Seventh Annual

Novel Strategies for Kinase Inhibitors

September 24 - 25, 2013

Session Topics:
- Beyond Cancer
- AllostERIC Kinase Inhibitors
- Overcoming Cancer Drug Resistance and Selective Kinase Inhibitors

PreMier SPonSors

Jeffrey Settleman, Ph.D., Senior Director, Discovery Oncology, Genentech
Donald L. Durden, M.D., Ph.D., Professor, Department of Pediatrics; Director Pediatric Oncology Research, University of California, San Diego and CEO, SignalRx Pharmaceuticals
Margrit Schwarz, Ph.D., MBA, MS Consulting, LLC; former Director, Research, Dyslipidemia and Atherosclerosis, Amgen

PLENaRY KEYNoTE SPEaKERS

Towards a Patient-Based Drug Discovery
Stuart L. Schreiber, Ph.D., Director, Chemical Biology, Founding Member, Broad Institute of Harvard and MIT; Howard Hughes Medical Institute Investigator; Morris Loeb Professor of Chemistry and Chemical Biology, Harvard University

Enteroendocrine Drug Discovery for Treatment of Metabolic Diseases
Paul L. Feldman, Ph.D., Senior Vice President, GlaxoSmithKline

Register Today!
About the Kinase and Cardio-Metabolic Drug Discovery Events:

Kinases are now well established as a validated drug target class in cancer. However this kinase meeting will cover progress on promising preclinical and early clinical phase kinase inhibitor drug candidates being developed for indications beyond cancer such as inflammation. Other presentations will address assay development for allosteric modulators of kinases and issues related to the role and potential of kinase inhibitors in combating cancers resistant to conventional therapies.

Our ‘Cardio-Metabolic Drug Targets’ meeting in the second half of our Discovery on Target event, is an expansion of last year’s ‘Diabetes Drug Targets’ meeting. It will cover progress on promising preclinical and early clinical drug candidates for areas such as cardiovascular disease, diabetes, obesity and dyslipidemia. Though traditionally treated as separate entities, researchers are now seeking compounds that target these conditions’ biological points of intersection because the conditions often appear together in individuals due to defects in underlying metabolic processes.

Attendees of both meetings will be able to network with colleagues attending concurrent tracks in the event during coffee/exhibit and poster session breaks. Audience-participatory panel and roundtable/breakout discussions are also a key feature of our meetings.

Plenary Keynote Speakers

Towards a Patient-Based Drug Discovery
Stuart L. Schreiber, Ph.D., Director, Chemical Biology, Founding Member, Broad Institute of Harvard and MIT; Howard Hughes Medical Institute Investigator; Morris Loeb Professor of Chemistry and Chemical Biology, Harvard University

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Paul L. Feldman, Ph.D., Senior Vice President, GlaxoSmithKline

Recommended Short Courses*

**MONDAY, SEPTEMBER 23 | 12:00 – 3:00 PM**
SC1: New Class of Kinase Inhibitors: Covalent Modifiers
Instructors: Alan Corin, Ph.D., Senior Director, Biochemistry and Molecular Pharmacology, Celgene Avilomics Research
Eric Schwartz, Ph.D., Senior Director, Chemistry, Celgene Avilomics Research

**MONDAY, SEPTEMBER 23 | 3:30 – 6:30 PM**
SC4: Allosteric Modulators of GPCRs
Instructors: Corey Hopkins, Ph.D., Research Assistant Professor, Pharmacology, Vanderbilt University
Debra Kendall, Ph.D., Distinguished Professor & Department Head, Pharmaceutical Sciences, University of Connecticut
Stephan Schann, Ph.D., Head, Research, Domain Therapeutics SA

SC5: Advancing Tools and Technologies for Fragment-Based Design
Instructors: Daniel A. Erlanson, Ph.D., Co-Founder, Carmot Therapeutics, Inc.
Edward R. Zartler, Ph.D., President & CSO, Quantum Tessera Consulting

