Cambridge Healthtech Institute 2nd Annual

WORLD PHARMA WEEK

DRIVING INNOVATION IN DRUG R&D

Register by March 20
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Final Agenda

JUNE 2 - 4, 2020 • BOSTON, MA • HYNES CONVENTION CENTER

250+ **Presentations**

Two **Receptions** + **Networking** App

Three Outstanding **Plenary Sessions**

Drug Discovery **Focused Exhibit Hall**

Design Your Program **Across 12 Tracks**

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Featured Speakers

Barbara Sosnowski,
Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer

Hans Clevers, MD, PhD,
Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Stephen Fesik, PhD,
Chair in Cancer Research, Vanderbilt University School of Medicine

Dmitri Wiederschain, PhD,
Global Head, Immuno-Oncology Research Therapeutic Area, Sanofi

Anthony Philippakis,
Chief Data Officer, Broad Institute; Venture Partner, GV

Hua Gong, MD, PhD,
Senior Director, Head of Genomics Biomarker Development, Navigate Biopharma

PharmaWeek.com

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About the Event

Today pharma innovation is advancing at an incredible pace, with opportunities to address diseases once considered intractable using advanced technologies. At the Second Annual World Pharma Week, we will bring together technical leaders, scientists, executives, visionaries, and biotech entrepreneurs to drive measurable innovation in biopharma R&D. Disruptive technologies, novel therapeutic modalities and platforms, data-driven approaches, as well as strategies to cut costs and increase productivity of drug R&D will be featured at 12 themed conferences, 3 keynote sessions, and numerous networking events. Taking place in the Boston/Cambridge biopharma hub, a global powerhouse of drug discovery and development, provides unique networking opportunities both in the Exhibit Hall and in the session rooms with a core biopharma audience. World Pharma Week is enhanced by the legacy of two Cambridge Healthtech Institute's well established and extremely successful events, World Preclinical Congress and Biomarker World Congress, that joined forces under its umbrella. Also new this year, we made it easier for you to customize your 3-day agenda between the concurrent conference tracks by delineating the theme of each conference day within its tagline.

Concurrent Conferences

- Accelerating Target Discovery
- Expanding Chemical & Druggable Space
- New Small Molecule Drug Targets
- Emerging Indications & Modalities
- Immuno-Oncology Advances
- Disease Modeling
- Preclinical Strategies, Models & Tools in Oncology
- Advances in Drug Metabolism & Safety Testing
- Immuno-Oncology Biomarkers
- Clinical & Translational Biomarkers
- AI for Drug Discovery & Development
- Drug Discovery Technologies

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Concurrent Conference Programs

JUNE 2 - 4

Drug Discovery | Preclinical | Biomarkers & Translational Science | Technology & Innovation

Accelerating Target Discovery
CRISPR • Chemical Biology & Phenotypic Screening • Protein Degradation

Expanding Chemical & Druggable Space
Macrocyclics & Encoded Libraries • FBDD & Lead Generation • PROTACs

New Small Molecule Drug Targets
RNA • Immunology & Oncology • Microbiome

Emerging Indications & Modalities
CNS & Neuroscience • Gene & Cell Therapy • Fibrosis & Liver Diseases

Immuno-Oncology Advances
Translational IO • Immune Profiling • Small Molecule Targets

Disease Modeling
3D Cellular Modeling • iPSCs • Bioengineered Models

Immuno-Oncology Biomarkers
Patient Selection • Immune Profiling • Companion Diagnostics

Preclinical Strategies, Models & Tools in Oncology
Platforms and Combinations • Novel Therapeutics • Tumor Models

Advances in Drug Metabolism & Safety Testing
Lead Optimization • Predicting Toxicity • Safety for New Modalities

Clinical & Translational Biomarkers
Precision Medicine • Liquid Biopsy • Clinical Trials

AI for Drug Discovery & Development
AI in Drug Discovery • AI in Translational Research • AI in R&D Strategy

Drug Discovery Technologies
Enabling Disruptive Innovation

Takes place in the Exhibit Hall!

**The tagline of each conference delineates the theme of each day (separated by dots) so that if you want to customize your agenda, you can easily plan your 'track hopping' among our concurrent conference tracks.*

I really enjoyed the speaker lineup and the overall meeting. This was my first time at WPW and will not be my last.

- Associate Project Scientist, Department of Surgery, UC San Diego

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Sponsorship, Exhibit & Lead Gen Information

Comprehensive sponsorship packages allow you to achieve your objectives before, during, and long after the event. Signing on earlier will allow you to maximize exposure to hard-to-reach decision-makers.

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, breakfast, or lunch. Package includes exhibit space, on-site branding, and access to cooperative marketing efforts by CHI. For the luncheon option, lunches are delivered to attendees already seated in the main session room. Presentations do sell out early

One-on-One Meetings
Select your top prospects from the pre-conference registration list. CHI will reach out to your prospects and arrange the meeting for you. A minimum number of meetings will be guaranteed, depending on your marketing objectives and needs. A very limited number of these packages will be sold.

Reception / VIP Dinner
Sponsors will select their top prospects from the conference pre-registration list for an evening of networking at the hotel or local venue. CHI will extend invitations and deliver prospects, helping you to make the most out of this invaluable opportunity. Evening will be customized according to sponsor's objectives (i.e.: purely social, focus group, reception style, plated dinner with specific conversation focus).

Exhibit
Exhibitors will enjoy facilitated networking opportunities with qualified delegates, making it the perfect platform to launch a new product, collect feedback, and generate new leads. Exhibit space sells out quickly, so reserve yours today!

Additional Branding Opportunities include:

- Double-Sided Meter Boards
- Solutions Theatre Presentation
- Notepads
- Product Launch
- Lanyards
- Seating Area Sponsorship
- Foot Trails
- Aisle Sign (wherein booth located)
- Keynote Chair Drop
- Staircase Wrap
- Tote Bag Exclusive Sponsorship
- Tote Bag Insert
- Chair Drop in Session Roo
- Water Bottles
- Hotel Room Key Cards

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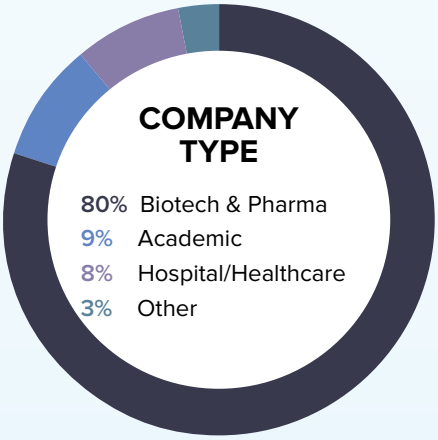
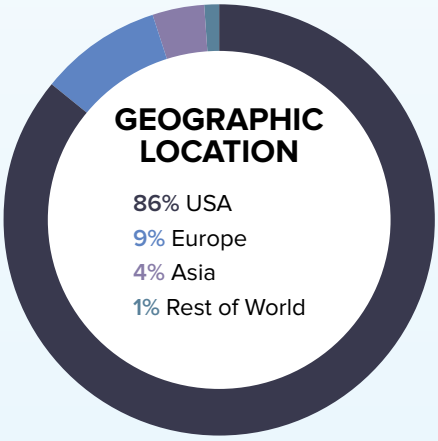
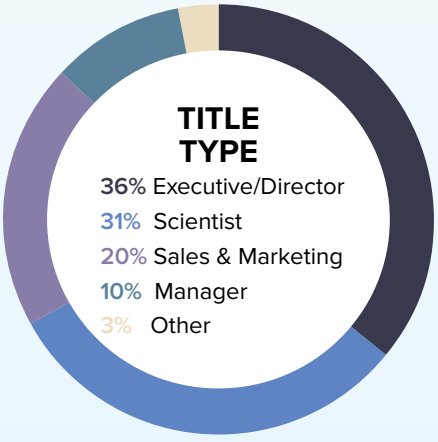
Manager, Business Development
781-247-6268
reymael@healthtech.com

Companies L-Z
Joseph Vacca, MS
Director, Business Development
781-972-5431
jvacca@healthtech.com

2019 Attendee Demographics







Plenary Keynote Sessions

JUNE 2 - 4

DAY 1

TUESDAY, JUNE 2, 4:25 - 6:05 PM

The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare. Scientific innovation and opportunity continues to stimulate a surge in entrepreneurship to deliver life-changing therapeutics to patients and their caregivers.

PANEL DISCUSSION: Driving Entrepreneurial Innovation To Accelerate Therapeutic Discoveries

Investing in drug discovery and development continues to face inherent challenges:

- Scale and duration of investment required;
- Risk and attrition in drug discovery and development;
- Uncertainties around pricing and reimbursement of new medicines;
- Leveraging the intersection of life-sciences and technology

Several novel business and investment models have been explored, and continue to be developed, to meet these challenges, and ensure medical breakthroughs continue to be delivered to address unmet patient needs. This session will explore such models, and potential new opportunities, with leaders within the biopharma, investment and related sectors who are at the cutting-edge of driving entrepreneurial innovation for therapeutic discovery.

Moderator: Nadeem Sarwar, PhD, Founder & President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai, Inc.

Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV

Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer

John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council




This panel discussion will focus on novel collaborative business models in biopharma. The purpose of this panel will be to highlight examples of innovative investment and collaborative models being used to accelerate the discovery and development of game-changing new medicines, and discuss future opportunities in this space.

DAY 2

WEDNESDAY, JUNE 3, 1:45 - 3:15 PM

Wednesday's Plenary Keynote session focuses on the innovative science spurring new drugs to market. Advances in stem cell and 3D cell culture for better disease modeling will be covered. Another topic focuses on new approaches that are 'breaking the barrier' to finding compounds against a common cancer-causing molecule, the mutant form of KRAS, that is notoriously difficult to inhibit because of its structure.

Keynote Introduction: *Speaker to be Announced, Reprints Desk, Inc*

Lgr5 Stem Cell-Based Organoids in Human Disease

Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Bio: Hans Clevers obtained his MD degree in 1984 and his PhD degree in 1985 from the University Utrecht, the Netherlands. His postdoctoral work (1986-1989) was done with Cox Terhorst at the Dana-Farber Cancer Institute of the Harvard University, Boston, USA. From 1991-2002 Hans Clevers was Professor in Immunology at the University Utrecht and, since 2002, Professor in Molecular Genetics. From 2002-2012 he was director of the Hubrecht Institute in Utrecht. From 2012-2015 he was President of the Royal Netherlands Academy of Arts and Sciences (KNAW). From June 2015-2019 he was director Research of the Princess Máxima Center for Pediatric Oncology.

Systematically Drugging Ras

Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry; Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine

Bio: Dr. Fesik's research focus is on cancer drug discovery using fragment-based approaches and structure-based drug design. Prior to joining Vanderbilt in May 2009, Dr. Fesik was the Divisional Vice President of Cancer Research at Abbott (2000-2009) where he built a pipeline of compounds that are showing promising anti-cancer activities in early stage clinical trials. While at Abbott, he also developed new NMR methods, determined the three-dimensional structures of several proteins and protein/ligand complexes, pioneered a method for drug discovery called SAR by NMR, and applied this method to identify and optimize ligands for binding to many protein drug targets. Dr. Fesik has published more than 285 papers, trained 59 postdoctoral fellows, has been a reviewer for several government funding agencies and has served as a member of the Editorial Boards of many peer-reviewed journals. He won numerous awards including the Life Time Achievement Award in Nuclear Magnetic Resonance from Eastern Analytical Society (2003), the NIH Director's Pioneer Award (2010), and the AACR Award for Outstanding Achievement in Chemistry in Cancer Research (2012).

Plenary Keynote Sessions

JUNE 2 - 4

DAY 3

THURSDAY, JUNE 4, 8:30 - 9:40 AM

Digital innovations, especially Artificial Intelligence (AI) is coming out as disruptive technology for the faster discovery and development of innovative therapies. There is a lot of excitement about the opportunities associated with the application of AI, but at the same time, a gap exists in understanding these possibilities and applying them to drug discovery and development processes. Thursday's plenary session aims to discuss how AI and digitization can supercharge the pharma R&D and also delve into the practical considerations and challenges in its adoption and implementation.

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility

Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics

Over the last few years, there has been tremendous interest in the application of artificial intelligence and machine learning in drug discovery. Ultimately, the success of any predictive model comes down to three factors: data, representation, and algorithms. This presentation will provide an overview of these factors and how they are critical to the successful implementation and deployment of AI methods.

