many binders that effectively inhibited binding of the target to its receptor.

9:30 Accelerating Drug Discovery Success with Integrated Computational and Experimental Sciences

Douglas Kitchen, Research Fellow Computer-Aided Drug Discovery, Discovery Services, Curia

Curia was founded in 1992 and the Computer-assisted drug discovery group began in 1997. The CADD group has applied computational and cheminformatics calculations to dozens of projects as part of project teams from Curia and multiple drug discovery entities. We have found that the expert use of computational chemistry in collaboration with experimentalists leads to successful projects with the generation of novel chemical matter and preclinical leads. Several example projects will illustrate the use of virtual screening, traditional physics-based modeling, reaction modeling and library design in early drug discovery.

9:45 Sponsored Presentation *(Opportunity Available)*

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

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12:15 pm **Close of AI/ML-Enabled Drug Discovery - Part 1 Conference**

Targeting MASH & Obesity

Drug Discovery and Development for Obesity and Fatty Liver Disease

TUESDAY, SEPTEMBER 23

7:00 am Registration Open and Morning Coffee

7:55 Welcome Remarks

BEYOND GLP1: NEW OBESITY DRUG TARGETS

8:00 Chairperson's Remarks
Florence Brunel, PhD, Senior Principal Scientist, Novo Nordisk Inc

8:05 The Promise of Synergistic Pharmacology: LY3457263, a Novel NPY2 Receptor Agonist for Type 2 Diabetes and Obesity
Avinash Muppidi, PhD, Director, Peptide Therapeutics, Eli Lilly and Company

8:35 Structural Basis of Lipid-Droplet Localization of 17-Beta-Hydroxysteroid Dehydrogenase 13
Shenping Liu, PhD, Associate Research Fellow, Exploratory Medicinal Sciences, Pfizer Global R&D Groton Labs
Loss of function of HSD17B13, a membrane protein associated with lipid droplet in liver, protects against chronic liver diseases. Here we report two series of HSD17B13 inhibitors and their complex structures, and developments of artificial substrates. These results provide understandings of HSD17B13's lipid droplet association and its variants' protection functions. Structure-based design of inhibitors and artificial substrates is used in developing compounds in the treatment of liver disease.

9:35 Networking Refreshment Break
Join your colleagues for a cup of coffee or refreshments and make new connections

10:05 Presentation to be Announced

10:35 PANEL DISCUSSION: Drug Development Challenges for MASH & Obesity
Moderator: Rebecca A. Taub, MD, CMO, President of R&D, Madrigal Pharmaceuticals

11:35 Sponsored Presentation *(Opportunity Available)*

12:05 pm Transition to Lunch

12:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:40 Session Break

TARGETING MASH

1:15 Chairperson's Remarks
Feng Liu, PhD, Executive Director, R&D, Regor Pharmaceuticals Inc.

1:20 FEATURED PRESENTATION: MASH Drug Development Lessons Learned from Taking a THRb Agonist to Market
Rebecca A. Taub, MD, CMO, President of R&D, Madrigal Pharmaceuticals

1:50 Tirzepatide for MASH
YoSon Park, PhD, Senior Advisor, DOCTA, Eli Lilly and Company

2:20 Sponsored Presentation *(Opportunity Available)*

2:50 In-Person Breakouts
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4:35 Pegozafermin: Reversing Fibrosis and Tackling Metabolic Dysfunction in MASH
Hank Mansbach, MD, CMO, 89bio, Inc.
This session will review the latest data and insights surrounding 89bio's lead investigational candidate, pegozafermin, a specifically engineered glycoPEGylated analog of fibroblast growth factor 21 (FGF21), for the treatment of Metabolic Associated Steatohepatitis (MASH). Pegozafermin is in Phase 3 ENLIGHTEN trials for MASH and the Phase 3 ENTRUST trial for severe hypertriglyceridemia (SHTG), demonstrating direct anti-fibrotic and anti-inflammatory effects in the liver, as well as other benefits and favorable saftey.

5:05 Efimosfermin Alfa: A Once-Monthly FGF21 Analog for the Treatment of MASH
Matthew Bryant, PharmD, Vice President, Medical Affairs, Boston Pharmaceuticals
Once-monthly efimosfermin treatment demonstrated statistically significant improvement in liver fibrosis and MASH resolution, reductions in liver fat content, improved markers of liver injury, and metabolic biomarkers with a favorable safety profile compared to placebo over 24 weeks in participants with biopsy-confirmed F2/F3 MASH. Efimosfermin was generally well tolerated with low discontinuation rates due to adverse events and an overall low incidence of gastrointestinal side effects and injection-site reactions.

5:35 Identification of Antibodies that Block the WISP1 Signaling for Treating Tissue Fibrosis
Yue Zhao, PhD, Principal Scientist, Biochemical Cellular & Pharmacology, Genentech Inc.
WISP1 was identified as a highly upregulated gene in human fibrotic tissues. WISP1 activates the MRTF signaling to transcriptionally activate cellular motility and is involved in recruiting the effector cells, such as fibroblasts, to the tissue injury site and promoting fibrosis progression. We developed WISP1-blocking antibodies and the preclinical study of the anti-WISP1 program will be presented.

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7:05 Close of Day

WEDNESDAY, SEPTEMBER 24

7:30 am Registration and Morning Coffee

2ND GENERATION INCRETIN-TARGETED COMPOUNDS

7:55 Chairperson's Remarks
Robert D. Mazzola, PhD, Director & Principal Scientist, Chemical Research, Merck & Co.

8:00 Small Molecule Agonists for GLP-1R and Other Obesity-Related GPCRs
Yingli Y. Ma, PhD, CTO, Platform Technology, Structure Therapeutics

8:30 Orally Bioavailable Small Molecule GLP1R Full Agonists with Best-in-Class Potential for Diabetes, Obesity, MASH & Beyond
Feng Liu, PhD, Executive Director, R&D, Regor Pharmaceuticals Inc.
GLP1 is a key incretin hormone involved in metabolic homeostasis, exerting effects that include enhanced insulin sensitivity, reduced inflammation, and appetite suppression—mechanisms highly relevant to the pathophysiology of metabolic disorders and MASH. GLP1R agonists have demonstrated efficacy in reducing hepatic steatosis and fibrosis in preclinical and clinical studies. Regor is developing orally bioavailable small molecule GLP1R agonists, offering potential for improved pharmacokinetics, patient adherence, and broader therapeutic reach.

9:00 Tuning Multi-Receptor Peptide Agonists through Molecular Design
Krishna Kumar, PhD, Professor, Chemistry, Tufts University
We describe here the design and development of potent peptide analogs that are completely refractory to hydrolytic enzyme action while retaining full biological activity, potency, and efficacy. This lecture will describe the fundamental design principles, molecular pharmacology, and *in vivo* data detailing, fine tuning such activity by simple chemical modification of peptides. Some of the compounds described rival or better those used in the clinic.

9:30 Sponsored Presentation *(Opportunity Available)*

10:00 Coffee Break in the Exhibit Hall with Poster Viewing
Start your morning with coffee, connections, and cutting-edge research! Vote for the Best of Show Poster and stay to celebrate the winner! Visit with industry-leading service providers, fill out the Game Card to win a raffle prize and vote for the People's Choice Best of Show Exhibitor.

PLENARY KEYNOTE PROGRAM

10:50 Welcome Remarks from the Discovery on Target Team Lead

11:00 Plenary Keynote Chairperson's Remarks

11:05 PLENARY KEYNOTE: The Radicalization of Drug Discovery
Gregory L. Verdine, PhD, President & CEO, LifeMine Therapeutics
The field of drug discovery stands at a watershed moment of scientific, medical, and commercial opportunity. Realization of this opportunity will require radical innovations that fundamentally expand the functional capabilities of therapeutic interventions and management of the attendant risks. This talk will focus on the discovery, development, and deployment of radically new therapeutic modalities, inspired by nature, that thrust the field forward in non-obvious, impactful, and exciting new directions.

11:40 PLENARY KEYNOTE: GLP-1 Unveiled: Key Takeaways for Next-Generation Drug Discovery
Lotte Bjerre Knudsen, PhD, Chief Scientific Advisor, Head of IDEA (Innovation&Data Experimentation Advancement), Novo Nordisk AS
This talk explores the evolution of GLP-1 as a significant component in diabetes and obesity treatment, and its direct impact on multiple co-morbidities. It highlights the role of industry innovation and scientific persistence in overcoming challenges posed by its short half-life, ultimately leading to the successful development of GLP-1 therapies. Key lessons will inform future drug discovery strategies, emphasizing that today's drug discovery must be based on human data.