**WEDNESDAY, SEPTEMBER 25 | 6:45 – 9:30 PM**
Dinner will be provided
SC9: Setting Up Effective Functional Screens Using 3D Cell Cultures
Instructors: Geoffrey A. Bartholomeusz, Ph.D., Assistant Professor and Director, siRNA Core Facility, Department of Experimental Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center
Lesley Matthews, Ph.D., Research Scientist, Biomolecular Screening and Profiling/Probe Development Group, National Center for Advancing Translational Sciences, NIH
Additional Instructors to be Announced
Conference-at-a-Glance

Mon., Sept. 23
12:00-3:00 PM SC1: New Class of Kinase Inhibitors: Covalent Modifiers
3:30-6:30 PM SC4: Allosteric Modulators of GPCRs
SC5: Advancing Tools and Technologies for Fragment-Based Design

Tues., Sept. 24
12:00-9:30 PM Targeting Epigenetic Readers
Targeting Histone Methyltransferases
GPCR-Based Drug Discovery
Functional Genomics Screening Strategies – Part 1
Novel Strategies for Kinase Inhibitors
Antibodies Against Membrane Protein Targets – Part 1

Wed.AM, Sept. 25
Targeting Epigenetic Readers
Targeting Histone Methyltransferases
GPCR-Based Drug Discovery
Functional Genomics Screening Strategies – Part 1
Novel Strategies for Kinase Inhibitors
Antibodies Against Membrane Protein Targets – Part 1

Wed. PM, Sept. 25
Next-Generation Histone Deacetylase Inhibitors
Targeting Histone Demethylases
GPCR-Targeted Therapeutics
Functional Genomics Screening Strategies – Part 2
Cardio-Metabolic Drug Targets
Antibodies Against Membrane Protein Targets – Part 2

Thurs., Sept. 26
Next-Generation Histone Deacetylase Inhibitors
Targeting Histone Demethylases
GPCR-Targeted Therapeutics
Functional Genomics Screening Strategies – Part 2
Cardio-Metabolic Drug Targets
Antibodies Against Membrane Protein Targets – Part 2

6:45 - 9:30 PM Conference Short Courses - Dinner will be provided*
SC9: Setting Up Effective Functional Screens Using 3D Cell Cultures

*Separate Registration Required.

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 a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by August 16, 2013. Please see registration page for details.

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- Receive $50 off your registration
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Assistant Professor, U. of Connecticut

MEDIA PARTNERS

DiscoveryOnTarget.com
EMD Millipore has generated a full length human recombinant ataxia telangiectasia mutated (ATM) protein, and developed an assay for detecting inhibitors of its kinase activity. Here, we discuss the ATM enzyme and an assay that monitors its phosphorylation of p53, one of the target substrates for ATM within the cell.

11:45 Deregulated Cdk5-Targeted Inhibitor for Neuro-inflammation
Harish C. Pant, Ph.D., Chief; Laboratory of Cytoskeleton Protein Regulation, National Institute of Neurological Disease and Stroke/NIH

12:15 pm Orally Available, CNS Penetrant MLK Inhibitors for Treatment of Neurodegenerative Diseases
Val Goodfellow, Ph.D., CEO, Califia Bio, Inc.
We have developed two series of orally available and CNS penetrant mixed lineage kinase inhibitors that have significant activity in animal models of HIV-Associated Neurocognitive Disease. We have developed two classes of compounds, one which inhibits several kinase pathways and one which is quite specific for MLK3. These compounds show contrasting patterns of anti-inflammatory activity and may be useful for treatment of multiple sclerosis, Parkinson’s disease and heart failure.

12:45 Lunch on Your Own

ALLOSTERIC KINASE INHIBITORS

2:15 Chairperson’s Opening Remarks
William J. Pitts, Ph.D., Group Leader, Medicinal Chemistry, Bristol Myers Squibb Co.