Bio: Pat Walters heads the Computation & Informatics group at Relay Therapeutics in Cambridge, MA. His group focuses on novel applications of computational methods that integrate computer simulations and experimental data to provide insights that drive drug discovery programs. Pat is co-author of the book "Deep Learning for the Life Sciences", published by O'Reilly and Associates. His work in AI began with expert systems in the late 1980s, moved to machine learning in the 1990s, and has continued through 25 years in the pharmaceutical industry. Prior to joining Relay, Pat spent more than 20 years at Vertex Pharmaceuticals where he was Global Head of Modeling & Informatics.

women in PHARMA

Join the conversation. Be inspired.

The World Pharma Week team is proud to recognize the importance of Women in Pharma. We are delighted to announce a NEW event at World Pharma Week 2020 to honor women in pharma and STEM programs.

THURSDAY, JUNE 4, 12:00 - 1:00 PM

On Thursday, June 4 from 12:00 – 1:00 pm join your peers for a Women in Pharma Luncheon Panel Discussion. This session will create a forum to share thought-provoking questions, inspiring stories, practical advice, and networking opportunities with influencers in the field.

INNOVATION STATION

WEDNESDAY, JUNE 3, 5:45 - 6:45

Life science researchers in Massachusetts, and especially the Boston/ Cambridge areas, are world renown for their ability to revolutionize drug discovery and development. Come and visit the Innovation Station, now a part of World Pharma Week on Wednesday, June 3 from 5:45 – 6:45 pm to chat with local venture capitalists, accelerators, entrepreneurs, start-ups and small companies to see what new ideas are brewing in this thriving ecosystem.

Short Courses*

JUNE 2, 8:00-10:45 AM

SC1: *In vitro* and *in vivo* Modeling for Cancer Research

This short course will describe the use of cutting-edge models to study human tumor biology, including both *in vivo* and *in vitro* approaches to advance our understanding of interactions between human immune systems and the tumor microenvironment. The use of humanized mice to study tumor biology will be discussed, including a description of the unique models available currently, highlighting the strengths and limitations of the models and the specific application of humanized mice in the field of cancer immunotherapy. The development and use of 3D models and patient-derived organoids will also be discussed, including a description of the technologies needed to establish these models and their application to study tumor physiology, growth and specific therapies. Key concepts that will be emphasized in the course include the development of optimal strategies and study designs to effectively interrogate questions focused on immuno-oncology.

Instructors:

Michael Brehm, PhD, Associate Professor, Diabetes Center of Excellence, Program in Molecular Medicine, University of Massachusetts Medical School

Aaron Goldman, PhD, Faculty and Principal Investigator, Goldman Laboratory Drug Resistance Group, Harvard Medical School

Mithun Khattar, PhD, Scientist II, Immuno-Oncology Lead, Takeda Oncology

SC2: Immunology Basics: Focusing on Autoimmunity and Cancer

This short course provides an introduction to immunology and immuno-oncology for discovery pharmacologists, biologists and chemists working in the biopharmaceutical industry. It will review how the immune system is organized and gives rise to both normal and pathogenic immune responses. Topics will include pathogen recognition by innate immune cells, antigen generation and presentation to lymphocytes, effector mechanisms of T cells and therapeutic modulation of the immune responses to control inflammation or promote anti-tumor immunity (immuno-oncology).

Instructors:

Thomas Sundberg, PhD, Senior Group Leader, Center for Development of Therapeutics, Broad Institute of MIT and Harvard

SC3: Fit-for-Purpose Biomarker Assay Development – Performance Characterization and Validation to "Context of Use"

This course will provide recommendations on the "fit-for-purpose" best practices in the development and validation of biomarker assays for exploratory or advanced biomarker applications. Strategies for different applications at various phases of biomarker development will be described. Key elements in the method of development and validation will be illustrated with examples, including reference to standard material, sample stability and collection integrity, validation and QC samples, validity of reference standards, calibration curve fitting methods, method optimization and feasibility studies. Special challenges in protein biomarker assays will be discussed, including strategies for moving from biomarker panels in the exploratory phase to the few markers chosen to support clinical trials, cross-validation of biomarker assays, etc.

Instructors:

John L. Allinson, FIBMS, Vice President, Biomarker Services, Immunologix Labs

Viswanath Devanarayan, PhD, Global Health of Statistics & Data Sciences, Charles River Laboratories

SC4: Optimizing Drug Metabolism, Drug Clearance and Drug-Drug Interactions

This short course will focus on concepts that will help you understand how drug clearance and drug-drug interactions (DDI) can impact decisions in drug discovery and development. Topics will include basic drug metabolism, CYP regulation, the role of bioactivation and how they all affect lead optimization. Common assays and methodologies for predicting clearance and drug-drug interactions will be discussed. Those scientists involved in medicinal chemistry, pharmacology and drug metabolism will benefit from this overview.

Instructors:

Zhengyin Yan, PhD, Principal Scientist, Department of Drug Metabolism and Pharmacokinetics, Genentech, Inc.

Donglu Zhang, PhD, Principal Scientist, Department of Drug Metabolism and Pharmacokinetics, Genentech, Inc.

SC5: Chemoproteomics Enabling Drug Discovery

This course explores the use of chemical biology approaches, particularly chemoproteomics, as an avenue for generating new targets and leads for drug discovery. Design, synthesis and applications of activity-based probes, reactivity-based probes, photoaffinity probes and utility of bioorthogonal chemistry in chemoproteomics will be discussed in detail. Case studies highlighting applications of chemoproteomics for target and off-target identification, target engagement and/or selectivity profiling in cells will be reviewed.

Instructors:

Doug Johnson, PhD, Senior Director, Chemical Biology & Proteomics, Biogen

Jaimeen Majmudar, PhD, Principal Scientist, Chemical Biology, Pfizer Inc.

Christopher am Ende, Senior Principal Scientist, Pfizer Inc.

SC6: An ML/AI Tutorial: From Basics to Advanced

This tutorial will simplify key AI concepts to help you connect the dots when you need to understand an AI project. The course will also help you appreciate the hype and hope areas of AI, which should further enable you to make the right strategic decisions for drug development at your organization.

Instructor:

Bino John, PhD, Associate Director, Data Science, Clinical Pharmacology & Safety Sciences, Data Science and AI, AstraZeneca

SC7: Intro to OOAC and Bioprinting for Disease Modeling

This is an introductory course that will review organs-on-a-chip and bioprinting and their applications for disease modeling. The speakers will describe the technique, how people in drug discovery and development are applying it, address common challenges, and more.

Instructor:

Jianbo Zhang, PhD, Linda Griffith Lab, Massachusetts Institute of Technology

**Separate registration required.*

Accelerating Target Discovery

CRISPR • Chemical Biology • Phenotypic Screening • Protein Degradation

Recommended Short Course*

SC5: Chemoproteomics Enabling Drug Discovery

Separate registration required; see page 8 for details.

TUESDAY, JUNE 2

ADVANCED GENOMICS

Day 1 of the Accelerating Target Discovery conference will focus on the use of existing and emerging functional genomics tools, in particular CRISPR-based screens, for generating novel drug targets. The use of such genomics-based tools and screens for validating existing targets or identifying off-target effects will also be discussed.

10:00 am Main Conference Registration Open

EXPLORING GENETICS-BASED TARGET DISCOVERY

11:15 Chairperson's Remarks

Jason Sheltzer, PhD, Principal Investigator, Cold Spring Harbor Laboratory

11:25 FEATURED PRESENTATION: CRISPR Screening for Target and Off-Target Identification

Jason Sheltzer, PhD, Principal Investigator, Cold Spring Harbor Laboratory

We have recently discovered that many anticancer drugs function through off-target interactions. By deploying a variety of spontaneous and directed mutagenesis approaches, we can identify resistance-granting mutations, and thereby uncover their true targets. Using these techniques, we have recently discovered the first potent and specific inhibitor of the cyclin-dependent kinase, CDK11.

11:55 CASE STUDIES: Using Targeted and Genome-Wide CRISPR Screens for Drug Target and Pathway Analysis

Michael Bassik, PhD, Assistant Professor, Department of Genetics, Stanford University

Studies highlighting the use of both genome-wide, as well as targeted CRISPR screens, for identifying novel potential therapeutic targets in cancer and neurodegenerative diseases will be presented.

12:25 pm Multiscale Network Biology Approach to Identify Novel Targets of Parkinson's Disease

Bin Zhang, PhD, Professor, Department of Genetics & Genomic Sciences; Director, Mount Sinai Center for Transformative Disease Modeling, Icahn Institute for Data Science and Genomic Technology, Icahn School of Medicine at Mount Sinai

Molecular mechanisms underlying idiopathic PD, which account for 80% of the PD cases, remain elusive. We performed multiscale gene network analysis of a large gene expression dataset in the *substantia nigra* from 83 PD cases and 70 controls and systematically identified and prioritized co-expressed gene modules and key regulators in PD. This study lays down a foundation for developing a comprehensive signaling map and novel therapeutics for PD.

12:55 Transition to Lunch

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:30 Session Break

CRISPR-BASED TARGET SCREENING

2:00 Chairperson's Remarks

John Doench, PhD, Director R&D, Genetic Perturbation Platform, Broad Institute of Harvard and MIT

2:05 Deeper, Finer, and Wider with CRISPR Screens for Gene Function

John Doench, PhD, Director R&D, Genetic Perturbation Platform, Broad Institute of Harvard and MIT

Genome-wide CRISPR screens have revitalized functional genomics. Large-scale data sets enable rapid hypothesis generation, and focused screening efforts can provide detailed mechanistic insights into the function of any gene of interest. Here I will discuss how CRISPR screens are being employed in gene function discovery projects, with an emphasis on the latest technological advances.

2:35 *In vivo* T Cell CRISPR Screen for Immunotherapy Target Discovery

Sidi Chen, PhD, Assistant Professor, Department of Genetics and Systems Biology Institute, Yale University; Member, Yale Cancer Center and the Yale Stem Cell Center

In vivo CRISPR screen is a powerful means for discovering therapeutic targets in physiologically relevant settings. Here we describe recent advancements in *in vivo* T cell CRISPR screen for immunotherapy target discovery and characterization of example targets.

3:05 Use of *in vivo* Screening in Target Discovery

Danilo Maddalo, PhD, Lab Head, ONC Pharmacology, Novartis Institutes for BioMedical Research, Novartis Pharma AG

Identification of novel-cell and non-cell autonomous targets has proven challenging as tumor cells display crucial differences in a 2D culture as opposite to an *in vivo*, 3D setting. To overcome such limitation, the ability to perform *in vivo* screening is key. I will give a brief overview of the current approaches to perform target identification and validation in *in vivo* models, their caveats, and the future perspectives.

3:35 Functional CRISPR Screening and Cell Barcoding to Identify Genes Driving Biological Responses and Disease Progression

Sponsored by CELLECTA Discovery is *Yours.*

Paul Diehl, PhD, COO, Cellecta

- Pooled lentiviral libraries of CRISPR sgRNA have proven to be highly effective in identifying genes and other genetic elements driving biological responses
- Libraries containing unique barcode sequences enable cell-specific labeling of individual cells in a target population to identify sub-populations that express specific features or phenotypes
- Barcoded CRISPR guide libraries with single-cell expression profiling enable parallel analysis of differences in gene activation across and within cell populations as a result of perturbation

4:05 Networking Refreshment Break and Transition to Keynote

PLENARY KEYNOTE SESSION
4:25 - 6:05

Driving Entrepreneurial Innovation to Accelerate Therapeutic Discoveries

The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare.

Moderator: Nadeem Sarwar, President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai Inc.

Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV

Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer

John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council

See Plenary Keynotes Page for More Information.

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

7:10 Close of Day

WEDNESDAY, JUNE 3

CHEMICAL BIOLOGY & PHENOTYPIC SCREENING

Day 2 of the Accelerating Target Discovery conference will discuss how phenotypic screening and chemical biology are being used to find and validate drug targets for diverse therapeutic indications. The talks will highlight the applications of chemical probes and proteomics-driven assays for inhibiting or activating potential drug targets to investigate their impact on cellular pathways, as well as the use of emerging single-cell technologies.

7:30 am Registration Open and Morning Coffee

PROTEOMICS-BASED TARGET DISCOVERY

8:10 Chairperson's Remarks

Doug Johnson, PhD, Senior Director, Chemical Biology & Proteomics, Biogen

8:15 Application of Chemical Biology Probes and Bioorthogonal Chemistry in Drug Discovery

Doug Johnson, PhD, Senior Director, Chemical Biology & Proteomics, Biogen

This talk will describe examples of how chemical biology probes and bioorthogonal chemistry were used for target identification and engagement, selectivity profiling (off-targets), and mechanism of action studies in drug discovery. Several different types of chemical biology probes were utilized including enzyme class-specific, activity-based probes, cysteine-specific reactivity-based probes, as well as target-specific clickable covalent inhibitor and photoaffinity probes. These probes proved to be invaluable for target discovery.