12:15 pm Close of Targeting MASH & Obesity Conference

Discovery on Target

By the Numbers

1100+ Attendees	220+ Presentations	110+ Research Posters	13 Conference Tracks	2 In-Person Training Seminars

90 Exhibitors	22 Countries Represented	12 In-Person Short Courses	5 Symposia

Degraders & Molecular Glues – Part 2

New Targets, Ligases, Assays for Induced Proximity and Degradation

WEDNESDAY, SEPTEMBER 24

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12:15 pm Enjoy Lunch on Your Own

ADVANCES IN MOLECULAR GLUES

1:45 Welcome Remarks

1:50 Chairperson's Remarks

Abbie Macmillan-Jones, Senior Scientist, Discovery Sciences, AstraZeneca

1:55 FEATURED PRESENTATION: Advances in the Systematic Discovery of Molecular Glue Degraders

Eric Fischer, PhD, Associate Professor, Biological Chemistry and Molecular Pharmacology, Harvard Medical School; Director Center for Protein Degradation, Dana-Farber Cancer Institute

While the discovery of PROTACs has become a mainstay of drug discovery, discovery of novel molecular glues beyond CRBN modulators remains a major challenge for the field. I will present recent work on understanding the principles that govern molecular glue interactions, updates on our discovery platforms and recent examples of success to expand the repertoire of ligases enabled for molecular glues.

2:55 Sponsored Presentation *(Opportunity Available)*

3:25 Refreshment Break in the Exhibit Hall with Poster Viewing

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VENTURE CAPITALIST INSIGHTS

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Moderator: Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation

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5:15 Dinner Short Course Registration*

COLLABORATIVE CONVERSATION

5:15 IN-PERSON PLENARY DISCUSSION: Connecting the DOTs to Spark Change!

Join us for an hour of inspiring, informal discussions on how to forge connections and create impactful ecosystems that will help you think, act, and thrive. We have invited pharma, biotech, and academic leaders to share their stories and experiences and to discuss key learnings. There will be time for open discussion and networking.

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Sean Ekins, PhD, Founder & CEO, Collaborations Pharmaceuticals
Shruthi Bharadwaj, PhD, Program Leader, MIT
Raquel Mura, DPharm, Founder, RGM Life Sciences Consulting; former VP & Head R&D, Sanofi
Nisha Perez, PhD, VP Preclinical Development & Clinical Pharmacology, ROME Therapeutics

6:00 Dinner Short Courses*

*All Access Package or separate registration required. See Short Courses page for details.

8:30 Close of Day

THURSDAY, SEPTEMBER 25

7:30 am Registration Open and Morning Coffee

Degraders & Molecular Glues – Part 2

New Targets, Ligases, Assays for Induced Proximity and Degradation

DEGRADING TRANSCRIPTION FACTORS

8:00 Chairperson's Remarks

Charles Wartchow, PhD, Associate Director, Discovery Sciences, Novartis Institutes for BioMedical Research

8:05 FEATURED PRESENTATION: Attenuating Oncogenic Transcription with Small Molecules

Angela Koehler, PhD, Associate Professor, Biological Engineering, Massachusetts Institute of Technology

The lecture reviews recent advances in the lab involving successful targeting strategies, including discussion of compounds that modulate MYC-driven transcription via mechanisms involving the MAX partner protein or the transcriptional kinase CDK9. Additionally, new and unpublished work related to targeting fusion oncoproteins arising in pediatric cancers such as alveolar rhabdomysosarcoma will be discussed.

8:50 FEATURED PRESENTATION: Development of Orally Bioavailable MDM2 Degraders

Shaomeng Wang, PhD, Warner-Lambert/Parke-Davis Professor of Medicine, Pharmacology & Medicinal Chemistry; Co-Director, Molecular Therapeutics Program, University of Michigan

The human murine double minute 2 (MDM2) protein is a primary, endogenous cellular inhibitor of the tumor suppressor p53. MDM2 inhibitors have major limitations in the clinic, including insufficient efficacy and development of clinical resistance. In this presentation, I will discuss the development of highly potent and orally efficacious MDM2 PROTAC degraders for the treatment of human AML and other types of human cancers.

9:35 Targeting MYC and Oncogenic p53 through LZK Inhibition or Degradation to Treat Head and Neck Cancers

John Brognard, PhD, Senior Investigator, Laboratory of Cellular & Developmental Signaling, National Cancer Institute, National Institutes of Health

The worldwide frequency of head and neck squamous cell carcinoma (HNSCC) is approximately 800,000 new cases, with 430,000 deaths annually. We found that the kinase activity of LZK stabilized c-MYC and that LZK stabilized gain-of-function (GOF) p53 through a kinase-independent mechanism in this cancer. Our lead PROTAC promotes LZK degradation and suppresses expression of GOF p53 and c-MYC, leading to impaired viability in HNSCC and is a promising new therapy.

10:05 In-Person Breakouts

In-Person Breakouts are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator, or facilitators, who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Breakouts page on the conference website for a complete listing of topics and descriptions.

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DEGRADER OPTIMIZATION

11:30 Delivering on Cascades for Next-Generation Degraders: Translating Innovation into Impact

Abbie Macmillan-Jones, Senior Scientist, Discovery Sciences, AstraZeneca

Following the success of PROTACs laying the framework for modulation of protein levels as a therapeutic strategy, the field of protein degradation has witnessed an unprecedented expansion in new drug modalities. This talk will discuss strategies to discover and develop these next generation molecules, translating basic research innovation into therapeutically active compounds.

12:00 pm Physicochemical Guides for the Design of Orally Bioavailable PROTAC Protein Degraders

Erika Vieira Araujo, PhD, Principal Research Investigator, Discovery Chemistry, Arvinas Inc.

Through a retrospective analysis of the pharmacokinetic profiles of a large set of PROTAC molecules, we have derived PROTAC design constraints on physicochemical properties associated with higher probability of oral bioavailability. This data was further used to train a machine-learning model to predict oral-absorption performance to further prospective design efforts of orally bioavailable molecules.

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1:00 Transition to Lunch

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SCREENING & ASSAY DEVELOPMENT FOR DEGRADERS

2:15 Chairperson's Remarks

Gisele Nishiguchi, PhD, Group Leader, St. Jude Children's Research Hospital

2:20 Multimodal Screening Strategies to Identify Novel Cereblon Neosubstrates

Gisele Nishiguchi, PhD, Group Leader, St. Jude Children's Research Hospital

The design of molecular glue degraders (MGD) has been challenging and the discovery of novel MGD/neosubstrate pairs has relied primarily on different screening strategies. In this talk, I will discuss our multipronged screening approaches (phenotypic, targeted, and proteome-wide) against a molecular glue library based on cereblon binders and the discovery of novel degrader-neosubstrate pairs.

2:50 NanoBRET-Powered High-Throughput Platform for the Discovery of Molecular Glues

Milad Rouhimoghadam, PhD, Senior Scientist I, Small Molecule Therapeutics & Platform Technology, AbbVie

We introduce a NanoBRET-powered high-throughput platform that lights up molecular glue activity in live cells. By capturing real-time E3 ligase–substrate interactions, this assay enables rapid, scalable discovery of glue degraders with high sensitivity and physiological relevance, offering a powerful tool to unlock new therapeutic mechanisms and expand the degradable proteome.

3:20 Expanding the Set of Zinc Finger Proteins Accessible to Drug-Induced Protein Degradation by CRBN

Mikolaj Slabicki, PhD, Assistant Professor, MGH/Broad Institute

The Slabicki Laboratory investigates the mechanistic basis of protein degradation by leveraging functional genomics and reprogramming the ubiquitin-proteasome system. Using advanced screening and biochemical approaches, we elucidate target-ligase interactions to accelerate therapeutic discovery for diseases lacking effective treatments. In our current work, we characterize neosubstrate recognition by CRBN, revealing how auxiliary degron interactions define and expand target scope and selectivity, enabling the rational design of more selective protein degraders.