2:20 JNK Inhibitor Discovery at Celgene – Tansisertib and Beyond
Yoshitaka Satoh, Ph.D., Senior Principal Scientist, Medicinal Chemistry, Celgene

2:50 Highly Selective Allosteric FMS Kinase Inhibitors
Bryan Smith, Ph.D., Director, Biology, Deciphera Pharmaceuticals LLC
FMS kinase has been implicated as a major effector of cancer metastasis to bone. FMS signaling is also the primary mechanism whereby tumor-associated macrophages mediate invasiveness and metastasis of a variety of cancers. Deciphera has generated novel allosteric FMS kinase inhibitors, exhibiting extreme selectivity for FMS in a large panel of enzymatic and cellular assays. Lead compounds exhibit profound inhibition of FMS in vivo, and efficacy has been realized in a variety of cancer models. Deciphera’s FMS inhibitors also exhibit exceptional pharmaceutical, pharmacokinetic, and safety profiles.
3:20 The Design and Optimization of selective PKCθInhibitors for the Treatment of MS
Philip Collier Ph.D., Senior Research Scientist, Medicinal Chemistry, Vertex Pharmaceuticals
Protein kinase C theta (PKCθ) has a central role in T cell activation and survival. Studies in PKCθ-deficient mice have demonstrated that whilst anti-viral responses are PKCθ-independent, T cell responses associated with autoimmune diseases are PKCθ-dependent. Thus, selective inhibition of PKCθ is expected to block autoimmune T cell responses without compromising antiviral immunity. The presentation will describe the design and optimization of a novel class of potent and selective PKCθ inhibitors, which show exceptional potency in cells and efficacy in an animal model of MS.

3:50 Refreshment Break in the Exhibit Hall with Poster Viewing

4:30 P529, An Allosteric Modifier of the TORC1 and TORC2 Complexes of the PI3K/Akt/mTOR Pathway
David Sherris, Ph.D., President and CEO, Paloma Pharmaceuticals, Inc.
P529 is a first-in-class, allosteric dual dissociative TORC1/TORC2 inhibitor of the PI3K/Akt/mTOR pathway. It has been shown to have broad activity inhibiting the PI3K pathway through multiple sites showing activity in a variety of diseases including age-related macular degeneration and cancer, among other diseases. Discussion will be made on the mechanism of action and results from our Phase I ophthalmic studies.

5:00 Allosterically Targeting Polo-Like Kinase 1 for Selective Cancer Cell Killing
Kyung Lee, Ph.D., Senior Investigator, Section Head, Laboratory of Metabolism, National Cancer Institute
Polo-like kinase 1 (Plk1) is thought to be an attractive anti-cancer drug target selectively required for the viability of activated Ras or inactivated p53-containing cancer cells, but significantly less for the respective normal cells. The C-terminal non-catalytic domain called polo-box domain (PBD) is critically required for the function of Plk1. We present the multi-faceted approaches we’ve taken to generate a new class of allosteric Plk1 PBD-specific inhibitors.

5:30 Interactive Breakout Discussion Groups

6:30 Welcome Reception in the Exhibit Hall with Poster Viewing

7:30 Close of Day

WEDNESDAY, SEPTEMBER 25

7:30 am Registration and Morning Coffee

OVERCOMING CANCER DRUG RESISTANCE AND SELECTIVE KINASE INHIBITORS

8:00 Chairperson’s Opening Remarks
Jordan S. Fridman, Ph.D., Senior Director, Pharmacology, Incyte Corp.

8:05 FEATURED SPEAKER: The Role of Growth Factors in Resistance to Anti-Cancer Kinase Inhibitors
Jeffrey Settleman, Ph.D., Senior Director, Discovery Oncology, Genentech
Selective kinase inhibitors have been clinically validated as an important class of oncology drugs. While mutational activation of the targeted pathway largely defines the patient population most likely to benefit from treatment, there is considerable variability among patients with respect to the magnitude and duration of benefit, implicating intrinsic resistance mechanisms. We find evidence of a potentially broad role for stromally-produced growth factors in clinical response to kinase inhibitors.