8:45 Design of Photoaffinity and Electrophilic Probes for Target Identification and Validation

Christopher am Ende, PhD, Senior Principal Scientist, Pfizer Inc.

Photoreactive and electrophilic probes are valuable tools in chemical biology to identify small-molecule/protein interactions. This presentation will compare and evaluate different photoreactive groups and electrophilic compounds in the context of drug discovery programs, with emphasis on target deconvolution, off-target identification, and activity-based protein profiling. Additional focus on the advancement of new sulfur (VI) fluoride probes, the development of a chemical biology toolbox, and synthetic chemistry advancements will also be discussed.

9:15 FEATURED PRESENTATION: Small-Molecule Phenotypic Screening: Biological Tools, Novel Targets or Leads?

Sujatha Gopalakrishnan, PhD, Head, Molecular Screening and Characterization, AbbVie

Phenotypic screens present a unique opportunity to uncover novel biology and discover druggable targets. At AbbVie, a combination of phenotypic and target-based screening strategies is in place to augment our early discovery pipeline. I will highlight recent phenotypic screens conducted using disease-relevant cellular models to identify and validate novel targets and mechanisms of action. Using an integrated approach of cell-based and target-based screening, we successfully progressed these targets to the next step in drug discovery.

9:45 Sponsored Presentation *(Opportunity Available)*

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 Uncovering Targets with Potential Cardiotoxicity

Eric Miele, PhD, Team Leader, Proteomics - Chemical Biology, AstraZeneca Pharmaceuticals

Janus Kinase 1 (JAK1) plays an important role in mediating signaling of cytokine family members resulting in downstream activation of STAT3 and STAT1, which have been shown to be oncogenic. A lead

JAK1 inhibitor resulted in cardiotoxicity during a 28-day rat study. Using a combination of three label-free techniques, CETSA-MS, KiNativ and Digiwest, showed a convergence towards MAPK proteins. A putative mechanistic pathway has been identified and tested in cardiomyocytes and will be discussed.

11:30 Large-Scale Proteomics Approaches to Enable Degrader Development for Challenging Targets in Cancer

Katherine Donovan, PhD, Scientist, Laboratory of Dr. Eric Fischer, Cancer Biology, Dana-Farber Cancer Institute/Harvard Medical School

Small molecules that induce protein degradation through ligase-mediated ubiquitination have shown considerable promise as a new pharmacological modality. We and others have demonstrated that efficacious degradation of kinases and other targets can be achieved *in vitro* and *in vivo*, however, many targets remain recalcitrant to degradation. In this presentation, I will discuss the use of large-scale chemical proteomics approaches to accelerate the development of degraders as novel chemical probes for kinases and other disease targets.

Sponsored by

PELAGO BIOSCIENCE

12:00 pm Presentation to be Announced

12:15 Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Session Break

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease

Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras

Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine

See Plenary Keynotes Page for More Information.

3:15 Refreshment Break in the Exhibit Hall with Poster Viewing

SINGLE-CELL TECHNOLOGIES FOR TARGET DISCOVERY

4:00 Chairperson's Remarks

Neville Sanjana, PhD, Assistant Professor, Departments of Neuroscience and Physiology, New York University; Faculty, New York Genome Center

4:05 Pooled CRISPR Screens with Single-Cell Chromatin Accessibility Profiling

Neville Sanjana, PhD, Assistant Professor, Departments of Neuroscience and Physiology, New York University; Faculty, New York Genome Center

Forward genetic screens using CRISPR-associated nucleases are a powerful tool to pinpoint genes involved in disease. Recently, we have combined pooled CRISPR perturbations with single-cell measurements of chromatin accessibility to provide genome-wide, multidimensional phenotypes of altered chromatin. Using this new technology, we perturb chromatin modifiers commonly mutated in tumors and pinpoint specific promoters and enhancers with altered chromatin accessibility across many transcription factor binding sites.

4:35 The State of the Art in Highly Multiplexed Multi-*in situ* OMICs

Richie Kohman, PhD, Senior Research Scientist and Lead, Synthetic Biology Platform, Wyss Institute for Biologically Inspired Engineering, Harvard University

Biological tissues are immensely complex containing a huge diversity of chemical motifs in specific, three-dimensional locations. Most OMICs techniques, such as single-cell transcriptomics, do not retain the location of the targets they are analyzing. This talk will cover the state of the art in *in situ* OMICs, where molecules are analyzed within their endogenous environment, providing a crucial insight into the content of healthy and diseased tissues.

5:05 Find Your Table, Meet Your Moderator

5:10 Roundtable Breakout Discussions

TABLE: Leveraging Advanced Genomics Tools for Target Identification

Moderators: Neville Sanjana, PhD, Assistant Professor, Departments of Neuroscience and Physiology, New York University; Faculty, New York Genome Center

Richie Kohman, PhD, Senior Research Scientist and Lead, Synthetic Biology Platform, Wyss Institute for Biologically Inspired Engineering, Harvard University

TABLE: Impact of Chemical Biology and Phenotypic Screening on Drug Discovery

Moderators: Jaimeen Majmudar, PhD, Principal Scientist, Chemical Biology, Pfizer Inc.

Sujatha Gopalakrishnan, PhD, Head, Molecular Screening and Characterization, AbbVie

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5:45 Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

THURSDAY, JUNE 4

TARGET DECONVOLUTION & DEGRADATION

Day 3 of the Accelerating Target Discovery conference highlights the use of computational tools and techniques for target engagement and deconvolution. The emerging area of targeted protein degradation using proteolysis-targeting chimeric molecules (PROTACs) for seeking out previously "undruggable" protein targets will also be discussed using relevant case studies.

8:00 am Registration Open and Morning Coffee

PLENARY KEYNOTE SESSION
8:30 - 9:40

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility

Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics

See Plenary Keynotes Page for More Information.

9:40 Coffee Break in the Exhibit Hall with Poster Viewing

EMERGING TOOLS FOR TARGET DECONVOLUTION

10:25 Chairperson's Remarks

John Brognard, PhD, NIH Stadtman Investigator, Laboratory of Cell and Developmental Signaling, National Cancer Institute, National Institutes of Health

10:30 Quantum Mechanics-Based Deep Learning Drug-Repurpose Screening System

Wenjin Zhou, PhD, Assistant Professor, Department of Computer Science, University of Massachusetts Lowell

Current drug design practice either employs a "blind" drug search for all possible molecules or limits the search to proteins' 3D structural shape. Using quantum mechanics, we dramatically reduce the search space by computing the electron structure of the protein so as to gain information on the active binding sites and atoms. We then provide a deep learning-based drug screening system that can repurpose existing Food and Drug Administration (FDA)-approved drugs. We will demonstrate our initial success.

11:00 Gating and Drug Modulation in 5-HT3A Receptor: Insights from Cryo-EM

Sandip Basak, PhD, Postdoctoral Fellow, Laboratory of Dr. Sudha Chakrapani, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University

Serotonin receptor (5-HT3R) is a pentameric ligand gated ion channel and a common therapeutic target to manage nausea/vomiting during cancer therapies and for treating irritable bowel syndrome. To develop newer drugs, detailed molecular understanding of the gating mechanism and inhibition is important. We have solved the apo-, two serotonin-, and antagonists-bound structures of the full-length 5-HT3AR in distinct conformations using cryo-EM that reveal the mechanism underlying channel activation and inhibition.

11:30 Mining the Unexplored Cancer Kinome for Novel Therapeutic Targets in Squamous Cell Carcinomas

John Brognard, PhD, NIH Stadtman Investigator, Laboratory of Cell and Developmental Signaling, National Cancer Institute, National Institutes of Health

This presentation aims to identify new therapeutic targets for intervention in head and neck cancers and lung squamous cell carcinomas. The presentation will also include the synthesis of new molecules targeting novel activated drivers in squamous cell carcinomas.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

OPTIMIZING & ENGINEERING TARGETED DEGRADATION

2:00 Chairperson's Remarks

Joe Patel, PhD, Director, Biochemistry, Biophysics & Crystallography, C4 Therapeutics, Inc.

2:05 Finding a Way Out of the Labyrinth: Degrader-Induced Ternary Complex Modelling

Joe Patel, PhD, Director, Biochemistry, Biophysics & Crystallography, C4 Therapeutics, Inc.

With targeted protein degraders come significant challenges in structural biology and computational modelling. Numerous examples now exist in the literature of the exquisite SAR possible through modifications of these molecules and this has driven a need to generate atomic-level ternary complex information to assist degrader design and elucidate mechanism of action. Here we will present our approach combining biophysical and computational methods to generate weighted models to support medicinal chemistry.

2:35 FEATURED PRESENTATION: Discovery of Novel Degraders Targeting Oncogenic Proteins

Jian Jin, PhD, Mount Sinai Endowed Professor in Therapeutics Discovery; Professor, Department of Pharmacological Sciences and Department of Oncological Sciences; Director, Mount Sinai Center for Therapeutics Discovery, Icahn School of Medicine at Mount Sinai

The Jian Jin Laboratory at Mount Sinai is a leader in developing novel small-molecule degraders targeting oncogenic proteins. Our recent progress in this area, including discovery of first-in-class EZH2 and MEK1/2 selective degraders, will be presented.

3:05 Immunotherapeutic Approaches for Degrading Tau Pathology in Alzheimer's Disease

Gilbert Gallardo, PhD, Assistant Professor, Hope Center for Neurological Disorders, Washington University School of Medicine

Alzheimer's disease is a tauopathy with no disease-modifying treatments currently available. However, an emerging therapeutic approach is anti-tau immunotherapies. While conventional immunotherapies are promising, they are limited to targeting extracellular proteins, whereas the majority of pathological tau remain in the cytosol of cells. Therefore, we have engineered anti-tau intrabodies for expression intracellularly that contain distinct tags to shuttle tau to either the proteasome or lysosome for degradation.

3:35 Close of Conference

Expanding Chemical & Druggable Space

Macrocyclics & Encoded Libraries • FBDD & Lead Generation • PROTACs

Recommended Short Course*

SC5: Chemoproteomics Enabling Drug Discovery

**Separate registration required; see page 8 for details.*

TUESDAY, JUNE 2

MACROCYCLICS & ENCODED LIBRARIES

Day 1 focuses on progress in macrocyclic peptide synthesis and applications of encoded libraries, two approaches that are widening the "base" from which successful drugs can be found.

10:00 am Main Conference Registration Open

MACROCYCLICS

11:15 Chairperson's Remarks

Tomi Sawyer, PhD, President, Maestro Therapeutics

11:25 Development of Macrocyclic Peptides for Intracellular Targets

David Tellers, PhD, Principal Scientist, Discovery Chemistry, Merck Research Labs

Modulating intracellular protein-protein interactions (PPI) remains a compelling therapeutic opportunity. Peptides bridge the gap between small molecules and antibodies in terms of size and physical properties. As such, peptides potentially have the right balance between target affinity and permeability to potentially address these challenges. This talk will focus on our efforts to develop macrocyclic peptides inhibitors of intracellular PPIs.

11:55 Passively Permeable Macrocycles: Inspiration from Nature and the Translation to the Bench

Cameron Pye, PhD, CEO and Co-Founder, Unnatural Products

We've been using passively permeable macrocycles found in nature as therapeutics for decades. However, designing this property into synthetic cyclic peptides has proved to be challenging despite the myriad of screening and selection platforms available. This talk will explore how we leverage our platform to turn impermeable binders into passively permeable leads.

12:25 pm Engineering Cell-Permeable Proteins as Intracellular Biologics

Dehua Pei, PhD, Professor of Chemistry and Biochemistry, The Ohio State University

Current biologic drugs work almost exclusively against extracellular targets, because they cannot cross the cell membrane. We show that proteins (e.g., enzymes and nanobodies) can be rendered cell-permeable by genetically grafting short "cyclic" cell-penetrating motifs into their surface loops. The engineered proteins are proteolytically stable and biologically active in cellular assays.

12:55 Transition to Lunch

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

Speaker

1:30 Session Break

ENCODED LIBRARIES

2:00 Chairperson's Remarks

Thomas Kodadek, PhD, Professor of Chemistry, The Scripps Research Institute; Co-Founder, Deluge Biotechnologies

2:05 Towards Macrocyclic Peptide Therapeutics using mRNA Encoded Libraries

Wayne Fairbrother, PhD, Director and Senior Staff Scientist, Early Discovery Biochemistry, Genentech

Development of small molecules modulating protein-protein interactions can be difficult due to large and shallow interaction interfaces. Antibodies are ideal for targeting PPIs, but they lack cell-permeability. Macrocycles occupy an intermediate space between small molecules and antibodies, having sufficient size and functionality to interact specifically and with high affinity with PPI surfaces. Accordingly, mRNA display is a highly valuable technology to identify and optimize peptide-based macrocycles.