Degraders & Molecular Glues – Part 2

New Targets, Ligases, Assays for Induced Proximity and Degradation

3:50 A Highly Productive Platform for Discovery of Targeted Protein Degraders

Shigeru Furukubo, PhD, Vice President, Chemistry, FIMECS Inc.

Our proprietary platform, RaPPIDS, facilitates the rapid production of degrader molecules and effective evaluation of targeted protein degradation. The high productivity of this platform enables us to discover not only novel E3 ligase binders by taking phenotypic-first approach but also well-optimized degraders with suitable DMPK profile. In this talk, I will share some case studies from our ongoing research programs.

4:20 Close of Conference

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12:15 pm Enjoy Lunch on Your Own

COMBINING LEAD GENERATION APPROACHES

1:45 Welcome Remarks

1:50 Chairperson's Remarks

Dean G. Brown, PhD, Vice President & Head, Chemistry, Jnana Therapeutics

1:55 FEATURED PRESENTATION: Integrated Hit Discovery for the Next Generation of Drug Targets

Emma Rivers, PhD, Director, Medicinal Chemistry, AstraZeneca

The challenge to identify high-quality hit chemical matter for novel targets has fueled the development and adoption of numerous new screening approaches, whereby the contemporary hit-identification toolbox comprises a growing number of orthogonal and complementary technologies. Here, I will describe how we apply an integrated strategy for hit discovery to maximize our likelihood for success, with an emphasis on the application of affinity-based methods such as DEL screening.

2:25 RCSB Protein Data Bank: An Open-Access Research Resource that Benefits All Humanity

Stephen K Burley, MD, DPhil, Henry Rutgers Chair and University Professor, Chemistry & Chemical Biology, Rutgers University

More than 240,000 experimentally determined, atomic-level, three-dimensional structures of biomolecules housed in the Protein Data Bank (PDB) support basic and applied research and education across the sciences, impacting fundamental biology, biomedicine, biotechnology, and energy sciences. This talk will explore how open access to PDB data at RCSB.org facilitates small-molecule drug discovery/development in both academia and the biopharmaceutical industry, encompassing target validation, target druggability, fragment screening, and structure-guided drug discovery.

2:55 CPSA: A Novel Assay Technology for High-Throughput Assessment of Drug-Target Engagement

Martin Main, CSO, Medicines Discovery Catapult

3:10 Sponsored Presentation *(Opportunity Available)*

3:25 Refreshment Break in the Exhibit Hall with Poster Viewing

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5:15 Dinner Short Course Registration*

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Nisha Perez, PhD, VP Preclinical Development & Clinical Pharmacology, ROME Therapeutics

6:00 Dinner Short Courses*

*All Access Package or separate registration required. See Short Courses page for details.

8:30 Close of Day

THURSDAY, SEPTEMBER 25

7:30 am Registration Open and Morning Coffee

DNA-ENCODED LIBRARY APPLICATIONS

8:00 Chairperson's Remarks

Timothy L. Foley, PhD, Senior Principal Scientist & Lab Head, DNA Encoded Library Selection & Pharmacology, Pfizer Global R&D Groton Labs

8:05 Combining DEL and HTS to Expedite Hit ID: A De-Ubiquitinase Case Study

Lindsay Trammell, Principal Associate Scientist, In Vitro Pharmacology, Valo Health

DUBs play an important role in cellular physiology and protein regulation, making them desirable as potential therapeutic targets. DUBs are responsible for cleaving the bond between a ubiquitin and its selective protein. We uncovered potent and selective inhibitors by leveraging Valo's DEL capabilities alongside an HTS campaign. Both HTS and DEL campaigns identified similar motifs in the chemical structure of the top hits, and conclusions from both influenced molecule design.

8:35 Insights and Analysis from Leveraging 15 Years' Worth of DNA-Encoded Library Data

Lucas Mastromatteo, Investigator, Data Analyst, GSK

At GSK, we improve decision-making from DNA Encoded Library (DEL) selections by leveraging extensive internal datasets from past experiments involving numerous target proteins. In this talk, we will demonstrate that calibrating results with historical background binders and evaluating chemical series with known "frequent hitters" enhances our ability to discern chemical series that interact with target proteins. Additionally, we can assess the historical productivity of individual DELs.

9:05 DNA-Encoded Library Technology Case Study on Cleavable Linkers

Broderick Corless, PhD, Senior Scientist, DNA Encoded Libraries, Pfizer

DEL screening has become an established hit-identification strategy employed at Pfizer. Our hit confirmation toolbox includes an on-DNA confirmation workflow. We developed a cleavable linker platform that enables us to access off-DNA samples directly from the products of on-DNA resynthesis. This talk will describe how we utilize this Cleavable Linker Platform to deliver microgram quantities of DEL hits from on-DNA synthesized samples for further analysis.

9:35 Protein-Ligand Data Generation at-Scale to Support Computational Hit Discovery

Aled M. Edwards, PhD, Structural Genomics Consortium and Professor, Medical Biophysics, University of Toronto

Our objective is to generate protein-ligand-binding at scale. To accomplish this, we will screen human proteins with two direct binding assays—enantioselective affinity-selection mass spectrometry and DNA-encoded library screening. All the binding data (both positive and negative) will be placed into the public domain. I will speak about our technological approaches and some of the emerging data.

10:05 In-Person Breakouts

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11:30 The Discovery Strategy for a Difficult-to-Drug Target

Haixia Liu, PhD, Senior Principal Scientist, Medicinal Chemistry, Roche

Protein X is a key regulator in the immune system and is associated with multiple autoimmune and inflammatory diseases. Despite its intriguing biological role, the development of small-molecule inhibitors has been challenging due to the target's difficult-to-drug nature. By adopting an integrated screening approach, several hits were identified through both HTS and DELT screening. The lead-generation strategy will be presented.

12:00 pm PANEL DISCUSSION: Is the Screening Era Over? Reviewing Current Trends & Innovations

Moderator: Jeff A. Messer, Director, Analytics, Encoded Libraries Technology, GlaxoSmithKline

12:30 Sponsored Presentation *(Opportunity Available)*

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BIOPHYSICAL APPROACHES FOR LEAD GENERATION

2:15 Chairperson's Remarks

Ching-Hsuan Tsai, PhD, Executive Director, Structure Therapeutics

2:20 Covalent and Photoaffinity Library Screening and Hit Characterization to Accelerate Targeted Drug Discovery

Sherry Ke Li, PhD, Principal Scientist, Biochemical & Cellular Pharmacology, Genentech, Inc.

We present an optimized MS-based covalent screening platform designed to maximize throughput, streamline hit triaging, and enable mechanistic characterization. Platform capabilities have been expanded to include photoaffinity library screening of reversible hits and the development of competition assays with covalent probes to accelerate early discovery efforts. We will also discuss leveraging integrated screening data to facilitate the identification of tractable, selective hits as actionable starting points.

2:50 KNOMATIC Platform: Accelerating Drug Discovery for Novel ATPase Targets

Brian Sosa-Alvarado, PhD, Director, MOMA Therapeutics

MOMA Therapeutics was launched to understand ATPases, systematically target and define them as a target class. Our KNOMATIC platform successfully addresses these historically challenging targets through an integrated approach combining novel target-ID, structural prediction, covalent fragment screening and DEL technology. Within six months of target validation for a novel DDR ATPase, the platform delivered three chemical series with nanomolar biochemical potency, enabled structure-based design, and demonstrated cellular target engagement assays.

TARGETING MEMBRANE PROTEINS

3:20 Discovery of First-In-Class Selective Acid Sensing Small Molecule Ion Channel Inhibitors

Joseph AL Mancini, PhD, VP Research, Research, adMare Bioinnovations

Acid-sensing ion channels (ASICs) are sensory receptors that are therapeutic targets for opioid-free pain management. I describe the discovery of first- and best-in-class orally bioavailable ASIC1 inhibitors. We screened a small molecule library using a calcium-based high-throughput FLIPR screen. We used functional selectivity assays via electrophysiology (manual and automated patch-clamp) for lead optimization using proprietary stable mammalian cell lines expressing human ASIC subtypes.

3:50 Enabling High-Throughput Electron Cryo-Microscopy for Structure-Based Design

Miguel Zamora-Porras, PhD, Astex

Access to high resolution structural data on protein–ligand complexes is a prerequisite for structure-based drug design. For proteins refractory to X-ray crystallography, high-throughput structure determination by cryo-EM has the potential to be transformational for medicinal chemistry. This talk will describe a workflow, from protein production through to end-user accessible high resolution structural data, applied to a biologically important ion channel target in complex with a diverse range of ligands.