8:35 FEATURED SPEAKER: Stromal Factors that are Targets for PI-3 Kinase Inhibitor Therapeutics in the Control of Metastasis
Donald L. Durden, M.D., Ph.D., Professor, Department of Pediatrics: Director Pediatric Oncology Research, University of California, San Diego and CEO, SignalRx Pharmaceuticals
Although it is well established that the macrophage M1 to M2 transition plays a role in tumor progression, the molecular basis for this process remains incompletely understood. We present data that demonstrate a role for the kinase, Syk and small GTPase, Rac2 in the control of macrophage M1 to M2 differentiation and the metastatic phenotype in vivo. Specifically, we identify a macrophage autonomous process by which the Syk-Rac2 signaling axis acts in concert with the p110δ isoform and the integrin α4β1 to control metastasis. The results define a novel molecular mechanism by which signals transmitted from the extracellular matrix via the α4β1 integrin and MCSF lead to the activation of Syk and Rac2 to regulate macrophage M2 differentiation. Finally, we demonstrate that Syk or PI-3K inhibitors block the M1 to M2 transition and metastasis and our findings suggest that α4β1-Syk-Rac2 signaling axis represents a novel therapeutic target for the disruption of tumor metastasis in vivo.

9:05 mTOR Inhibitor Torin-1 for Effective Targeting of Resistant Human Colon Cancer Stem Cells
Maria Giovanna Francipane, Ph.D., Post Doctoral Research Scholar, Pathology, University of Pittsburgh
Mammalian target of Rapamycin (mTOR) activation has been suggested as a crucial modulator of metastatic colorectal cancer biology. Among a panel of six inhibitors, we identified Torin-1 as a powerful drug candidate for metastatic colorectal cancer therapy because Torin-1 was the only inhibitor class that could hinder cell growth, motility, invasion, and survival of distinct colon CSC subpopulations which need to be eradicated for successful tumor growth suppression.

9:35 Panel Discussion: Kinase Inhibitor Discovery Challenges

10:05 Coffee Break in the Exhibit Hall with Poster Viewing
10:50 Development of c-MET Kinase Inhibitors for Cancer Therapy and Drug Resistance
Xiangdong Liu, Ph.D., Drug Discovery Group, Incyte Corporation
The c-MET receptor tyrosine kinase plays important roles in the formation, progression and dissemination of human cancer. Activated c-MET signaling also contributes to cancer drug resistance. I’ll describe the discovery and characterization of a novel small molecule c-MET kinase inhibitor INCB28060 and present data to support its therapeutic potential in human cancers.

11:20 Exploiting a Serendipitous Binding Opportunity in the Development of Highly Selective Rho Kinase Inhibitors
Erick Young, Ph.D., Distinguished Research Fellow, Medicinal Chemistry and Research Administration, Boehringer Ingelheim Pharma

11:50 Enjoy Lunch On Your Own

1:40 pm PLENARY KEYNOTE PRESENTATIONS:
Towards a Patient-Based Drug Discovery
Stuart L. Schreiber, Ph.D., Director, Chemical Biology and Founding Member, Broad Institute of Harvard and MIT; Howard Hughes Medical Institute Investigator; Morris Loeb Professor of Chemistry and Chemical Biology, Harvard University
Small-molecule drugs were originally discovered using compound based drug discovery: opportunistic discovery of a biologically active compound, often a natural product (e.g., penicillin) followed by a search for a disease that might be treated with the compound. This remains a common approach to modern drug discovery (e.g., rapamycin and analogs for use as antifungal agents; immune suppression agents; anticancer agents; possibly others in the future). The advent of recombinant DNA accelerated a second approach – target-based drug discovery – where the therapeutic target is selected and subjected to methods that yield candidate drugs (mechanism-based design; structure-based design; screening). But this approach has its shortcomings – 97% of drug candidates that enter into clinical investigation eventually fail, many due to unanticipated toxicity and many others due to a lack of efficacy despite successful modulation of the target. Selecting therapeutic targets based on information derived from surrogates of patients has proved challenging. Advances in human biology, including human genetics and physiology, and in small-molecule science, including chemistry and chemical biology, are now accelerating a third approach – patient-based drug discovery. This lecture will present examples that aim to use: 1) information from heritable or somatic human genetics in human disease; for example, in Crohn's Disease and cancer, 2) advances in diversity-oriented synthetic chemistry and chemical biology to accelerate the discovery of safe and effective small-molecule therapeutics, and 3) an understanding of the relationship of human genetic variation to drug efficacy.