2:35 Development of Scaffold-Diverse, Stereochemically-Rich DNA-Encoded Libraries and Their Application to Targeting the "Undruggable" Proteome

Thomas Kodadek, PhD, Professor of Chemistry, The Scripps Research Institute; Co-Founder, Deluge Biotechnologies

DNA-encoded libraries (DELs) are increasingly popular as a source of protein ligands. An important issue moving forward is to develop more structurally diverse and stereochemically complex DELs, particularly with respect to "largish" molecules such as non-peptidic macrocycles that may be suitable for targeting difficult to drug proteins such as transcription factors. Recent efforts along these lines will be described.

3:05 Applications of ELT outside Therapeutic Lead Discovery

Christopher Arico-Muendel, PhD, Manager, Platform Capabilities, Encoded Library Technologies, R&D Platform Technology & Science, GlaxoSmithKline Discovery

Most applications of DEL seek stand-alone small molecule ligands to biological targets. However, the attached DNA tag identifies a site for linkage of additional moieties to create bispecific drugs, tool compounds, and affinity reagents. This presentation describes the discovery of a novel, highly potent, specific binder to human serum albumin. Utility of the ligand for therapeutic half-life extension and for affinity purification of albumin containing therapeutics will be discussed.

3:35 Sponsored Presentation *(Opportunity Available)*

4:05 Networking Refreshment Break and Transition to Keynote

PLENARY KEYNOTE SESSION
4:25 - 6:05

Driving Entrepreneurial Innovation to Accelerate Therapeutic Discoveries

The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare.

Moderator: Nadeem Sarwar, President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai Inc.

Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV

Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer

John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council

See Plenary Keynotes Page for More Information.

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

7:10 Close of Day

WEDNESDAY, JUNE 3

FRAGMENT-BASED DRUG DESIGN & LEAD GENERATION

Day 2 focuses on applications of fragment-based drug design (FBDD) and associated biophysical techniques that are providing drug leads against more difficult targets. Now part of most drug discovery efforts, FBDD is a method for finding new drug leads by screening libraries of low molecular weight fragments of drug-like organic compounds. Fragment-based libraries are especially suited for screening against newer types of drug targets such as intracellular protein-protein interactions (PPIs).

7:30 am Registration Open and Morning Coffee

FRAGMENT-BASED DRUG DESIGN

8:10 Chairperson's Remarks

Scott Cowen, PhD, Independent Medicinal Chemistry Consultant

8:15 Optimizing a Fragment Hit into Undruggable Space: A Case Study

Justin Dietrich, PhD, Senior Scientist III, Fragment Based Drug Discovery, AbbVie

We present a story on going from a small molecule fragment to an oral drug candidate with *in vivo* efficacy for a PPI program. For that story, we optimized a fragment into undruggable space to learn about the protein target and then used that information and tools generated along the way to guide a second fragment program that focused on efficiency and maintaining drug-like properties for the final drug candidate.

8:45 From Fragment to Clinical Candidate: The Role of Biophysical Methods in Protein-Protein Interaction (PPI) Inhibitor Development

Chiara Valenzano, PhD, Senior Research Associate, Molecular Sciences Group, Astex Pharmaceuticals

This talk will offer the opportunity to discuss the impact that biophysical methods can have at different stages of the drug discovery process. By presenting case studies taken from the Astex pipeline, the advantages and limitations of applying biophysical techniques such as NMR, SPR and X-ray crystallography to fragment-based drug discovery will be discussed.

9:15 The Application of Fragment Methods to Identify Allosteric Compounds

Ian Storer, PhD, Director of Chemistry, Head of FBLD, Astra Zeneca

A presentation covering examples of both structural (X-ray) and biophysical fragment screening to identify allosteric binders, providing examples from several AstraZeneca projects to illustrate the screening strategy and chemical optimisation from hits to leads.

9:45 Sponsored Presentation *(Opportunity Available)*

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

NEW BIOPHYSICAL TECHNIQUES FOR DRUG LEAD GENERATION

11:00 SAR by 19F NMR: Using Protein-Observed Fluorine NMR for Targeting Protein Complexes

William Pomerantz, PhD, Professor, Chemistry, University of Minnesota

Inspired by the protein-observed NMR approach using 1H-15N-HSQC NMR, we have applied a complementary protein-observed 19F NMR (PrOF NMR) approach using 19F-labeled side-chains that are enriched at protein-protein interaction interfaces. This talk will describe several case studies where PrOF NMR has been applied for fragment screening, ligand deconstruction, and screening of protein mixtures. Several new inhibitors of epigenetic complexes will also be highlighted.

11:30 CryoEM for Drug Discovery

Seungil Han, PhD, Cryo-EM Lab Head, Structural & Molecular Sciences, Pfizer Global R&D

This talk will describe applications of cryo-EM to investigations of solute carrier transporter proteins to enable drug discovery. The prospects of studying large disease-relevant macromolecular complexes without having to generate a single crystal are very appealing, and cryo-EM is becoming a part of lead generation in more and more research departments. The introduction of direct electron detectors, the resolution and range of biological molecules amenable to single particle cryo-EM, have enabled this.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Session Break

Expanding Chemical & Druggable Space

Macrocyclics & Encoded Libraries • FBDD & Lead Generation • PROTACs

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease
Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras
Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine
See Plenary Keynotes Page for More Information.

3:15 Refreshment Break in the Exhibit Hall with Poster Viewing

ORTHOGONAL APPROACHES FOR LEAD GENERATION

4:00 Chairperson's Remarks
Gottfried Schroeder, PhD, Senior Scientist, Department of Pharmacology, Merck Research Labs Bo

4:05 Next-Generation Inhibitors of Bruton's Tyrosine Kinase (BTK) and Clinical Trial Results of BIIB068, a Selective, Potent, Reversible BTK Inhibitor
Bin Ma, PhD, Senior Scientist, Medicinal Chemistry, Biogen
Covalent modification of BTK has been proven to be beneficial for cancer patients with multiple drugs on market while their safety profiles are concerned for autoimmune disease indications. A reversible non-covalent BTK inhibitor will have the promise to address this unmet need. We will report our discovery of BIIB068, an exquisitely selective, potent, reversible BTK inhibitor, together with the med chem strategy and Phase I clinical results.

4:35 Talk Title to be Announced
Rachel Palte, PhD, Senior Scientist, Computational and Structural Chemistry, Merck & Co.

5:05 Find Your Table, Meet Your Moderator

5:10 Roundtable Breakout Discussions

TABLE: Advances and Challenges in Macrocyclic Peptide Therapeutic Development
Moderator: Vincent Guerlavais, PhD, New Modalities, Drug Discovery Consultant

TABLE: Comparing New Biophysical Methods: When to Use What
Moderator: Scott Cowen, PhD, Independent Medicinal Chemistry Consultant

TABLE: Designing and Optimizing Small Molecule Protein Degraders
Moderators: Joe Patel, PhD, Director, Biochemistry, Biophysics & Crystallography, C4 Therapeutics, Inc.
Guangrong Zheng, PhD, Associate Professor, Department of Medicinal Chemistry, College of Pharmacy, University of Florida

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5:45 Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

THURSDAY, JUNE 4

PROTACs

The final day of the Expanding Chemical & Druggable Space conference highlights the use of targeted protein degradation using proteolysis-targeting chimeric molecules (PROTACs) for disrupting protein-protein interactions and hijacking the ubiquitin-proteasome system. The talks discuss the development and optimization of a new generation of protein degrader molecules for diverse therapeutic applications.

8:00 am Registration Open and Morning Coffee

PLENARY KEYNOTE SESSION
8:30 - 9:40

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility
Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics
See Plenary Keynotes Page for More Information.

9:40 Coffee Break in the Exhibit Hall with Poster Viewing

DISCOVERY OF NOVEL PROTAC-BASED DEGRADERS

10:25 Chairperson's Remarks
Jessie Hsu, PhD, Oncology R&D, Senior Scientist, Bioscience, AstraZeneca Pharmaceuticals

Expanding Chemical & Druggable Space

Macrocyclics & Encoded Libraries • FBDD & Lead Generation • PROTACs

10:30 EED-Targeted PROTACs Degrade EED, EZH2, and SUZ12 in the PRC2 Complex

Jessie Hsu, PhD, Oncology R&D, Senior Scientist, Bioscience, AstraZeneca Pharmaceuticals

The polycomb repressive complex 2 (PRC2) is frequently deregulated in cancer. We have discovered a highly potent and selective EED-targeted PROTAC that can inhibit PRC2 activity. The PROTACs target EED and its associated proteins including EZH2 and SUZ12 for elimination and inhibit cell proliferation in PRC2-dependent cancer cells.

11:00 Discovery of Bcl-xL Degraders: A PROTAC Strategy for Tissue-Selective Targeting

Guangrong Zheng, PhD, Associate Professor, Department of Medicinal Chemistry, College of Pharmacy, University of Florida

Bcl-xL plays a key role in cancer cell survival. However, development of drugs targeting Bcl-xL has been thwarted by the on-target platelet toxicity because platelets depend on Bcl-xL to maintain their viability. To circumvent this toxicity, we have applied the proteolysis targeting chimera (PROTAC) technology to design small-molecules that target Bcl-xL to E3 ligases for degradation. This proof-of-concept study demonstrates the potential of utilizing a PROTAC approach to achieve tissue selectivity.

11:30 Expanding the Chemical Space of PROTACs with Novel E3 Ligase Ligands

Kumar Suresh, PhD, Senior Director R&D, Progenra, Inc.

Chemical knock-down of proteins by PROTACs is a paradigm shift in the drug discovery field. Currently, PROTACs based on Cereblon, VHL, HDM2 and cIAPs have been exploited by medicinal chemists to degrade a limited set of therapeutic targets. By focusing on novel ubiquitin ligases, Progenra has discovered entirely new classes of PROTACs with applications in oncology, inflammation, and neuroscience.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

OPTIMIZING & ENGINEERING TARGETED DEGRADATION

2:00 Chairperson's Remarks

Joe Patel, PhD, Director, Biochemistry, Biophysics & Crystallography, C4 Therapeutics, Inc.

2:05 Finding a Way Out of the Labyrinth: Degrader-Induced Ternary Complex Modeling

Joe Patel, PhD, Director, Biochemistry, Biophysics & Crystallography, C4 Therapeutics, Inc.

With the exponential growth in the development of targeted protein degraders comes significant challenges for the structural biology and computational modelling communities. Numerous examples now exist in the literature of the exquisite SAR possible through modifications of these molecules, and this has driven a need to generate atomic-level ternary complex information to assist degrader design and elucidate mechanisms of action. Here we will present our approach combining biophysical and computational methods to generate weighted models to support medicinal chemistry campaigns.

2:35 FEATURED PRESENTATION: Discovery of Novel Degraders Targeting Oncogenic Proteins

Jian Jin, PhD, Mount Sinai Endowed Professor in Therapeutics Discovery; Professor, Department of Pharmacological Sciences and Department of Oncological Sciences; Director, Mount Sinai Center for Therapeutics Discovery; Icahn School of Medicine at Mount Sinai

The Jian Jin Laboratory at Mount Sinai is a leader in developing novel small-molecule degraders targeting oncogenic proteins. Our recent progress in this area, including discovery of first-in-class EZH2 and MEK1/2 selective degraders, will be presented.

3:05 Immunotherapeutic Approaches for Degrading Tau Pathology in Alzheimer's Disease

Gilbert Gallardo, PhD, Assistant Professor, Hope Center for Neurological Disorders, Washington University School of Medicine

Alzheimer's disease is a tauopathy and the leading cause of dementia worldwide with no disease-modified treatments currently available; however, an emerging therapeutic approach is anti-tau immunotherapies. While conventional immunotherapies are promising, they are limited to targeting extracellular proteins, whereas the majority of pathological tau remain in the cytosol of cells. Therefore, we have engineered anti-tau intrabodies for expression intracellularly that contain distinct tags that shuttle tau to either the proteasome or lysosome for degradation.

3:35 Close of Conference

"WPW is a must-attend event to better understand how the pharma industry is moving forward. We will definitely return next year. "

-Director, Marketing, NanoSurface Biomedical

New Small Molecule Drug Targets

RNA • Immunology & Oncology • Microbiome

Recommended Short Course*

SC2: Immunology Basics: Focusing on Autoimmunity and Cancer

Separate registration required; see page 8 for details.

TUESDAY, JUNE 2

RNA AS A NOVEL DRUG TARGET

RNA molecules are crucial for delivering cellular information and genetic regulation, but until recently, the drug discovery world has emphasized protein drug targets. Our lack of knowledge in RNA biology prevented us from exploring possibilities of RNA drug targets, but with recent advances in technologies, such as sequencing, new therapeutic strategies are being explored. Join us as we discuss methods and tools to identify specific, potent, novel, small molecule binders of RNA.