4:20 Close of Conference

Cambridge Healthtech Institute's Inaugural

Emerging Cancer Targets for Multispecifics, ADCs, and Biologics

Synergy & Discovery: Combining Validated and Identifying Promising Novel Targets

WEDNESDAY September 24 — THURSDAY September 25

WEDNESDAY, SEPTEMBER 24

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EMERGING IMMUNE MODULATORS

1:45 Welcome Remarks

1:50 Chairperson's Opening Remarks

Dori Thomas-Karyat, PhD, Founder & CEO, Synthis Therapeutics

1:55 Osmotic Assistance for Targeting Soluble and Cell-Surface Molecules for Complete Immunotherapy

Miroslaw Janowski, MD, Associate Professor, Diagnostic Radiology, University of Maryland Baltimore

The larger size of biological drugs may limit their ability to penetrate tissues. While cellular targets can lead to some preferential accumulation of antibodies in tumors, such mechanisms are unlikely to assist in scavenging soluble immune-inhibiting molecules. Intra-arterial pre-injection of osmotically active substances, such as a combination of 25% mannitol and 4% saline, dramatically improves antibody delivery to the target organs, such as the brain, tongue, and likely others.

2:25 PB203: Next-Generation Immunotherapy Targeting PD-L1/VEGF-A/PLGF to Transform the Pancreatic Cancer Microenvironment

David Yang, PhD, Director, Research, Panolos Biosciences

PB203 is a bi-modal, multispecific Fc fusion protein targeting PD-L1, VEGF-A, and PLGF simultaneously. In humanized pancreatic cancer mouse models, PB203 demonstrated synergistic anti-tumor efficacy with gemcitabine, reducing fibrosis and activating immune responses via PD-L1 inhibition. Its unique dual blockade (VEGF-A/PLGF) combined with immune activation provides a novel approach to comprehensively reshape the tumor microenvironment beyond current VEGF-A/PD(L)-1 inhibitors attracting global interest.

2:55 Technology Spotlights *(Sponsorship Opportunity Available)*

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Nisha Perez, PhD, VP Preclinical Development & Clinical Pharmacology, ROME Therapeutics

6:00 Dinner Short Courses*

*All Access Package or separate registration required. See Short Courses page for details.

8:30 Close of Day

THURSDAY, SEPTEMBER 25

7:30 am Registration Open and Morning Coffee

Emerging Cancer Targets for Multispecifics, ADCs, and Biologics

Synergy & Discovery: Combining Validated and Identifying Promising Novel Targets

TARGETING THE TME AND TAAs

8:00 Chairperson's Remarks

Anqi Zhang, PhD, Postdoctoral Associate, Binghamton University

8:05 Overcoming CXCR4 Antibody Discovery Challenges: High-Affinity Antagonists via Salipro Nano-Membrane Particles & Phage Display

Robin Loeving, PhD, CSO, Salipro Biotech AB

CXCR4 is a well-studied chemokine receptor found upregulated in several cancers, yet developing therapeutic antibodies against it has proven challenging. The best-in-class antibody, Ulocuplumab, was discontinued in clinical development. Using the Salipro DirectMX technology to isolate wildtype CXCR4 together with the Bio-Rad Pioneer antibody discovery platform, novel CXCR4 antibodies were made with higher affinity and improved antagonistic properties compared to Ulocuplumab.

8:35 FEATURED PRESENTATION: Illuminating the Disease Surfaceome: Exploiting Conformational Targets for First-in-Class Cancer Therapies

Dan Benjamin, PhD, CTO, Radical.Bio

Driven by the need for unique, tumor-specific targets, Radical Bio is pioneering the discovery of Surface Protein Conformers (SPCs)—disease-specific protein conformations that expose novel epitopes. By combining native-state structural proteomics with AI-enabled antibody engineering, we develop next-generation ADCs that maximize tumor specificity and eliminate off-disease effects. This approach broadens the druggable space, transforming the therapeutic paradigm by exploiting hidden protein conformations for superior efficacy.

9:05 Maximizing the Power of Bispecific Therapies for Treating Solid Tumors

Brian Avanzino, PhD, Director, Rondo Therapeutics

T cell engaging bispecific antibodies targeting CD3 have had notable success in treating hematologic tumors but have had limited efficacy in treating solid tumors. Employing safe and potency-optimized bispecific antibodies targeting immune co-stimulatory receptors may help overcome challenges related to solid tumors, such as the immuno-suppressive tumor microenvironment. Here, we describe our bispecific platforms and our lead program, RNDO-564, a CD28 x Nectin-4 bispecific antibody for treatment of metastatic bladder cancer.

9:35 Extra-Domain B of Fibronectin Is a Tumor-Specific Extracellular Matrix Target for the First-in-Concept ADC PYX-201

Marsha Crochiere, PhD, Head of Translational Medicine & Research, Pyxis Oncology

EDB+FN, an ECM protein, is highly expressed in tumors but not normal tissue. PYX-201, an ADC, targets this matrix. Tumor-specific proteases cleave the linker, releasing a payload that kills cancer cells. This induces bystander effects and neoantigen release, stimulating immunogenic cell death. EDB+FN's differential tumor expression makes it a novel cancer therapy target.

10:05 In-Person Breakouts

In-Person Breakouts are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator, or facilitators, who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Breakouts page on the conference website for a complete listing of topics and descriptions.

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11:30 GV20 STEAD Platform for Simultaneous Target Evaluation and Antibody Discovery

Xiaole Shirley Liu, PhD, CEO, GV20 Therapeutics

GV20 Therapeutics' proprietary platform STEAD harnesses AI to decode patients' natural B cell responses from large cohorts of tumor profiles, enabling simultaneous discovery of novel targets and therapeutic antibodies. GV20's discovery pipeline spans best-in-class and first-in-class monoclonal and bispecific antibodies, as well as antibody-drug conjugates (ADCs), reflecting their comprehensive approach to innovative cancer therapy.

12:00 pm Discovery and Engineering of Peptide-HLA (pHLA)-Targeting Therapeutics via Large Yeast Libraries

Garrett Rappazzo, PhD, Scientist, Platform Technologies, Adimab

Peptide-HLA (pHLA)-targeting therapeutics, including soluble TCRs and TCR-mimic antibodies, kill infected/cancerous cells. High affinity is crucial, but native TCRs lack it. We created fully-human libraries in yeast to rapidly discover and engineer high-affinity TCRs and TCR-mimic antibodies. This accelerates preclinical development of potent, specific pHLA-targeting therapeutics.

12:30 Sponsored Presentation *(Opportunity Available)*

1:00 Transition to Lunch

1:05 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:35 Dessert Break in the Exhibit Hall with Last Chance for Poster Viewing

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CYTOKINES AND GROWTH FACTORS

2:15 Chairperson's Remarks

Marsha Crochiere, PhD, Head of Translational Medicine & Research, Pyxis Oncology

2:20 Lack of Glycosylation Enhances Immune-Stimulating Antibody Conjugates by Preventing Target-Independent Uptake

Anqi Zhang, PhD, Postdoctoral Associate, Binghamton University

Immunostimulatory antibody conjugates (ISACs) typically depend on Fcγ receptor (FcγR) engagement to activate immune cells, but this can lead to off-target toxicity. We show that non-glycosylated, Fcγ-ablated ISACs enhance tumor immunogenicity and immunotherapy efficacy independently of FcγR binding. Instead, they trigger a bystander effect, mediating immune activation *in vitro* and *in vivo*. This approach offers a safer, targeted strategy for improving cancer treatment by minimizing systemic toxicity.

2:50 Enhanced Cancer Targeting: Advancements in Peptide Drug Conjugates

Keykavous Parang, PhD, Professor, Biomedical and Pharmaceutical Sciences, Chapman University

Cyclic peptides with alternating tryptophan and arginine act as tyrosine kinase inhibitors and molecular transporters. To improve anticancer efficacy and reduce toxicity, these peptides were conjugated to doxorubicin (Dox). The conjugates retained potency in wild-type cells, showed enhanced activity in resistant cancer cells, and reduced heart and kidney toxicity. Mechanistic studies suggest they bypass efflux, improve nuclear delivery, and offer a promising approach to overcome Dox resistance with minimal cardiotoxicity.