Enteroendocrine Drug Discovery for Treatment of Metabolic Diseases
Paul L. Feldman, Ph.D., Senior Vice President, GlaxoSmithKline
The Enteroendocrine Discovery Performance Unit at GlaxoSmithKline is focused on discovering and developing medicines that mimic the efficacy of Roux-en-Y gastric bypass surgery to treat metabolic diseases. Our strategy emanates from the findings that there are significant metabolic benefits to obese and obese diabetic patients that undergo Roux-en-Y gastric bypass surgery. In general, these patients experience ~30% weight loss while >80% of obese diabetics who undergo this surgery have complete “remission” of diabetes. Our strategy is focused on three areas: 1) enteroendocrine science: discovery efforts focused on targets expressed on the luminal surface of the GI tract and peptides secreted from the GI tract or other peptides known to have metabolic effects, 2) combination therapies: by first intent progress combinations of assets that work synergistically to manifest significant, differentiated metabolic efficacy, and 3) assets that minimize safety risks: peptide based therapeutics and GI luminally restricted small molecules. In this presentation, I will describe the strategy our Unit has taken to discover novel combination peptide-based and GI luminally restricted small molecule therapeutics.

3:10-3:50 Refreshment Break in the Exhibit Hall with Poster Viewing
3:50 Close of Conference
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4:00 FEATURED SPEAKER: Atherosclerosis and Cardio-Metabolism Research Overview: Promising Targets
Margrit Schwarz, Ph.D., MBA, MS Consulting, LLC; former Director, Research, Dyslipidemia and Atherosclerosis, Amgen
Dyslipidemia as a risk factor for cardiovascular disease (CVD) is being effectively treated with statins, though residual CVD risk in most patients has prompted the development of new therapies. PCSK9 inhibitors have emerged as a new class of LDL-C lowering drugs with promising efficacy in clinical trials. Will they effectively address residual CVD risk, or is there a need for additional therapies that target atherosclerosis more directly? Drug discovery strategies beyond PCSK9 are being discussed.

4:30 Combining Next-Generation Phenytophory with Panomics – A New Standard for Biomarker and Drug Discovery
Szilard Voros, M.D., Founder & CEO, Global Genomics Group LLC
We present a comprehensive and integrated approach for biomarker and target discovery that addresses the
shortcomings of current approaches to investigate disease-relevant pathways. By combining next-generation phenotyping through the use of advanced imaging with panomics, we investigate and analyze comprehensive, multidimensional biological networks. Our current focus is atherosclerosis in cardiovascular diseases.

5:00 Novel Treatment for Dyslipidemia: Liver-Directed Thyroid Hormone Receptor-β Agonist
Rebecca Taub, M.D., Ph.D., CEO, Madrigal Pharmaceuticals

Insulin resistant type 2 diabetics have a high incidence of atherosclerosis, and 85-80% of diabetics die of cardiovascular (CV) disease such as heart attacks and strokes. Diabetes is associated with a dyslipidemia characterized by fatty liver, elevated triglycerides (TGs), atherogenic LDL particles and low HDL cholesterol. MGL-3196, a liver-targeted THR beta agonist has a unique profile including insulin sensitization, reduction of cholesterol, triglycerides and liver triglycerides in animal models and reduction in LDL cholesterol (30%), triglycerides (60%) in human studies. MGL-3196 may be highly effective treatment for diabetic dyslipidemia that can reduce CV risk in type-2 diabetics.