10:00 am Main Conference Registration Open

TARGETING RNA WITH SMALL MOLECULES

11:15 Chairperson's Remarks

Pramod Pandey, PhD, Principal Scientist, Merck Research Labs Exploratory Science Center

11:25 FEATURED PRESENTATION: Drugging RNA with Small Molecules — A Drug Discovery Perspective

Jennifer Petter, PhD, Founder & CSO, Arrakis Therapeutics

RNA is upstream of all biology and thus presents a vast array of therapeutically attractive targets. Most therapeutic agents that bind directly to RNA are either antibiotics blocking bacterial ribosome function or oligonucleotides with their attendant pharmaceutical limitations. At Arrakis, we have identified druggable RNA sub-structures in mRNA and orally available small molecules that bind to those structures selectively and thereby modulate mRNA function. In this talk I will describe recent results that support this larger mission.

11:55 Drugging RNA

Natalie Dales, PhD, Director, Global Discovery Chemistry, Novartis

12:25 pm Discovering Novel RNA-Binding Proteins for Small Molecule Drug Discovery

Pramod Pandey, PhD, Principal Scientist, Merck Research Labs Exploratory Science Center

A large fraction of the genome is transcribed into non-coding RNAs and many of these have been implicated in influencing diseases. We are studying these in the context of diseases, relating to barrier function/dysfunction. Towards that goal, we are developing chemical biology tools to study the RNA protein interactions and find novel targets for small molecule drug discovery.

12:55 Transition to Lunch

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:30 Session Break

TARGETING RNA WITH SMALL MOLECULES (CONT.)

2:00 Chairperson's Remarks

Samie Jaffrey, MD, PhD, Greenberg-Starr Professor, Pharmacology, Weill Cornell Medicine

2:05 Detecting Interactions of Small Molecules with RNA Using Genetically Encoded Fluorescent RNAs

Samie Jaffrey, MD, PhD, Greenberg-Starr Professor, Pharmacology, Weill Cornell Medicine

Detecting and measuring small molecule binding to RNA in living cells has limited the development of therapeutic small molecule ligands of RNA. Here we show how small molecule target engagement on RNA can be imaged in real-time. In this approach, disease-relevant RNA sequences can be converted into fluorescent sensors for detecting small molecule binding, optimizing compounds, and for developing small molecule therapeutics.

2:35 Targeting Pre-mRNA Splicing with Small Molecules

Marla Weetall, PhD, Vice President, Pharmacology, PTC Therapeutics

Pre-mRNA splicing is emerging as a key control point in the expression of disease-modifying genes. Mutations causing alterations in splicing may result in diseases. Small molecules that affect pre-mRNA splicing have been identified and are being clinically developed. At PTC, we have developed a general approach to discover and develop drugs targeting splicing. Here we describe the application of this approach to spinal muscular atrophy, familial dysautonomia, and Huntington's disease.

3:05 PANEL DISCUSSION: What Challenges Come with Targeting a New Modality

Moderator: Natalie Dales, PhD, Director, Global Discovery Chemistry, Novartis

RNA and its many different forms are a new target for small molecules. What challenges come with this new target? With so many new types of targets – mRNA, RNA-protein complexes, lncRNA, epitranscriptomics – what are the best practices moving forward?

3:35 Sponsored Presentation *(Opportunity Available)*

4:05 Networking Refreshment Break and Transition to Keynote

New Small Molecule Drug Targets

RNA • Immunology & Oncology • Microbiome

PLENARY KEYNOTE SESSION
4:25 - 6:05

Driving Entrepreneurial Innovation to Accelerate Therapeutic Discoveries

The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare.

Moderator: Nadeem Sarwar, President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai Inc.

Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV
Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer
John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council

See Plenary Keynotes Page for More Information.

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

7:10 Close of Day

WEDNESDAY, JUNE 3

IMMUNOLOGY & ONCOLOGY

Day 2 focuses on new disease targets in immunology and oncology which are being discovered at a rapid pace. Many are intracellular targets and therefore especially suited to modulation by small molecule-based drugs, as opposed to biologics, because small molecules can cross the cell membrane. Many of these new targets are also part of protein-protein interactions or large molecular complexes, which add to the challenges of new drug discovery.

7:30 am Registration Open and Morning Coffee

TARGETING AUTOIMMUNITY & INFLAMMATION

8:10 Chairperson's Remarks

Dustin McMinn, PhD, Senior Director, Head of Chemistry, Kezar Life Sciences

8:15 An IL36 Antagonist for Probing Psoriasis

Chaohong Sun, PhD, Director & Research Fellow, Protein Sciences and Fragment Based Drug Discovery, AbbVie

IL-36 cytokines are pro-inflammatory members of the IL-1 superfamily that are upregulated in inflammatory disorders. Targeting IL-36 signaling has been an attractive approach for several dermatological diseases including psoriasis. In this talk, I will present our discovery of A-552, a novel first in class small molecule antagonist of the IL-36 signaling pathway. A-552 binds potently and selectively to human IL-36g and was capable of attenuating IL-36g induced responses in mouse and human disease models.

8:45 Targeting Metabolic Pathway Regulators for Inflammation and Autoimmunity

Masha Poyurovsky, PhD, Vice President, Discovery Biology, Kadmon Corporation, LLC

The talk will provide an introductory overview of the metabolic pathways involved of immune cell function under the physiologic and pathologic conditions, providing specific examples of targeting metabolic pathways as means of regulating autoimmune inflammation. Primarily, we will present Kadmon's programs targeting glucose transporters (GLUTs) and PAICS, an enzyme in the purine biosynthesis pathway, showing promise in *in vitro* and *in vivo* models of autoimmune disease.

9:15 Targeting the Mitochondria for Inflammation

Glenda Trujillo, PhD, Principal Scientist, CV and Fibrosis Drug Discovery Disease Sciences and Biology, R&D, Bristol-Myers Squibb

9:45 Sponsored Presentation *(Opportunity Available)*

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

NEW MOLECULAR TARGETS FOR CANCER

11:00 Inhibitors of Sec61 as Novel Anti-Cancer Therapeutics

Dustin McMinn, PhD, Senior Director, Head of Chemistry, Kezar Life Sciences

Targeting and functionalization of most secreted and transmembrane proteins require co-translational translocation to the ER through the Sec61 translocon. Translocation is negotiated by interactions between Sec61 and signal sequences unique to each translating protein. Disruption of these interactions in specific or multi-signal sequence fashion presents an opportunity to modulate protein homeostasis toward therapeutic benefit. Development of signal and multi-signal sequence-selective Sec61 inhibitors as novel anti-cancer agents will be discussed.

11:30 Targeting Metabolic Susceptibilities in the Treatment of Hematologic Malignancies

Josh Murtie, PhD, Senior Director, Head of Cancer Biology, Agios

The treatment of hematologic malignancies has seen significant advances in the past decade, particularly in specific subgroups of patients. While many patients have benefited from these treatments, the prognosis for numerous others remains poor. Agios has focused on identifying metabolic vulnerabilities in a variety of cancers and has developed inhibitors of mutant IDH1 (AG-120; TIBSOVO®) and DHODH (AG-636) with the goal of treating these malignancies.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Session Break

New Small Molecule Drug Targets

RNA • Immunology & Oncology • Microbiome

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease
Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras
Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine
See Plenary Keynotes Page for More Information.

3:15 **Refreshment Break in the Exhibit Hall with Poster Viewing**

SMALL MOLECULE IO TARGETS

4:00 **Chairperson's Remarks**
Masha Poyurovsky, PhD, Vice President, Discovery Biology, Kadmon Corporation, LLC

4:05 **Targeting the Adenosine Receptor for Immuno-Oncology**
Olivier De Henau, MD, Medical Director, iTeos Therapeutics SA

4:35 **IDO1 Inhibitors Discovered from DNA-Encoded Libraries**
Bing Xia, PhD, NCE Encoded Library Technologies, RD Medical Science & Technology, GlaxoSmithKline
Indoleamine 2,3-dioxygenase-1 (IDO1) is induced and activated in response to viral and bacterial infection causing a dysfunctional immune response in clearing pathogens. IDO1 inhibitors (IDO1i) have the potential to restore immune function in indications such as cancer and infection. A structurally-unique IDO1i class was discovered through the affinity selection of a novel DNA-encoded library. After additional medicinal chemistry iterations, the compound series was elaborated into potential best-in-class preclinical molecules.

5:05 **Find Your Table, Meet Your Moderator**

5:10 **Roundtable Breakout Discussions**

TABLE: Targeting Cellular Metabolism: Not Just for Treating Cancer Anymore
Moderator: Masha Poyurovsky, PhD, Vice President, Discovery Biology, Kadmon Corporation, LLC

TABLE: Microbiome-Based Drug Development
Moderator: Mark Charbonneau, PhD, Head, Quantitative Biology, Synlogic

TABLE: What Happens When You Get Off-Target Effects When You Target RNA?
Moderator to be Announced

5:45 **Reception in the Exhibit Hall with Poster Viewing**

6:45 **Close of Day**

THURSDAY, JUNE 4

MICROBIOME

Awareness of the impact of the human microbiome (microbe communities residing in our bodies) on our health has been steadily increasing over the past decade. The last day of the conference will explore strategies for either modulating the microbiome, sometimes specific targets, for controlling responsiveness to specific treatments, or to treat particular disease states.

8:00 am **Registration Open and Morning Coffee**

PLENARY KEYNOTE SESSION
8:30 - 9:40

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility
Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics
See Plenary Keynotes Page for More Information.

9:40 **Coffee Break in the Exhibit Hall with Poster Viewing**

CHARACTERIZING THE MICROBIOME

10:25 **Chairperson's Remarks**
Christopher Weidenmaier, PhD, Principal Scientist, Biology, Finch Therapeutics

10:30 **Engineering Microbes to Treat Metabolic and Immunological Diseases**
Mark Charbonneau, PhD, Head, Quantitative Biology, Synlogic
There is a growing appreciation of how the complex interactions occurring between the host and the gut microbiome play a role in human health and disease. At Synlogic, we engineer pathways into bacteria to enable secretion or consumption of known metabolites to modulate disease processes. This presentation will review the design and translational development of engineered *E. coli* Nissle strains designed for the treatment of metabolic diseases.

11:00 Drugs and Bugs: Microbiome Metabolism of Small Molecules

Julia Kemis, PhD, Postdoctoral Fellow, Cheminformatics, Merck

Although the intestinal microbiome is a known modulator of drug pharmacokinetics and metabolism, we lack a comprehensive understanding of how drug metabolism varies among individual microbiomes. To address this challenge, we developed an informer set of compounds encompassing diverse drug-like chemical space that can be applied to functionally characterize microbiome samples. The informer set presents a novel strategy to compare and group microbiome samples of interest based on metabolic activity.

11:30 It Takes Guts to Rev Up CARs: Using the Gut Microbiome to Modulate Response to CAR T Cells

Bilal Abid, MD, Assistant Professor of Medicine, Medical College of Wisconsin

The gut microbiome has been shown, in pre-clinical and clinical settings, to homogenize and improve responses to immunotherapy, by enhancing innate and adaptive anti-cancer immune responses. Based on shared immunological and microbiological mechanisms, we are examining the potential of the gut microbiome in enhancing responses to CAR T-cells and as biomarkers of response and survival. Chimeric Antigen Receptor (CAR) T cells are autologous T cells re-directed towards a tumor-specific antigen and are FDA-approved for patients with refractory B-cell ALL and DLBCL.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

TARGETING THE MICROBIOME

2:00 Chairperson's Remarks

Julia Kemis, PhD, Postdoctoral Fellow, Cheminformatics, Merck

2:05 Inflammatory Bowel Disease and the Microbiome

Christopher Weidenmaier, PhD, Principal Scientist, Biology, Finch Therapeutics

Inflammatory bowel diseases like ulcerative colitis and Crohn's disease are characterized by altered mucosal immune responses and a dysbiotic microbiome. Finch uses machine learning models on clinical and microbiome intervention data to identify clinically relevant bacterial strains. This human-first discovery platform allows to identify and isolate strains with the ability to therapeutically modulate disease pathophysiology. Building consortia from such strains enables Finch to develop therapeutic candidates while minimizing translational risk.

2:35 Therapeutic Applications Based on the Gut-Brain Axis: Small Molecule Based Approaches to Treat CNS Diseases

David Donabedian, CEO, Axial Biotherapeutics

Axial Biotherapeutics is taking a revolutionary approach to treating CNS diseases by focusing on developing gut retentive, small molecules and delivering them to the gut and not the brain.