3:20 Targeting Interleukin-6 as a Treatment Approach for Peritoneal Carcinomatosis

Patrick Wagner, Director of Surgical Oncology, Allegheny Health Network

Peritoneal carcinomatosis (PC) is a devastating condition with limited treatment options. Interleukin-6 (IL-6) plays a critical role in PC progression by promoting inflammation and tumor growth. This research explores targeting IL-6 as a therapeutic strategy to disrupt these processes. Preclinical and clinical studies suggest that IL-6 inhibition may offer a promising approach to improve outcomes for patients with PC.

3:50 **SYN101, First-in-Class, Non-Cytotoxic ADC That Reverses Immune Suppression in Cancer Patients**

Dori Thomas-Karyat, PhD, Founder & CEO, Synthis Therapeutics

We have developed SYN101, a first-in-class, non-cytotoxic ADC that selectively blocks TGF-b mediated immune suppression and drives tumor clearance in multiple tumor models *in vivo*. Our platform is enabled by our linkable TGF-b inhibitor payload, to improve safety, efficacy, and therapeutic window. Unlike systemic TGF-b inhibitors which cause heart toxicity, SYN101 is safe and does not cause tissue toxicity.

4:20 **Close of Conference**

GPCR-Based Drug Discovery

Targeting G Protein-Coupled Receptors for New Therapeutic Options

WEDNESDAY, SEPTEMBER 24

PLENARY KEYNOTE PROGRAM

10:50 am Welcome Remarks from the Discovery on Target Team Lead

11:00 Plenary Keynote Chairperson's Remarks

11:05 PLENARY KEYNOTE: The Radicalization of Drug Discovery
Gregory L. Verdine, PhD, President & CEO, LifeMine Therapeutics
The field of drug discovery stands at a watershed moment of scientific, medical, and commercial opportunity. Realization of this opportunity will require radical innovations that fundamentally expand the functional capabilities of therapeutic interventions and management of the attendant risks. This talk will focus on the discovery, development, and deployment of radically new therapeutic modalities, inspired by nature, that thrust the field forward in non-obvious, impactful, and exciting new directions.

11:40 PLENARY KEYNOTE: GLP-1 Unveiled: Key Takeaways for Next-Generation Drug Discovery
Lotte Bjerre Knudsen, PhD, Chief Scientific Advisor, Head of IDEA (Innovation&Data Experimentation Advancement), Novo Nordisk AS
This talk explores the evolution of GLP-1 as a significant component in diabetes and obesity treatment, and its direct impact on multiple co-morbidities. It highlights the role of industry innovation and scientific persistence in overcoming challenges posed by its short half-life, ultimately leading to the successful development of GLP-1 therapies. Key lessons will inform future drug discovery strategies, emphasizing that today's drug discovery must be based on human data.

12:15 pm Enjoy Lunch on Your Own

SELECTIVE GPCR ACTIVATION

1:45 Welcome Remarks

1:50 Chairperson's Remarks
Yamina A. Berchiche, PhD, Founder, Dr. GPCR

1:55 FEATURED PRESENTATION: The Kinetics of Allostery: The Added Benefits of Allosteric Function
Terrence P. Kenakin, PhD, Professor, Pharmacology, University of North Carolina at Chapel Hill
Estimation of drug activity parameters are traditionally made in equilibrium systems. However, drugs are used *in vivo*, where concentration is never constant, and equilibrium conditions are never attained. Critical differences between non-equilibrium kinetics (fluxes) and traditional assays will be discussed. Thus, the kinetic nuances around alpha (effect on affinity) and beta (effect on efficacy) will be delineated that differentiate modulators beyond the data attained in equilibrium systems.

2:25 FEATURED PRESENTATION: Targeting a Cryptic Pocket in Cannabinoid Receptors Drives Peripheral and Functional Selectivity
Susruta Majumdar, PhD, Professor, Clinical Pharmacology, Washington University School of Medicine
Cannabinoids represent potential alternatives as pain relievers, but centrally-acting cannabinoids have issues like psychoactivity and tolerance which limit their clinical use. We designed novel peripherally-selective cannabinoids with reduced tolerance by targeting a cryptic pocket in CB1 receptors that houses a conserved aspartate residue which biases GPCR signaling away from arrestin. The designed agonist was analgesic while showing reduced cannabinoid tetrad effects, in addition to tolerance compared to canonical cannabinoids.

2:55 Sponsored Presentation *(Opportunity Available)*

3:25 Refreshment Break in the Exhibit Hall with Poster Viewing
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VENTURE CAPITALIST INSIGHTS

4:15 PLENARY PANEL DISCUSSION: Venture Capitalist Insights into Trends in Drug Discovery

Moderator: Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation
Topics to be discussed:
- Key drivers of innovation in drug discovery
- Overcoming hurdles in translating discoveries from the lab to the clinic
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Brendan Kelly, PhD, Principal, Lightstone Ventures
Devin Quinlan, PhD, Principal, Investment, MPM BioImpact Inc.
Blair Willette, PhD, Associate, KdT Ventures

5:15 Dinner Short Course Registration*

COLLABORATIVE CONVERSATION

5:15 IN-PERSON PLENARY DISCUSSION: Connecting the DOTs to Spark Change!
Join us for an hour of inspiring, informal discussions on how to forge connections and create impactful ecosystems that will help you think, act, and thrive. We have invited pharma, biotech, and academic leaders to share their stories and experiences and to discuss key learnings. There will be time for open discussion and networking.
This session will not be recorded for on-demand viewing. See details on our Plenary Sessions Page.
Moderators:
Saudat Fadeyi, PhD, MBA, Head, Business Development & Strategy, Samyang Biopharm USA, Inc.
Sean Ekins, PhD, Founder & CEO, Collaborations Pharmaceuticals
Shruthi Bharadwaj, PhD, Program Leader, MIT
Raquel Mura, DPharm, Founder, RGM Life Sciences Consulting; former VP & Head R&D, Sanofi
Nisha Perez, PhD, VP Preclinical Development & Clinical Pharmacology, ROME Therapeutics

6:00 Dinner Short Courses*
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8:30 Close of Day

GPCR-Based Drug Discovery

Targeting G Protein-Coupled Receptors for New Therapeutic Options

THURSDAY, SEPTEMBER 25

7:30 am Registration Open and Morning Coffee

GPCRs IN DISEASE

8:00 Chairperson's Remarks

Huixian Wu, PhD, Structural Biology Lab Head, Discovery Sciences, Medicine Design, Pfizer Worldwide Research & Development

8:05 Discovery of a Novel Allosteric Inverse Agonist Mechanism against Orphan Receptor GPR61

Joshua Lees, PhD, Principal Scientist, Cryo EM, Pfizer

GPR61 is an orphan GPCR linked to BMI phenotypes. Pfizer undertook a GPR61-targeted inverse agonist program to treat cachexia, and the team used extensive protein engineering, aided by AlphaFold2, to enable structures of active and inactive GPR61 for SBDD and rationalization of SAR. Co-elucidation of GPR61 with the inverse agonist series revealed a novel G protein-competitive inverse agonist mechanism, offering key functional insights and new molecular tools for studying GPR61.

8:35 Structural Basis for the Activation of Proteinase-Activated Receptors PAR1 and PAR2

Aaron McGrath, PhD, Senior Scientist, Structural Biology, Takeda, San Diego

Members of the proteinase-activated receptor (PAR) subfamily are G protein-coupled receptors that play critical roles in processes such as inflammation, wound healing, and cancer progression. Using structural snapshots, we reveal how tethered ligands activate PAR1 and PAR2, uncovering a conserved orthosteric binding mechanism. We also highlight the structure of PAR2 bound to GB88, showcasing how pathway-selective inhibition mimics tethered ligand interactions, advancing our understanding of PAR signaling and therapeutic targeting.

9:05 Orphan Receptor GPR52 as a CNS Target

John A. Allen, PhD, Associate Professor, Pharmacology & Toxicology, University of Texas Galveston

This presentation will describe our efforts to create novel agonists for the brain orphan receptor GPR52. GPR52 is primarily expressed in the human striatum and is a recently identified schizophrenia risk gene. We have synthesized and pharmacologically evaluated multiple agonist series, including novel G protein-biased agonists that have reduced receptor desensitization. An advanced GPR52 agonist lead shows robust activity in preclinical models relevant to schizophrenia and substance use disorders.