5:30 Modulating Glycerolipid Metabolism in Myeloid Cells for Cardiometabolic Benefit
Suneil K. Koliwad, M.D., Ph.D. Assistant Professor, Diabetes Center/Department of Medicine, University of California San Francisco (UCSF)

Intestinal DGAT enzymes have been targeted to lower body weight and reduce the progression of metabolic syndrome. Unfortunately, DGAT inhibition is associated thus far with several unwanted side effects. We have used these targets to uncover a link between glycerolipid flux within myeloid cell types (macrophages, dendritic cells, microglia) and inflammatory responsiveness. The work from our group has focused on DGAT enzymes as tools to modulate the flux of fatty acids within innate immune cells that are activated in metabolic tissues in the face of diet-induced obesity.

6:00 Targeting PCSK9 for Hypercholesterolemia and Atherosclerosis
Hong Liang, Ph.D., Associate Research Fellow, Rinat Research Unit, Pfizer

PCSK9 promotes LDLR degradation and increases serum LDLc. We show that a humanized mAb (J16) potently and selectively reduces LDLc in cynomolgus monkeys and humans. This effect is additive to that of the HMG-CoA reductase inhibitor. Furthermore, we show that a Mab engineered to have pH-sensitive binding to PCSK9 (J17) minimizes PCSK9-mediated degradation leading to extension in antibody half-life and prolonged duration of efficacy.

6:30 Close of Day

THURSDAY, SEPTEMBER 26

7:30 am Registration

NEW ATHERO/LIPID/CARDIO-METABOLIC DRUG TARGETS

8:00 Breakfast Interactive Breakout Discussion Groups

9:05 Chairperson’s Opening Remarks
Jerome J. Schentag, PharmD, Professor of Pharmaceutical Sciences, University at Buffalo

9:10 ApoE derived ABCA1 agonists for the Treatment of Cardiovascular Disease
Jan Johansson, M.D., Ph.D., CEO, Artery Therapeutics, Inc.

The ATP Binding Cassette A1 (ABCA1) transporter regulates the cholesterol content in macrophage cells, and thereby plaque stability and atherosclerosis. ABCA1 also has effects on Amyloidbeta degradation in glial cells and potential utility in Alzheimer’s disease. We optimized mono-peptides from apolipoprotein E for ABCA1 potency, selectivity and safety. The IND is in progress for the lead candidate Artprep2.

9:40 Blockade of Delta-Like Ligand 4 (Dll4)-Notch Signaling Reduces Macrophage Activation and Attenuates Atherosclerotic Vascular Diseases and Metabolic Disorders
Masanori Aikawa, Ph.D., Assistant Professor, Department of Medicine, Brigham and Women’s Hospital and Harvard Medical

Atherosclerosis and the metabolic syndrome closely associate with macrophage activation. Dll4-Notch signaling promotes macrophage activation and plays a central role in the shared mechanism for the pathogenesis of cardiometabolic disorders, serving as a novel therapeutic target. We previously linked Notch signaling triggered by Dll4 with macrophage activation in vitro. This talk presents results from in vivo experiments designed to determine whether Dll4-Notch signaling participates in the pathogenesis of major atherosclerotic vascular diseases and metabolic disorders.

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

10:55 AMPK as a Target in Lipid and Carbohydrate Metabolism
Ajit Srivastava, Ph.D., Adjunct Professor, Department of Pharmacology, Drexel University; Independent Consultant, Integrated Pharma Solutions, LLC

The adenosine monophosphate-activated protein kinase (AMPK) is a metabolic sensor of energy metabolism, involved in a wide range of biological activities that normalize lipid, glucose, and energy imbalances. AMPK, with multifaceted activities in various tissues, has emerged as an attractive drug target to manage lipid and glucose abnormalities and maintain energy homeostasis. This talk will focus on AMPK as a drug target in the treatment of cardiometabolic disease.