3:05 Presentation to be Announced

3:35 Close of Conference

Recommended Short Course*

SC4: Optimizing Drug Metabolism, Drug Clearance and Drug-Drug Interactions

Separate registration required; see page 8 for details.

TUESDAY, JUNE 2

CNS AND NEUROSCIENCE

A greater understanding of CNS-related disease biology and the emergence of new, improved targets and technologies are advancing the development of neurological therapeutics. This session focuses on the latest strategies, modalities and translational challenges driving CNS drug development.

10:00 am Main Conference Registration Open

MATCHING THE RIGHT MODALITY TO THE RIGHT MECHANISM

11:15 Chairperson's Remarks

Dario Doller, PhD, Director, Medicinal Chemistry, Sunovion Pharmaceuticals

11:25 Matching the Right Modality to the Right Mechanism for the Right Patient

Julie Chen, PhD, Chemical and Structural Biology Lead, Eisai Center for Genetics Guided Dementia Discovery (G2D2)

11:55 Small Molecule Treatment of Brain Diseases: A Perspective on the Path Forward, Looking Up from the Bottom

Dario Doller, PhD, Director, Medicinal Chemistry, Sunovion Pharmaceuticals

This presentation will analyze and discuss the key challenges facing CNS drug discovery and development, including: where we have been, contemporary neuroscience pipelines, success in CNS drug research, context, contrast and expectations, and where to now?

12:25 pm Leveraging the Power of Human Genetics to Go beyond A-Beta and Tau

Janna Hutz, PhD, Head, Data Sciences, Eisai Center for Genetics Guided Dementia Discovery (G2D2)

12:55 Transition to Lunch

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:30 Session Break

CNS DRUG DEVELOPMENT AND TRANSLATION

2:00 Chairperson's Remarks

Dario Doller, PhD, Director, Medicinal Chemistry, Sunovion Pharmaceuticals

2:05 Machine Learning Models in CNS Drug Discovery and Penetrating the BBB

Istvan Enyedy, PhD, Principal Scientist, Medicinal Chemistry, Biogen

The design of therapeutic agents that penetrate the blood-brain barrier is challenging mainly due to the promiscuity of efflux transporters. The structures of P-gp and BCRP have been published allowing us to build machine learning models that combine the transporter structural information with traditional ligand-based descriptors. The performance of these models will be presented.

2:35 PET Imaging of Neuroinflammation in Neurodegenerative Diseases

Changning Wang, PhD, Assistant Professor of Radiology, Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Harvard Medical School

Molecular imaging, such as PET, has been widely used in medical research and drug discovery. We have developed new imaging tools and applied them in clinical research and drug discovery. In this presentation, I will discuss the development and application of molecular neuroimaging techniques for brain research. Our work is a unique example on the multidisciplinary research, including molecular imaging, medicinal chemistry, clinical research and preclinical drug discovery.

3:05 A Neuroinflammatory Translational Pipeline for Neurodegenerative Diseases

Jonathan Levenson, PhD, Vice President, Translational Biology, Tiaki Therapeutics

Neuroinflammation is a pathological hallmark of CNS degenerative diseases, yet preclinical translational tools to support drug discovery programs are lacking. Tiaki has developed an *ex vivo* slice culture and an animal model that manifests a neuroinflammatory state that is aligned with Alzheimer's and Huntington's disease. Using these tools, a novel anti-inflammatory target for neurodegenerative disease, which was identified using curated human data, has been progressed to lead optimization.

3:35 Sponsored Presentation *(Opportunity Available)*

4:05 Networking Refreshment Break and Transition to Keynote

PLENARY KEYNOTE SESSION
4:25 - 6:05

Driving Entrepreneurial Innovation to Accelerate Therapeutic Discoveries

The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare.

Moderator: Nadeem Sarwar, President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai Inc.

Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV
Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer
John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council

See Plenary Keynotes Page for More Information.

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

7:10 Close of Day

WEDNESDAY, JUNE 3

RARE DISEASES, CELL AND GENE THERAPY

This session provides a platform for pharma, biotech, and academia to discuss and benchmark the latest advances in developing new drug targets and novel therapies across the fields of neuroscience, rare diseases, and gene and cell therapy. How do your drug discovery and translational strategies compare?

7:30 am Registration Open and Morning Coffee

GENE THERAPIES FOR NEUROLOGICAL DISEASES

8:10 Chairperson's Remarks
Dario Doller, PhD, Director, Medicinal Chemistry, Sunovion Pharmaceuticals

8:15 Gene Therapy Development for Neurological Diseases
Gabriele Proetzel, PhD, Director, External Neuroscience Innovation, Neuroscience Drug Discovery Unit, Takeda Pharmaceuticals

With the approval of Zolgensma, gene therapy for neurological disorders have become a reality. This presentation will discuss the recent advances for *in vivo* gene therapy development for the neuronal diseases with their challenges and opportunities. The focus will be on adeno-associated virus (AAV), key aspects for preclinical development and how this is different from classical drug discovery. Discussed will be payload options, delivery, and preclinical models critical for advancing gene therapy into the clinic and to the patient.

8:45 Preclinical Development of an Intrathecally-Administered ASO to Treat Spinal Muscular Atrophy
Kenneth S. Loveday, PhD, DABT, Principal Investigator, Preclinical Safety, Biogen

Patients with spinal muscular atrophy have a defect in the SMN1 gene. Nusinersen is an ASO designed to increase production of SMN protein from the SMN2 gene by modifying splicing of pre-mRNA. Toxicology studies in monkeys used intrathecal dosing to deliver nusinersen across the blood-brain barrier into CSF to its site of action: spinal cord motor neurons. The clinical development program was successful, and initial regulatory approval occurred in December of 2016.

9:15 Tissue Distribution and PK of Antisense Oligonucleotides following Intrathecal Administration
Natasha Penner, PhD, Director, Clinical Pharmacology and Pharmacometrics, Biogen

With oligonucleotides unable to penetrate the blood-brain barrier, this presentation describes tissue distribution and PK of antisense oligonucleotides following intrathecal administration. Nusinersen is an ASO designed to increase production of SMN protein from the SMN2 gene by modifying splicing of pre-mRNA. The clinical development program was successful, and initial regulatory approval occurred in December of 2016.

Sponsored by
NeuCyte
Translatable Neuroscience

9:45 Presentation to be Announced

10:00 Sponsored Presentation *(Opportunity Available)*

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

EMERGING TARGETS AND PATHWAYS

11:00 Lysosomal Dysfunction in Common Neurodegenerative Diseases: From Genetics to the Clinic
Pablo Sardi, PhD, R&D Senior Director, Rare and Neurological Diseases, Sanofi

This presentation will discuss: clinical, genetic and experimental evidence underlies the relevance of lysosomal dysfunction in Parkinson's disease (PD), and mutations in the lysosomal glucocerebrosidase gene (GBA) accelerate PD progression. First trial has begun testing a GBA pathway modulator in a genetically defined population, and modulation of the lysosomal pathway may also benefit a larger sporadic patient population.

Emerging Indications & Modalities

CNS & Neuroscience • Gene & Cell Therapy • Fibrosis & Liver Diseases

11:30 Targeting Ataxin-2 against TDP43 Pathology Associated with Amyotrophic Lateral Sclerosis and Frontotemporal Dementia

Yinghui Hu, PhD, Associate Principal Scientist, Neurodegeneration Group, Merck

Ataxin-2 has been identified as a potent modifier of TDP43-toxicity. We demonstrated that knockdown of Ataxin-2 or inhibition of Ataxin-2 interaction with TDP43 effectively reversed TDP43-induced toxicity in hu-iPSC neurons. Proteomic analysis was also performed to identify a specific set of proteins associated with the aberrant Ataxin-2/TDP43 interaction. These findings led us to explore various approaches and modalities that can be used as novel strategy for therapeutic intervention.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Session Break

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease

Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras

Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine

See Plenary Keynotes Page for More Information.

3:15 Refreshment Break in the Exhibit Hall with Poster Viewing

CELL AND GENE THERAPY

4:00 Chairperson's Remarks

Dario Doller, PhD, Director, Medicinal Chemistry, Sunovion Pharmaceuticals

4:05 Authentic Cell Therapies for Intractable Neurological Diseases

Stefan Irion, MD, Vice President, Translational Neuroscience, BlueRock Therapeutics

The convergence of cell biology and genetic engineering is creating fundamental new ways to impact disease. Founded in 2016 to capitalize on these technological breakthroughs, we are advancing our novel platform to develop, manufacture, and deliver an entirely new generation of authentic and engineered cell therapies across three therapeutic areas: neurology, cardiology, and immunology. This presentation will focus on cell therapies for intractable neurological diseases.

4:35 Disruption of RNA Metabolism in Neurological Diseases and Emerging Therapeutic Interventions

Matthew Nolan, PhD, Post Doc Research Fellow, Harvard Medical School and Massachusetts General Hospital

RNA binding proteins are critical to the maintenance of the transcriptome via controlled regulation of RNA processing and transport. Alterations of these proteins impact multiple steps of the RNA life cycle resulting in various molecular phenotypes such as aberrant RNA splicing, transport, and stability. Emerging therapeutic approaches to mitigate or reverse alterations of RNA binding proteins in neurological diseases are discussed.

5:05 Find Your Table, Meet Your Moderator

5:10 Roundtable Breakout Discussions

TABLE: Translational Strategies in CNS Drug Development

Moderator: Dario Doller, PhD, Director, Medicinal Chemistry, Sunovion Pharmaceuticals

TABLE: AI and Machine Learning in CNS Drug Development

Moderator: Istvan Enyedy, PhD, Principal Scientist, Medicinal Chemistry, Biogen

TABLE: Modeling Fibrosis

Moderator: Vanessa Morales-Tirado, PhD, Principal Research Scientist, Translational Immunology, Immunology Discovery, AbbVie Bioresearch Center

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5:45 Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

THURSDAY, JUNE 4

FIBROSIS AND LIVER DISEASE

Finding new medical treatments for fibrosis, especially of the lung and liver, is a growing area of activity in the drug development industry. Not only are the incidences of fibrotic or different types of liver disease rising as our population ages, but new scientic evidence is revealing points of therapeutic intervention. On the last day of this conference, join us to explore the translational challenges and hear about new dug targets in these areas of fibrosis and liver diseases.

8:00 am Registration Open and Morning Coffee

PLENARY KEYNOTE SESSION
8:30 - 9:40

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility
Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics
See Plenary Keynotes Page for More Information.

9:40 Coffee Break in the Exhibit Hall with Poster Viewing

TARGETING FIBROSIS

10:25 Chairperson's Remarks
John O'Neill, CSO, XYLYX BIO INC

10:30 Fibrosis Biomarker Tool Kit for the Lung and Beyond
Vanessa Morales-Tirado, PhD, Principal Research Scientist, Translational Immunology, Immunology Discovery, AbbVie Bioresearch Center
Efficient, novel therapeutics against fibrotic diseases are highly desirable. Identification of biomarkers contribute to understanding of disease mechanisms, acceleration of drug development and clinical management. Accessibility to tissues and disease target activities is a challenge in fibrotic diseases such as IPF and scleroderma, highlighting the need for the identification of non-invasive biomarkers to represent drug pharmacodynamics and disease biology. Here, we present novel tools to identify biomarkers in fibrotic diseases.

11:00 Role of Fibroblast Expression of Integrin-Alpha V in Fibrosis and Inflammation
Kevin Hart, PhD, Principal Scientist, Inflammation, Pfizer Inc.
Since some integrins can serve as master regulators of fibrosis, we investigated if integrin-alpha V is critical during polarized inflammatory responses during tissue damage disease models. While data confirmed a role for integrin-alpha V in type 17-associated fibrosis, integrin-alpha V was not critical to the development of type 2-driven fibrosis. However, our studies reveal a novel mechanism through which fibroblasts, via integrin-alpha V expression, are capable of regulating immune polarization.

11:30 Targeting Integrins for Fibrosis
Speaker to be Announced, Pliant Therapeutics
aV integrins are a subset of a family of heterodimeric transmembrane proteins that mediate cell-cell and cell-extracellular matrix signaling. Targeting aV integrins with small molecules has been a challenge in the drug discovery field, primarily due to limited approaches to selectivity, complex signaling mechanisms, poor ADME properties and poor translation to a clinical setting. This talk will focus on our approach to addressing these concerns, leading to *in vivo* active molecules that translate to human disease.

12:00 pm Disease-Specific Extracellular Matrix Cell Culture Substrates to Improve Predictive *in Vitro* Models of NASH
Sponsored by XYLYX
John O'Neill, CSO, XYLYX BIO INC
Introducing a standardized, fully humanized commercial 3D cell culture platform for fibrosis research and discussing how this platform can reduce the dependence on animal models, and enable more relevant scientific results leading to improved drug discovery process.