9:35 Conformational Dynamics of the μ-Opioid Receptor Revealed by Single-Molecule FRET

Jiawei Zhao, PhD, Post-doctoral Fellow, del Marmol Laboratory, Biological Chemistry and Molecular Pharmacology, Harvard University

The μ-opioid receptor (μOR) is the target of opioids that are critical analgesics for pain management. The molecular understanding of the μOR behavior in the presence of drugs will facilitate the development of better therapeutics. Using methods of single-molecule fluorescence resonance energy transfer (smFRET) and double electron-electron resonance (DEER), we show how ligand-specific conformational dynamics of the μOR translate into a broad range of intrinsic efficacies at the transducer level.

10:05 In-Person Breakouts

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BIOPHYSICAL TOOLS FOR GPCR-TARGETED DRUG DISCOVERY

11:30 Differential Role of Phosphorylation in Glucagon Receptor Family Signaling Revealed by Mass Spectrometry

Ian Lamb, PhD, Postdoctoral Research Fellow, Biophysics, Eli Lilly

12:00 pm Enabling Hit ID in GPCR Drug Discovery: Taking Down the Roadblocks with an Enhanced Toolbox

Alison Heick Varghese, Principal Scientist, Pfizer Inc.

GPCRs present unique challenges to drug discovery due to their low expression, complexity, and poor stability. Detergent extraction from their native environment is commonplace but can prohibit basic biochemical characterization and render false positives in downstream screening campaigns. To address this problem, we have implemented membrane mimics to generate detergent-free GPCRs to facilitate their characterization, enable Hit ID screening campaigns, and validation follow-up.

12:30 Sponsored Presentation *(Opportunity Available)*

1:00 Transition to Lunch

1:05 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:35 Dessert Break in the Exhibit Hall with Last Chance for Poster Viewing

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BIOPHYSICAL INNOVATIONS FOR TARGETING GPCRs

2:15 Chairperson's Remarks

Sujatha Gopalakrishnan, Director, Research Fellow, Head of HTS & Molecular Characterization, AbbVie

2:20 New Methodologies for *in vitro* Quantification of Drug Efficacy

Matthew T. Eddy, PhD, Assistant Professor, Chemistry, University of Florida, Gainesville

We present new NMR-based methodology for the characterization and quantification of GPCR drug efficacies and illustrate this method with the human A_{2A} adenosine receptor. The method is particularly valuable for compounds where precise information is needed, for example, in accurate characterization of inverse agonists and partial agonists. This new approach relates drug efficacy directly to receptor structural changes, rather than the detection of secondary metabolite production in traditional cell-based approaches.

2:50 Using CryoEM to Capture Multiple Activation States of an Orphan GPCR

Karen S. Conrad, PhD, Scientific Associate Director, Structural Biology, Takeda

GPCRs are intracellular receptors that mediate physiological functions through ligand binding. Numerous GPCRs remain classified as orphan GPCRs because their native ligands remain unidentified. GPCRs are attractive targets for numerous indications ranging from brain injury to obesity, but structural study has been hindered by their innate qualities. Here we present and compare novel structures of a class A orphan GPCR with bound ligand to inform mechanism and drug discovery.

3:20 Applying 19F-NMR to Elucidate the Structure of Intermediate GPCR-G Protein Complex

Libin Ye, PhD, Associate Professor, Molecular Biosciences, University of South Florida

Guided by 19F-qNMR, we resolved the first intermediate GPCR-G protein complex structure, and elucidated its function. This advance will facilitate structure-based drug development by screening drugs targeting individual conformations of GPCR and its complex with different signaling partners.

3:50 Measuring Small-Molecule Binding Kinetics to GPCRs via Plasmonic Nano-Oscillators

Shaopeng Wang, PhD, Research Professor, Bioelectronics & Biosensors Center, Arizona State University

This talk introduces a novel label-free, charge-sensitive method for multiplexed quantification of small-molecule binding kinetics to virion-displayed membrane proteins via wide-field plasmonic imaging of affinity barcoded nanocomposite oscillators. Virion display maintains native membrane protein environments. Affinity-resolved multi-state DNA barcoding efficiently addresses individual nano-oscillators and enables measurement of a library of G protein-coupled receptors on a single chip.

4:20 Close of Conference

Targeting Transcription Factors & Regulators

Innovative Chemistries, Assays, and Modalities for Increasing Druggability of Transcription Factors

WEDNESDAY, SEPTEMBER 24

PLENARY KEYNOTE PROGRAM

10:50 am Welcome Remarks from the Discovery on Target Team Lead

11:00 Plenary Keynote Chairperson's Remarks

11:05 PLENARY KEYNOTE: The Radicalization of Drug Discovery
Gregory L. Verdine, PhD, President & CEO, LifeMine Therapeutics
The field of drug discovery stands at a watershed moment of scientific, medical, and commercial opportunity. Realization of this opportunity will require radical innovations that fundamentally expand the functional capabilities of therapeutic interventions and management of the attendant risks. This talk will focus on the discovery, development, and deployment of radically new therapeutic modalities, inspired by nature, that thrust the field forward in non-obvious, impactful, and exciting new directions.

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12:15 pm Enjoy Lunch on Your Own

TARGETING CHROMATIN REMODELERS

1:45 Welcome Remarks

1:50 Chairperson's Remarks
Asad Taherbhoy, PhD, Director, Drug Discovery, Foghorn Therapeutics

1:55 FEATURED PRESENTATION: Biochemical and Functional Interplay between Cancer-Associated mSWI/SNF Chromatin Remodeling Complexes and Transcription Factors
Cigall Kadoch, PhD, Associate Professor, Pediatric Oncology, Dana-Farber Cancer Institute/Harvard Medical School; Scientific Founder, Foghorn Therapeutics
ATP-dependent chromatin remodeling complexes are multi-component molecular machines that govern genomic accessibility and gene expression and are among the most frequently implicated cellular entities in human cancer. This presentation highlights biochemical and structural advances that have enabled the mechanistic understanding of mSWI/SNF complex activities in normal and disease states, opening new opportunities for therapeutic intervention.

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3:25 Refreshment Break in the Exhibit Hall with Poster Viewing
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Shruthi Bharadwaj, PhD, Program Leader, MIT
Raquel Mura, DPharm, Founder, RGM Life Sciences Consulting; former VP & Head R&D, Sanofi
Nisha Perez, PhD, VP Preclinical Development & Clinical Pharmacology, ROME Therapeutics

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8:30 Close of Day

THURSDAY, SEPTEMBER 25

7:30 am Registration Open and Morning Coffee

Targeting Transcription Factors & Regulators

Innovative Chemistries, Assays, and Modalities for Increasing Druggability of Transcription Factors

DEGRADING TRANSCRIPTION FACTORS

8:00 Chairperson's Remarks

Charles Wartchow, PhD, Associate Director, Discovery Sciences, Novartis Institutes for BioMedical Research

8:05 FEATURED PRESENTATION: Attenuating Oncogenic Transcription with Small Molecules

Angela Koehler, PhD, Associate Professor, Biological Engineering, Massachusetts Institute of Technology

The lecture reviews recent advances in the lab involving successful targeting strategies, including discussion of compounds that modulate MYC-driven transcription via mechanisms involving the MAX partner protein or the transcriptional kinase CDK9. Additionally, new and unpublished work related to targeting fusion oncoproteins arising in pediatric cancers such as alveolar rhabdomysosarcoma will be discussed.

8:50 FEATURED PRESENTATION: Development of Orally Bioavailable MDM2 Degraders

Shaomeng Wang, PhD, Warner-Lambert/Parke-Davis Professor of Medicine, Pharmacology & Medicinal Chemistry; Co-Director, Molecular Therapeutics Program, University of Michigan

The human murine double minute 2 (MDM2) protein is a primary, endogenous cellular inhibitor of the tumor suppressor p53. MDM2 inhibitors have major limitations in the clinic, including insufficient efficacy and development of clinical resistance. In this presentation, I will discuss the development of highly potent and orally efficacious MDM2 PROTAC degraders for the treatment of human AML and other types of human cancers.