11:25 Macrophage ABC Transporters: Novel Targets to Promote Atherosclerotic Plaque Regression by Inducing Reverse Cholesterol Transport (RCT) Mechanism
Eralp “Ali” Bellibas, M.D., Senior Director, Head, Clinical Pharmacology, The Medicines Company

Cholesterol homeostasis in macrophages requires a balance between lipid influx and efflux. Storage of excessive amounts of lipids in vascular wall macrophages leading to foam cell formation is a key event in atheroma plaque formation. Cholesterol efflux from macrophages is the most important step of RCT by which HDL exerts its protective effect against atherosclerosis. ATP-binding cassette transporter A1 (ABCA1) mediates cholesterol efflux from macrophages to lipid-free apolipoprotein A-I, main protein component of HDL. Mutations in ABCA1 cause Tangier disease in patients that is characterized by HDL deficiency and increased susceptibility to atherosclerosis. Therefore new molecules targeting RCT mechanism are expected to provide major clinical benefits to patients with atherosclerotic cardiovascular disease.

11:55 Targeting Ubiquitin Signaling Mediated Disease Pathology of LDL Receptors
Udo Maier, Ph.D., Head of Target Discovery Research, DiscoveryOnTarget.com
Boehringer Ingelheim Pharma

Altering the proteasomal degradation of proteins by modulation of E3 ubiquitin ligases, and/or de-ubiquitinases offers a novel approach for therapeutic intervention for selected targets. IDOL is an E3 Ring Ligase, which marks selected target proteins for ubiquitin-mediated proteasomal degradation. The inhibition of IDOL offers a novel drug concept for the elevation of LDL-R and thereby induced improvement of lipid profile for patients suffering from dyslipidemia and/or atherosclerosis. In vitro and in vivo target characterization experiments confirmed the functional involvement of IDOL in ubiquitin-mediated regulation of LDL-R levels on hepatocytes.

12:25 pm Lunch on Your Own

CARDIO-METABOLIC MIMETICS

1:55 Chairperson’s Opening Remarks
Ajit Srivastava, Ph.D., Adjunct Professor, Dept Pharmacology, Drexel University and Independent Consultant, Integrated Pharma Solutions, LLC

2:00 Oral Mimetics of RYGB and GLP-1 in Metabolic Syndromes
Jerome J. Schentag, PharmD, Professor of Pharmaceutical Sciences, University at Buffalo

Patients who undergo RYGB surgery are more likely to resolve all of the major manifestations of metabolic syndrome, which ordinarily is treated with 3-6 separate medications. Accordingly, the actions of an oral mimetic on the L-cells of the ileum would activate the ileal brake and also resolve all of the major manifestations, since metabolic syndrome is driven by the imbalances between nutrition, hormones and exercise. We will demonstrate that Brake is highly active at the release of L-cell hormones, and when used for treatment of patients with metabolic syndrome, it shows as much as 80% of the actions of RYGB. We have also been developing oral formulations of insulin, GLP-1 and large monoclonal antibodies. Between Brake and the oral formulations, it is possible to envision a time when all-oral treatment of diabetes is feasible, with the benefit of great improvements in patient acceptance of therapy.

2:30 Expert Panel Discussion: Challenges in Diabetes and Atherosclerosis Drug Development
Moderator: Jerome J. Schentag, PharmD, Professor of Pharmaceutical Sciences, University at Buffalo
Panelists:
Paul L. Feldman, Ph.D., Senior Vice President, GlaxoSmithKline
Jan Johansson, M.D., Ph.D., CEO, Artery Therapeutics, Inc.
Ajit Srivastava, Ph.D., Independent Consultant, Integrated Pharma Solutions, LLC
Rebecca Taub, M.D., Ph.D., CEO, Madrigal Pharmaceuticals

3:00 TGR5 in Metabolic Diseases
Michael Orsini, Ph.D., Principal Scientist, Diabetes Drug Discovery, Bristol-Myers Squibb
TGR5 is a G protein-coupled receptor for bile acid. This talk will discuss the receptor’s role in metabolic diseases and our efforts in developing potential therapies targeting TGR5.