12:15 Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

Emerging Indications & Modalities

CNS & Neuroscience • Gene & Cell Therapy • Fibrosis & Liver Diseases

TARGETING LIVER DISEASE

2:00 Chairperson's Remarks

Vanessa Morales-Tirado, PhD, Principal Research Scientist, Translational Immunology, Immunology Discovery, AbbVie Bioresearch Center

2:05 Progress Toward a Combination Therapy to Cure HBV

Michael Sofia, PhD, CSO, Arbutus Biopharma, Inc.

It is widely held that a combination of agents with different mechanisms of action will be required to achieve an HBV functional cure that is broad-based and of finite duration. To deliver on such an HBV curative regimen, we believe that cessation of viral replication, reduction of HBsAg levels, stopping replenishment of cccDNA pools and reactivation of the host immune response against HBV will need to be achieved. Progress toward the development of a combination therapy that addresses these key objectives will be presented.

2:35 NASH: Drug Development Landscape with a Focus on Cirrhosis

Peter Traber, MD, Partner, Alacrita Consulting; Adjunct Professor of Medicine, University of Pennsylvania School of Medicine

NASH, non-alcoholic steatohepatitis, is a chronic, slowly progressive inflammatory and fibrotic disease of the liver which progresses in some individuals to cirrhosis with its attendant complications, including death and liver transplant. In this presentation, I will review the status of drug candidates in clinical trials and their MOA (no treatments are on the market yet). Additionally, the differences in the pathophysiology and impact on patients between precirrhotic and cirrhotic NASH will be reviewed. I will also put in the context of current ongoing development programs, the acceptable and potential regulatory endpoints for clinical trials.

3:05 Targeting Galectin-3 in Fibrotic Disease

Rob Slack, PhD, Director of Pharmacology, Galecto, Inc.

Galectin-3 is a β-galactoside-binding lectin highly expressed in fibrotic tissue of diverse etiologies and has been shown to play a key role in lung, liver and kidney fibrosis. Galecto, Inc. have developed a number of high affinity and selective galectin-3 inhibitors currently undergoing clinical investigation in fibrotic diseases of the lung and liver. This talk will focus on the translational pharmacology of these galectin-3 inhibitors and their potential as anti-fibrotic therapies.

3:35 Close of Conference

Immuno-Oncology Advances

Translational IO • Small Molecule Targets • Immune Profiling

Recommended Short Course*

SC1: *In vitro* and *in vivo* Modeling for Cancer Research

**Separate registration required; see page 8 for details.*

TUESDAY, JUNE 2

PLATFORMS AND COMBINATIONS

Immunotherapeutic strategies have changed the way cancers are being treated, providing significant benefit to patients. Despite success, a large fraction of patients does not respond to single-agent therapy. Combination approaches may be the key to improving response rates in these patients. Preclinical immuno-oncology models provide tremendous value for shaping clinical strategies, given that countless potential combinations exist with other immunotherapies, radiation, and/or standard of care.

10:00 am Main Conference Registration Open

MULTI-TARGETED PLATFORMS AND EXTERNAL COLLABORATIONS

11:15 Chairperson's Remarks

Michael Woo, PharmD, Head, Search & Evaluation, Immuno-Oncology, Business Development & Licensing, Novartis Institutes for BioMedical Research, Inc

11:25 KEYNOTE PRESENTATION: Leveraging Multi-Targeting for More Effective Cancer Immunotherapy

Dmitri Wiederschain, PhD, Global Head, Immuno-Oncology Research Therapeutic Area, Sanofi

Cancer immunotherapies with anti-PD-1/PD-L1 checkpoint blockers have revolutionized the treatment of a wide variety of malignancies. However, immunotherapy is ineffective in a significant subset of cancer patients or eventually results in the development of resistance with relapsed disease. Therefore, the future of immuno-oncology is identification of new multi-targeted agents that can elicit robust anti-tumor immunity as single agents and/or be combined with PD1/PDL1 inhibitors to increase the duration and durability of clinical responses. Sanofi is leveraging its rich internal toolbox of therapeutic modalities, including multispecific antibodies, nanobodies and ADCs, to reduce the concept of multi-targeting to practice and convert "cold" non-immunogenic tumors into "hot" tumors with rich and functionally active immune infiltrate.

11:55 Exploring Novel Immunotherapy Combinations to Overcome Resistance to PD-1 Blockade

Russell Jenkins, MD, PhD, Assistant Professor, Medicine, Center for Cancer Research, Massachusetts General Hospital

Cancer immunotherapy with immune checkpoint blockade has transformed the treatment of patients with advanced melanoma, but strategies to overcome resistance are limited. Using molecular and pharmacologic tools, we have confirmed TANK-binding kinase 1 (TBK1) as a novel target to overcome resistance to PD-1 blockade, further supporting the preclinical and clinical development of this novel combination strategy.

12:25 pm External Collaboration in Immuno-Oncology: New Approaches and Business Models

Michael Woo, PharmD, Head, Search & Evaluation, Immuno-Oncology, Business Development & Licensing, Novartis Institutes for BioMedical Research, Inc

The rapid expansion of the field of immune-oncology provoked a spike of venture capital activity and increased the level of external collaboration among pharmaceutical and biotechnology companies. This presentation will focus on strategic consequences of the IO wave for pharma, biotech, and the venture ecosystem.

12:55 Transition to Lunch

1:00 Luncheon Presentation to be Announced

Sponsored by

CHAMPIONS ONCOLOGY

1:30 Session Break

TRANSLATIONAL APPROACHES AND NOVEL TARGETS

2:00 Chairperson's Remarks

Viviana Cremasco, PhD, Investigator III, Exploratory Immuno-Oncology, Novartis

2:05 *In vivo* Imaging Techniques for Model Characterization and Guiding Combination Strategies

Tapan Nayak, PhD, Director, Translational Imaging Biomarkers, Merck & Co., Inc.

The success rate of experimental therapy is difficult to predict, as its efficacy often depends upon the characteristics of the preclinical animal models. The presentation will cover different non-invasive imaging techniques to characterize animal models and the information used to guide combination therapies in animal models.

2:25 TGFβ-Blockade Uncovers Stromal Plasticity in Tumors by Revealing the Existence of a Novel Subset of Interferon-Licensed Fibroblasts

Viviana Cremasco, PhD, Investigator III, Exploratory Immuno-Oncology, Novartis

By performing an unbiased interrogation of tumor mesenchymal cells, our study shows that TGFβ-neutralization leads to a profound remodeling of CAF dynamics, greatly reducing the frequency and activity of myofibroblasts, while promoting the formation of a novel fibroblast population characterized by strong response to interferon and heightened immunomodulatory properties. These changes are sufficient to drive productive anti-tumor immunity, laying the foundation for future investigations aimed at defining strategies to reprogram CAF composition for cancer therapy.

2:45 Driving Clinical Decisions about Indications and Combination Partners Using Patient-Derived Xenograft Models

Anderson Clark, PhD, Director, Translational in vivo Pharmacology, Translational Innovation Platform, Oncology, EMD Serono

Preclinical tumor models can provide data to drive clinical decisions about responsive indications, biomarkers, suitable combination partners (both standard-of-care and novel agents), and dosing strategies. In this talk, I will present the preclinical strategy that was used to support early clinical development of M2698, a dual inhibitor of p70S6K/AKT, at EMD Serono.

3:05 TAC Development for the Treatment of Solid and Liquid Tumors

Christopher Helsen, PhD, Director, R&D and Head, Platform Development, Triumvira Immunologics Inc.

Triumvira is a clinical-stage company developing T-cell therapies engineered with the proprietary T-cell antigen coupler (TAC). TAC is designed to co-opt the natural TCR independent of MHC showing safe and effective tumor rejection in mouse models of solid and liquid tumors. Triumvira successfully cleared IND/CTA submission for TAC01-CD19 to treat LBCL with a second solid tumor program in preclinical development.

3:35 Presentation to be Announced

Sponsored by

3:50 Sponsored Presentation *(Opportunity Available)*

4:05 Networking Refreshment Break and Transition to Keynote

PLENARY KEYNOTE SESSION
4:25 - 6:05

Driving Entrepreneurial Innovation to Accelerate Therapeutic Discoveries

The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare.

Moderator: Nadeem Sarwar, President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai Inc.

Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV

Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer

John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council

See Plenary Keynotes Page for More Information.

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

7:10 Close of Day

WEDNESDAY, JUNE 3

IMMUNE PROFILING

Immune profiling promises to identify biomarkers that predict response to immunotherapy and to help monitor its progress. Understanding the tumor microenvironment and mechanisms of tumor immune evasion are the goal of this session.

7:30 am Registration Open and Morning Coffee

INTEGRATED IMMUNE PROFILING AND TUMOR MICROENVIRONMENT

8:10 Chairperson's Remarks

Samir Hanash, MD, PhD, Director, McCombs Institute for Cancer Early Detection and Treatment, MD Anderson Cancer Center

8:15 Integrative Analyses of Environment, Microbiome, Immunity, and Tumor for Precision Oncology

Shuji Ogino, MD, PhD, MS, Professor of Pathology, Brigham & Women's Hospital, Harvard Medical School; Professor, Epidemiology, Harvard T.H. Chan School of Public Health; Chief of Molecular Pathological Epidemiology (MPE) Program, Brigham & Women's Hospital; Associate Member, Broad Institute of MIT and Harvard

The integrative field of immunology-MPE (molecular pathological epidemiology) is an emerging paradigm and can investigate influences of the exposome on tumor-immune interactions, thereby informing immunotherapy research. Using over 1500 colorectal cancer cases with rich data on immune response, whole exome sequencing, RNA-sequencing, tumor neoantigens, and clinical outcomes, proof-of-principle immunology-MPE studies have shown great promise for precision prevention and immuno-oncology.

8:45 The Tumor Immune Microenvironment of Pre-Malignant Lesion in the Pancreas

Elizabeth Thompson MD, PhD, Assistant Professor, Pathology and Oncology, The Johns Hopkins Hospital

While much work has focused on the tumor immune microenvironment of established cancers, little is known about the immune response to the earliest stages of tumor development. This talk will explore the immune microenvironment of neoplastic precursor lesions in the pancreas, focusing on pancreatic intraepithelial neoplasia and intraductal papillary mucinous neoplasms (IPMN) with emphasis on features predicting grade of dysplastic change and recurrence/progression to malignancies.

Immuno-Oncology Advances

Translational IO • Small Molecule Targets • Immune Profiling

9:15 Immune Profiling
Veena Kandaswamy, PhD, Immuno-Oncology Biomarkers, Eli Lilly

9:45 How Biospecimen Sourcing Can Impact Your R&D Results
Sponsored by TRANS-HIT BIO
Vanessa Tumilasci, PhD, Commercial Director, Trans-Hit Bio
Biospecimen sourcing is becoming a challenge for many scientists who need to respect timelines for R&D plans as well as regulatory and ethical constraints. Are the scientists working with the samples aware of all the imperatives to obtain them; quality, respect of laws, ethics and regulations?

10:00 Sponsored Presentation *(Opportunity Available)*

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

INTEGRATED IMMUNE PROFILING AND TUMOR MICROENVIRONMENT (CONT.)

11:00 Molecular Signatures of Tumor Immune Evasion
Samir Hanash, MD, PhD, Director, McCombs Institute for Cancer Early Detection and Treatment, MD Anderson Cancer Center
A wide world of mechanisms leading to tumor immune evasion have emerged. Assessment of these mechanisms has relevance to immunotherapy applications.

11:30 Multiplex Immunofluorescence Tyramide Signal Amplification and Multispectral Imaging Assay to Support Translational Oncology Studies
Edwin Roger Parra Cuentas, MD, PhD, Assistant Professor, Translational Molecular Pathology; Director of the Multiplex Immunofluorescence and Image Analysis Laboratory, MD Anderson Cancer Center
Multiplex immunofluorescence (mIF) have emerged in the last years as a very powerful tool to study tumor tissues. This revolutionary technology provides important visual technique for tumor examination in formalin-fixed paraffin-embedded specimens to improve the understanding of the tumor microenvironment, promote new treatment discoveries, aid in cancer prevention, as well as allowing translational studies to be carried out.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Session Break

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease
Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras
Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine
See Plenary Keynotes Page for More Information.