9:35 Targeting MYC and Oncogenic p53 through LZK Inhibition or Degradation to Treat Head and Neck Cancers

John Brognard, PhD, Senior Investigator, Laboratory of Cellular & Developmental Signaling, National Cancer Institute, National Institutes of Health

The worldwide frequency of head and neck squamous cell carcinoma (HNSCC) is approximately 800,000 new cases, with 430,000 deaths annually. We found that the kinase activity of LZK stabilized c-MYC and that LZK stabilized gain-of-function (GOF) p53 through a kinase-independent mechanism in this cancer. Our lead PROTAC promotes LZK degradation and suppresses expression of GOF p53 and c-MYC, leading to impaired viability in HNSCC and is a promising new therapy.

10:05 In-Person Breakouts

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ALLOSTERIC & COVALENT MODULATION

11:30 Small-Molecule Covalent Stabilization and Inhibition of TEAD•YAP1 Transcription Factor Activity in Cancer Cells

Samy O. Meroueh, PhD, Professor, Biochemistry; Member, Cancer Center Drug Discovery Program, University of Illinois Urbana-Champaign

Here we report acrylamide small molecules that form a covalent bond with a conserved cysteine at the TEAD palmitate pocket. Binding studies showed profound stabilization of TEADs by the small molecules, and co-crystal structures reveal that the compounds mimic the binding mode of palmitate. In mammalian cells, the compounds stabilize the TEAD• YAP1 interaction yet reduce TEAD and YAP1 protein levels and inhibit TEAD transcription factor activity.

12:00 pm First-in-Class TET2 Activators as a Novel Therapeutic Strategy for Cancer Treatment

Carles Galdeano, PhD, Co-Founder Oniria Therapeutics; Associate Professor, University of Barcelona

Following a computational and biophysical approach, we have discovered a first-in-class series of small molecules that allosterically activate TET2, a master epigenetic regulator enzyme that reprograms tumor cells by converting 5-methylcytosine (5-mC) to 5-hydroxymethylcytosine (5-hmC), ultimately leading to tumor cell death. Specifically, ONR-001 exhibits an optimal pharmacokinetic profile, high potency, and good tolerability in rodents. TET2 activation by ONR-001 resulted in strong antitumoral effects in melanoma and CRC models.

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STRUCTURAL & MECHANISTIC CHARACTERIZATION

2:15 Chairperson's Remarks

Sherry Niessen, PhD, Vice President, Proteomics, Belharra Therapeutics

2:20 Developing and Applying a Novel Chemoproteomics Platform for Transcription Factor Drug Discovery

Sherry Niessen, PhD, Vice President, Proteomics, Belharra Therapeutics

Belharra's platform discovers novel, functionally relevant binding pockets on elusive, high-value drug targets across the undrugged proteome and can reveal binding pockets, in any protein or protein complex, in any cell type. This talk will focus on the discovery of chemical probes and ligandable pockets across transcription factors.

2:50 Biophysical and Structural Characterization of the Molecular Glue-Mediated Interaction of Transcription Factors with Cereblon

Charles Wartchow, PhD, Associate Director, Discovery Sciences, Novartis Institutes for BioMedical Research

Transcription factors are known to bind to cereblon in the presence of molecular glues and some reports implicate interactions with multiple zinc fingers. We present biophysical and structural assessments of the minimal binding domains of IKZF2 and other transcription factors, revealing that multiple zinc fingers interact with cereblon:glue complexes. In these examples, the binding modes are distinct and may have implications for the design of selective degraders.

Targeting Transcription Factors & Regulators

Innovative Chemistries, Assays, and Modalities for Increasing Druggability of Transcription Factors

3:20 Structural Characterization of a TF-BAF Interaction

Yunji Davenport, PhD, Director, Drug Discovery, Foghorn Therapeutics

Dysregulation within the interaction between pioneer transcription factors and mSWI/SNF(BAF) has been increasingly implicated in oncogenesis. Here, we characterize the direct interaction between BAF and the TF PU.1 via biochemical studies to map the BAF-PU.1 binding site. We present the first high-resolution structure of a human TF–BAF complex as well as potential small molecule inhibitors of this PPI, opening a therapeutic avenue for targeting aberrant TF-BAF activity in cancer.

3:50 Targeting NONO to Modulate AR and ARv7 Signaling in Metastatic Castration-Resistant Prostate Cancer

Gaelle Mercenne, PhD, Head, Biology, Talus Bio

We used TF-Scan proteomics to identify covalent inhibitors of NONO, a key regulator of ARv7 in castration-resistant prostate cancer. Lead compounds reduced ARv7 activity, suppressed oncogenic transcription, and restored expression of repressed genes like B4GALT1. These findings validate NONO as a therapeutic target and demonstrate the power of TF-Scan to drug previously undruggable transcriptional regulators, offering a promising strategy for ARv7-driven, treatment-resistant prostate cancer.

4:20 Close of Conference

AI/ML-Enabled Drug Discovery - Part 2

Discovering and Validating New Targets, Pathways, and Drug Responses

WEDNESDAY, SEPTEMBER 24

PLENARY KEYNOTE PROGRAM

10:50 am Welcome Remarks from the Discovery on Target Team Lead

11:00 Plenary Keynote Chairperson's Remarks

11:05 PLENARY KEYNOTE: The Radicalization of Drug Discovery
Gregory L. Verdine, PhD, President & CEO, LifeMine Therapeutics
The field of drug discovery stands at a watershed moment of scientific, medical, and commercial opportunity. Realization of this opportunity will require radical innovations that fundamentally expand the functional capabilities of therapeutic interventions and management of the attendant risks. This talk will focus on the discovery, development, and deployment of radically new therapeutic modalities, inspired by nature, that thrust the field forward in non-obvious, impactful, and exciting new directions.

11:40 PLENARY KEYNOTE: GLP-1 Unveiled: Key Takeaways for Next-Generation Drug Discovery
Lotte Bjerre Knudsen, PhD, Chief Scientific Advisor, Head of IDEA (Innovation&Data Experimentation Advancement), Novo Nordisk AS
This talk explores the evolution of GLP-1 as a significant component in diabetes and obesity treatment, and its direct impact on multiple co-morbidities. It highlights the role of industry innovation and scientific persistence in overcoming challenges posed by its short half-life, ultimately leading to the successful development of GLP-1 therapies. Key lessons will inform future drug discovery strategies, emphasizing that today's drug discovery must be based on human data.

12:15 pm Enjoy Lunch on Your Own

ADOPTION & IMPACT OF AI/ML

1:45 Welcome Remarks

1:50 Chairperson's Remarks
Shruthi Bharadwaj, PhD, Program Leader, MIT Lincoln Laboratory

1:55 PANEL DISCUSSION: AI in Life Sciences & Healthcare: Balancing Innovation, Regulation, and Real-World Impact
Moderator: Shruthi Bharadwaj, PhD, Program Leader, MIT Lincoln Laboratory
As artificial intelligence continues to transform drug discovery, diagnostics, and healthcare delivery, collaboration between industry, academia, and government becomes increasingly vital. This panel brings together leaders from all three sectors to explore how to accelerate innovation while ensuring safety, equity, and effectiveness. Panelists will discuss the evolving regulatory landscape, ethical considerations, translational challenges, and the role of public-private partnerships in shaping the future of AI in life sciences and healthcare.
Panelists:
Sherri Cherry, MBA, Deputy CIO, Defense Health Agency
Nimita Limaye, PhD, Research Vice President, Life Sciences R&D Strategy and Technology, IDC
Raquel Mura, PharmD, Founder, RGM Life Sciences Consulting; Former Vice President & Head, R&D North America, Sanofi
William Streilein, PhD, Principal Staff, Biotechnology & Human Systems, Massachusetts Institute of Technology

2:55 Sponsored Presentation *(Opportunity Available)*

3:25 Refreshment Break in the Exhibit Hall with Poster Viewing

Recharge during our refreshment break! Visit booths, view posters, connect with peers, and turn in your Game Cards for a chance to win a raffle prize. Don't miss the opportunity to meet the Venture Capitalists who will be participating in the panel following the break. And Connect the DOT's with participants driving the Collaborations Discussion following the VC panel.