3:30 Ice Cream Refreshment Break in the Exhibit Hall with Poster Viewing

GPCRs IN METABOLIC DISEASES
4:00 Lactate Receptor, GPR81/HCA1, as a Novel Target for Metabolic Disorders
Changlu Liu, Ph.D., Scientific Director, Janssen Fellow, Head of Molecular Innovation, Neuroscience, Janssen Research & Development, LLC
We identified Lactate as the endogenous ligand for GPR81, predominantly expressed in adipocytes. The EC50 value of Lactate for GPR81 is 4 mM, which is in the middle of the physiological Lactate concentration range in the body (1-20 mM), allowing the receptor to best sense the change of lactate concentration under the physiological conditions. Administration of GPR81 agonists inhibits lipolysis, suggesting GPR81 is an attractive target for metabolic disorders.

4:30 Targeting GPR55 in Cancer and Diabetes
Marco Falasca, Ph.D., Professor of Molecular Pharmacology, Queen Mary University of London
Several studies, including work from our own laboratory, have revealed a role for the orphan G protein-coupled receptor 55 (GPR55) and its main agonist, lysophosphatidylinositol (LPI) in cancer and diabetes. Our work aims at validating GPR55, and GPR55-dependent signaling pathways, as a novel potential therapeutic target and LPI as a novel potential biomarker. Recent results have shown that GPR55 is expressed in the endocrine pancreas and revealed its function at stimulus-secretion coupling of insulin secretion, suggesting a role in glucose homeostasis.

5:00 Close of Conference
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HOTEL & TRAVEL INFORMATION

Conference Hotel:
Westin Boston Waterfront
425 Summer St.
Boston, MA 02210
T: 617-532-4600

Preferred Room Rate: $269 s/d
Discounted Room Rate Cut-off Date: August 26, 2013

Please visit our conference website or call the hotel directly to reserve your sleeping accommodations. You will need to identify yourself as a Cambridge Healthtech Institute conference attendee to receive the discounted room rate with the host hotel. Reservations made after the cut-off date or after the group room block has been filled (whichever comes first) will be accepted on a space and rate-availability basis. Rooms are limited, so please book early.

TOP REASONS TO STAY AT THE WESTIN BOSTON WATERFRONT HOTEL:
- Take advantage of the $269 group rate!
- No Commute, since meeting takes place at hotel
- Complimentary wireless internet access in guest rooms
- Lots of new restaurants within walking distances. Waterfront is the up and coming area of Boston!

Flight Discounts:
Special discount rentals have been established with American Airlines for this conference.
- Call American Airlines 1-800-433-1790 use Conference code 2593BF.
- Go to www.aa.com/group enter Conference code 2593BF in promotion discount box.
- Contact our designated travel agent, Rona Meizler, at 617-559-3735 or rona.meizler@protravel.com

Car Rental Discounts:
Special discount rentals have been established with Hertz for this conference.
- Call Hertz 1-800-654-3131 use our Hertz Convention Number (CV): 04KL0003
- Go to www.hertz.com use our Hertz Convention Number (CV): 04KL0003

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CONFERENCE DISCOUNTS

POSTER DISCOUNT ($50 Off) Poster abstracts are due by August 16, 2013. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact jring@healthtech.com. *CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

REGISTER 3 - 4th IS FREE: Individuals must register for the same conference or conference combination and submit completed registration form together for discount to apply.

ALUMNI DISCOUNT: Cambridge Healthtech Institute (CHI) appreciates your past participation at Discovery On Target. As a result of the great loyalty you have shown us, we are pleased to extend to you the exclusive opportunity to save an additional 20% off the registration rate.

GROUP DISCOUNTS: Discounts are available for multiple attendees from the same organization. For more information on group rates contact David Cunningham at +1-781-972-5472