VENTURE CAPITALIST INSIGHTS

4:15 PLENARY PANEL DISCUSSION: Venture Capitalist Insights into Trends in Drug Discovery

Moderator: Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation
Topics to be discussed:
• Key drivers of innovation in drug discovery
• Overcoming hurdles in translating discoveries from the lab to the clinic
• Impact of AI/machine learning, emerging drug modalities, pursuit of challenging drug targets
• Navigating the current regulatory and funding environment
• Perspectives on upcoming challenges and opportunities in drug development
Panelists:
Olga Danilchanka, PhD, Partner, MRL Ventures Fund
Chris De Savi, PhD, CSO Partner, Curie Bio
Jamie Kasuboski, PhD, Partner, Luma Group
Brendan Kelly, PhD, Principal, Lightstone Ventures
Devin Quinlan, PhD, Principal, Investment, MPM BioImpact Inc.
Blair Willette, PhD, Associate, KdT Ventures

5:15 Dinner Short Course Registration*

COLLABORATIVE CONVERSATION

5:15 IN-PERSON PLENARY DISCUSSION: Connecting the DOTs to Spark Change!
Join us for an hour of inspiring, informal discussions on how to forge connections and create impactful ecosystems that will help you think, act, and thrive. We have invited pharma, biotech, and academic leaders to share their stories and experiences and to discuss key learnings. There will be time for open discussion and networking.
This session will not be recorded for on-demand viewing. See details on our Plenary Sessions Page.
Moderators:
Saudat Fadeyi, PhD, MBA, Head, Business Development & Strategy, Samyang Biopharm USA, Inc.
Sean Ekins, PhD, Founder & CEO, Collaborations Pharmaceuticals
Shruthi Bharadwaj, PhD, Program Leader, MIT
Raquel Mura, DPharm, Founder, RGM Life Sciences Consulting; former VP & Head R&D, Sanofi
Nisha Perez, PhD, VP Preclinical Development & Clinical Pharmacology, ROME Therapeutics

6:00 Dinner Short Courses*
*All Access Package or separate registration required. See Short Courses page for details.

8:30 Close of Day

AI/ML-Enabled Drug Discovery - Part 2

Discovering and Validating New Targets, Pathways, and Drug Responses

THURSDAY, SEPTEMBER 25

7:30 am Registration Open and Morning Coffee

AI/ML FOR BIOLOGICS DRUG DEVELOPMENT

8:00 Chairperson's Remarks

Surge Biswas, PhD, Founder & CEO, Nabla Bio, Inc.

8:05 Combining Generative VAE and Protein Language Models for Drug Screening

Victor Guallar, PhD, Professor, Barcelona Supercomputing Center and Nostrum Biodiscovery

Active learning cycles in drug discovery are boosting hit finding in terms of true positive rates and generating diversity by means of screening ultra large libraries or using generative modelling. We are exploring to further boost their performance by adding a learning step based on affinity predictions through Protein Language models, significantly speeding up the process and allowing to implement it in parallel to dozens of targets.

8:35 AceFF: Machine-Learning Forcefield for Simulating Drug Discovery

Gianni De Fabritiis, PhD, Professor, Computational Biochemistry & Biophysics Lab, Universitat Pompeu Fabra; Founder, Acellera

Machine-learning potentials offer a revolutionary, unifying framework for molecular simulations across scales, from quantum chemistry to coarse-grained models. Here, I explore their potential to dramatically improve accuracy and scalability in simulating complex molecular systems.

9:05 Role of Next-Generation Sequencing for Lead Generation and Lead Optimization in Antibody Discovery

Sonia Agrawal, PhD, Associate Principal Scientist, Biologics Engineering, AstraZeneca

Next-generation sequencing (NGS) accelerates lead generation and optimization in antibody discovery by enabling high-throughput profiling of immune repertoires. It identifies diverse candidate sequences, tracks clonal evolution, and informs affinity maturation. Advanced clustering and machine learning techniques refine downselection, preserving diversity while reducing redundancy. Integrating NGS with computational pipelines enhances the efficiency of hit-to-lead workflows, improving the selection of high-affinity, developable therapeutic antibodies.

9:35 Target Druggability Enabled by Machine Learning

Diane M. Joseph-McCarthy, PhD, Professor of the Practice, Biomedical Engineering, Boston University

Target evaluation can be advanced through a combination of physics-based and machin- learning approaches. The use of large language models for rapid literature review to identify potential drug targets for a given indication will be discussed. Computational hot-spot mapping using protein structures and AlphaFold models to assess binding site druggability will be described. Finally, the machine learning-enabled prediction of antibody-antigen binding for the assessment of antibody targets will be presented.

10:05 In-Person Breakouts

In-Person Breakouts are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator, or facilitators, who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Breakouts page on the conference website for a complete listing of topics and descriptions.

10:50 Coffee Break in the Exhibit Hall with Poster Viewing and Best of Show Awards Announced

Meet new collaborators, and network with clients, colleagues, and exhibitors. Make your vote count for the People's Choice Best of Show Exhibitor award and plan to stay and cheer the winner!

11:30 *De novo* Design of Epitope-Specific Antibodies against Soluble and Multipass Membrane Proteins with High Specificity, Developability, and Function

Surge Biswas, PhD, Founder & CEO, Nabla Bio, Inc.

We present JAM, a generative protein design system that enables fully computational design of antibodies with therapeutic-grade properties for the first time. JAM generates antibodies that achieve double-digit nanomolar affinities, strong early-stage developability profiles, and precise targeting of functional epitopes without experimental optimization. We demonstrate JAM's capabilities across multiple therapeutic contexts, including the first fully computationally designed antibodies to multipass membrane proteins—Claudin-4 and CXCR7.

12:30 pm Sponsored Presentation *(Opportunity Available)*

12:45 Sponsored Presentation *(Opportunity Available)*

1:00 Transition to Lunch

1:05 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:35 Dessert Break in the Exhibit Hall with Last Chance for Poster Viewing

Enjoy dessert and coffee during our final exhibit hall break. Did you connect with all the service providers and poster presenters? You never know what you missed! Stay till the end to maximize your time in the exhibit hall and to celebrate our Best of Show Poster award winner!

ADOPTION & INTEGRATION OF AI/ML TOOLS

2:15 Chairperson's Remarks

Yuan Wang, PhD, Head of Research Analytics, UCB Pharma

2:20 Automated Characterization of Naturalistic Behaviors in Mouse Models of Epilepsy

Joeri Nicolaes, PhD, Computer Scientist & DT Lead, AI Solutions & Multimodal AI, UCB Pharma

Epilepsy encompasses a set of complex, multifaceted disorders presenting a large panel of disease symptoms. We developed and validated a computational pipeline to measure behavioral phenotypes of an epilepsy animal model in an unbiased manner. We leveraged open-source ML algorithms to automatically process long-term video data and uncover behavioral fingerprints. We analyzed the usage of behavioral fingerprints across treatment groups and explored the associations between behavioral transitions and seizure events.

2:50 Integrating AI and Computational Strategies to Overcome Resistance in Cancer Therapeutics

Aleksandra Karolak, PhD, Assistant Professor, Department of Machine Learning, Moffitt Cancer Center & Research Institute

We integrate predictive and generative AI, computational chemistry, and computational combinatorial approaches to design and optimize small molecules targeting resistant Ras-driven tumors with complex resistance mechanisms. Through this multidisciplinary approach, we aim to accelerate the design of next-generation inhibitors and the molecular expansion of existing libraries, followed by rigorous computational optimization and experimental testing to enhance efficacy, reduce toxicity, and overcome therapeutic resistance.

AI/ML-Enabled Drug Discovery - Part 2

Discovering and Validating New Targets, Pathways, and Drug Responses

3:20 Accelerating Target Discovery & Validation Using a Scientific Knowledge Graph

John Piccone, Founder & CEO, URIKA bioworks

Few organizations apply a systematic approach to elucidating disease biology, discovering and characterizing novel targets. Systematically applying target discovery and validation strategies to a comprehensive corpus of scientific knowledge can yield novel targets and accelerate target discovery and validation.

3:50 Advancements in Drug Discovery: Protein Swarm-Based Analysis Technology

Shama Kajiji, PhD, CEO & Co-Founder, Emergent System Analytics, LLC

Drug discovery faces significant challenges in aligning chemical and biological function spaces due to system plasticity. To enhance precision of effect predictions, we have developed a data-driven, swarm-intelligence platform that integrates Pharmacological Cause-Effect Analysis, Information Theory, and Particle Swarm Optimization. It enhances AI-driven drug discovery, unlocks deeper insights into complex biochemical interactions, and uncovers innovative solutions. Applications in cardiovascular and infectious diseases will be discussed.

4:20 Close of Conference