3:15 Refreshment Break in the Exhibit Hall with Poster Viewing

BIOMARKERS FOR ONCOLOGY CLINICAL TRIALS

4:00 Chairperson's Remarks

Samir Hanash, MD, PhD, Director, McCombs Institute for Cancer Early Detection and Treatment, MD Anderson Cancer Center

4:05 Pharmacodynamic Profiling of Patients Treated with BLZ945 Demonstrates On-Target Peripheral and Tumor Immune Microenvironment Modulation

Jennifer Mataraza, PhD, Head, Translational Immuno-Oncology, Novartis Institutes for BioMedical Research

BLZ945 is an oral, highly selective and potent kinase inhibitor of CSF-1R. Both preclinical and clinical evidence demonstrates that blocking (CSF-1R) signaling may lead to depletion of TAMs and increased T cell activation. BLZ945X2101 is an ongoing clinical trial investigating the use of BLZ945 as single agent and in combination with spartalizumab (anti-PD-1) in advanced solid tumors. Biomarker analyses will be discussed as evidence of on-target pharmacodynamic effects of BLZ945 in treated patients.

4:35 Overview of Genomic Biomarkers in Clinical Trials

Chetan Deshpande, Clinical Biomarker Assay Lead, Pfizer

Genomics biomarkers have been implemented routinely in clinical trials, especially in oncology, for exploratory endpoints. Over the last few years, molecular testing by NGS has been applied not only to understand the molecular mechanism of the underlying disease, but also to gain insights into resistance mechanism. This presentation will review the current trends in implementing genomic biomarkers in oncology clinical trials.

5:05 Find Your Table, Meet Your Moderator

5:10 Roundtable Breakout Discussions

TABLE: Tumor Immune Microenvironment

Moderator: Elizabeth Thompson MD, PhD, Assistant Professor, Pathology and Oncology, The Johns Hopkins Hospital

TABLE: Theranostics in Immuno-Oncology

Moderator: Michael Roehrl, MD, PhD, Director, Precision Pathology Center, Memorial Sloan Kettering Cancer Center; Associate Professor, Pathology and Laboratory Medicine, Weill Cornell Medicine

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5:45 Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

THURSDAY, JUNE 4

TUMOR MODELS

Preclinical tumor models are key tools to evaluate the activity of cancer therapies. They are instrumental to understanding the mechanism of action of tested compounds and help with identifying rational combination partners for best anti-tumor efficacy. Next-generation tumor models, preclinical imaging, and translational strategies will be featured at Day 3 of this conference.

8:00 am Registration Open and Morning Coffee

PLENARY KEYNOTE SESSION 8:30 - 9:40

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility

Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics

See Plenary Keynotes Page for More Information.

9:40 Coffee Break in the Exhibit Hall with Poster Viewing

NEXT-GENERATION MODELING SYSTEMS AND WHAT WE CAN LEARN WITH THEIR HELP

10:25 Chairperson's Remarks

Christopher Kemball, PhD, Scientist, Biochemical & Cellular Pharmacology, Genentech

10:30 Preclinical Modeling Using Human Cancer Xenografts Grown in Immune-Deficient Zebrafish

David Langenau, PhD, Associate Chief of Research and Director of Molecular Pathology, Massachusetts General Hospital; Associate Professor, Pathology, Harvard Medical School

We have generated immune-compromised zebrafish that lack T-, B- and NK-cells that robustly engraft human cancers. Capitalizing on the optical clarity of zebrafish and facile imaging approaches, we have documented small-molecule therapy responses and dynamic cell killing by CAR T cell- and bispecific T cell-engager antibodies (BITES) at single-cell resolution. Our studies credential the immune-deficient zebrafish as a new platform for preclinical drug studies.

Immuno-Oncology Advances

Translational IO • Small Molecule Targets • Immune Profiling

11:00 CD34+ Stem Cell-Derived Human Dendritic Cells Provide a Physiologically Relevant System to Evaluate the Pharmacology of Therapeutic Molecules

Christopher Kemball, PhD, Scientist, Biochemical & Cellular Pharmacology, Genentech

Anti-tumor immunity may be enhanced by therapeutic agents that promote dendritic cell expansion and differentiation. To better characterize the pharmacology of these therapies, *in vitro* models are needed that recapitulate physiologically relevant human DC subsets. DCs generated *in vitro* from human CD34+ progenitor cells closely resemble primary blood DCs. We show that CD34-derived DCs can be used to characterize the potency of a therapeutic molecule to drive cDC1 differentiation.

11:30 Is There a Key Node in the TME to Tip the Balance?

Zhao Chen, PhD, Investigator III, Exploratory Immuno-Oncology, Novartis Institutes for BioMedical Research, Inc.

The efficacy of the host immune response against cancer largely depends on the behavior of the tumor microenvironment (TME). Many TME components were shown to impact different aspect of cancer immunity, ranging from T cell priming, effector function, exhaustion to memory. However, the highly heterogeneous TME is often a big hurdle for the clinical translation of TME targets. We are interested in the interplay between components of the TME and the key node that can truly perturb the TME balance.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

2:00 Chairperson's Remarks

Virna Cortez-Retamozo, PhD, Lab Head, Senior Principal Scientist, Oncology-Pharmacology, Sanofi

2:05 Transplanted Syngeneic Metastasis Models for Preclinical Applications

Viswanathan Muthusamy, PhD, Research Scientist; Executive Director, Center for Precision Cancer Modeling, Yale School of Medicine

There is a great need for robust *in vivo* preclinical models for evaluation of drugs interfering with metastasis. We have developed several transplantable, syngeneic metastasis models and used these to assess: 1) interventions to prevent colonization and growth in distant organs; and 2) treatment-induced abscopal effects on distant metastases. In preliminary studies, an immune-targeting, intratumorally injected drug candidate reduced metastatic burden and improved survival in one such model.

2:35 Using Humanized Mouse Models to Evaluate IO Therapeutics

Virna Cortez-Retamozo, PhD, Lab Head, Senior Principal Scientist, Oncology-Pharmacology, Sanofi

The success of early cancer immunotherapies has led to the development of several new therapeutic approaches, including T cell engagers. T cell engagers are typically bispecific Abs directed against the T cell and a tumor-associated antigen, whose therapeutic strategy is to: 1) engage T cells; 2) activate the T cells; and 3) engage tumor cells and induce tumor cell killing. Preclinical evaluation relies on development of models that mirror some properties of a human setting to assess the therapeutic properties of T cell engagers.

3:05 PANEL DISCUSSION: Next-Generation Modeling Systems and What We Can Learn with Their Help

Moderator: Zhao Chen, PhD, Investigator III, Exploratory Immuno-Oncology, Novartis Institutes for BioMedical Research, Inc.

Panelists: Speakers of the Session

3:35 Close of Conference

Disease Modeling

3D Cellular Modeling • iPSCs • Bioengineered Models

Recommended Short Course*

SC7: Intro to OOAC and Bioprinting for Disease Modeling

Separate registration required; see page 8 for details.

TUESDAY, JUNE 2

3D CELLULAR MODELS

In the past decade, a lot of momentum has been gaining for three-dimensional (3D) cell culture; proponents state that this is more physiologically relevant, but admit that we still need to discuss standardization, validity, scalability and more. Join us on Day 1 of the Disease Modeling conference at World Pharma Week as we discuss innovations, specific-use cases of 3D-oids (organoids, spheroids or tumoroids), and applications for drug discovery and development.

10:00 am Main Conference Registration Open

MOVING TOWARDS A 3D PHYSIOLOGICALLY RELEVANT CELLULAR MODEL

11:15 Chairperson's Remarks

Virneliz Fernandez Vega, Scientific Associate, Molecular Medicine, Scripps Research

11:20 Combining 3D Models and Functional Genomics in Preclinical Drug Development

Alejandro Amador, PhD, Scientific Leader, Platform Biology Automation, GSK

The current preclinical oncology drug discovery paradigm involves lengthy and costly optimization/lead discovery campaigns, often using cellular or *in vivo* tumor models with weak translational relevance that don't closely resemble human solid tumors. I will highlight opportunities/challenges in implementing 3D solid tumor models. I will outline key components that should be considered when developing, validating, scaling, and automating 3D solid tumor models that are more physiologically relevant.

11:40 Adult Stem Cell Organoids: A Patient in the Lab

Robert Vries, PhD, CEO, Hubrecht Organoid Technology (HUB)

Key to the development of the HUB Organoid Technology was the discovery of adult stem cells by Hans Clevers. Provided with the appropriate growth factors, the adult stem cells form a polarized epithelium in which stem cells and their differentiated offspring maintain their natural hierarchy and function. In addition, the organoids are genetically stable during prolonged culture. Subsequently, we developed Organoid technology for most other epithelia. High-establishment efficiency means that we can use the Organoid Technology to generate disease models from virtually all patients.

12:00 pm Understanding Donor-to-Donor Variability in Healthy Human Gut-Derived Organoids

Linda Lieberman, PhD, Principal Scientist, Merck Exploratory Science Center

Primary organotypic cultures need to be robust and reproducible with limited donor-to-donor variability to advance discovery research toward complex functional tissue biology, yet donor-to-donor variability has not been characterized systematically for many human organoid systems. We established intestinal organoid cultures from adult stem cells of healthy donors and characterized inter- and intra-culture variability. We found that differentiation patterns were consistent among cultures and passages, producing all expected intestinal cell types.

12:20 *In vitro* Generation of Cancer-Associated Fibroblasts for 3D Culture Modeling of Immune-Excluded Tumors

Joanna Lee, PhD, Scientist, Genentech

The transcriptional regulator YAP is considered a universal mechanotransducer, based largely on 2D culture studies. We show a lack of YAP activity in cells in 3D culture and *in vivo*, which is associated with drastic changes in nuclear morphology relative to cells in 2D culture. This work highlights the context-dependent role of YAP in mechanotransduction, and establishes that YAP does not mediate mechanotransduction in breast cancer.

12:55 Transition to Lunch

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:30 Session Break

HOW TO SCALE UP 3D MODELS FOR HTS OR UHTS

2:00 Chairperson's Remarks

Virneliz Fernandez Vega, Scientific Associate, Molecular Medicine, Scripps Research

2:05 3D Enteroid-Derived "Gut-in-a-Dish" Model for Developing Personalized Therapies for Chronic Inflammatory Diseases

Soumita Das, PhD, Associate Professor, Department of Pathology, Chief Scientific Director, HUMANOID Center of Research Excellence (CoRE), University of California, San Diego

We have developed a Gut-in-a-dish model from 3D organoids isolated from the intestinal specimens of healthy and diseased patients. This

model consisting of epithelial cells, immune cells, and microbes could be utilized to investigate mechanisms for gastrointestinal inflammatory diseases, both oncogenic and non-oncogenic. A semi-HTP format of the model can be useful for the identification of new diagnostic and therapeutic targets, personalization of therapies through Phase "0" human trials, and much more.

2:35 3D Models of Brain Cancer for Precision Medicine Therapeutic Profiling

Virneliz Fernandez Vega, Scientific Associate, Molecular Medicine, Scripps Research

Our goal is to develop and validate a precision medicine therapeutic profiling technology by implementing rapid, cost-effective, physiologically relevant, functional 3D models of brain cancer for phenotypic evaluation of anti-cancer drugs. This combined with molecular pathology has been implemented into clinically pertinent information, which will improve the quality and speed of a physician's decision-making for drug selection in treating cancer in a patient-specific manner.

3:05 Development of a Miniaturized 3D Organoid Culture Platform for Ultra-High-Throughput Screening (uHTS)

Yuhong Du, PhD, Associate Professor, Department of Pharmacology and Chemical Biology, Associate Director, Emory Chemical Biology Discovery Center (ECBDC), Emory University School of Medicine

"Organoids" with an extracellular matrix to support 3D architecture offer a new approach for drug discovery. However, it has been challenging for high-throughput screening (HTS)-based drug discovery due to technical difficulties. We have developed such a 3D organoid culture with an extracellular matrix in high-density, 1536-well plate for ultra-HTS (uHTS), and validated its application for large-scale primary compound screening. Our miniaturized platform provides an enabling technology to accelerate organoid-based drug discovery.

3:35 Methods and Media for the Differentiation of Human Intestinal Organoids and Organoid-Derived Monolayers

Sponsored by STEMCELL™ TECHNOLOGIES

Martin Stahl, Scientist, R&D Intestinal, Stemcell Technologies Inc.

Organoid cultures have redefined the limits of biological data that can be obtained *in vitro*. Learn about how IntestiCult™ Organoid Differentiation Medium drives the differentiation of organoids and organoid-derived monolayer cultures into a more functional, differentiated epithelium that better recapitulates the cellular composition and function of the human intestinal epithelium.

3:50 CO-PRESENTATION: Advanced Peptide Hydrogels for 3D Models, Lab-on-Chip, and hiPSCs

Sponsored by PepGel

Susan Sun, CTO, PepGel LLC

Todd Ringhouse, General Manager, PepGel LLC

PGmatrix 3D Models for cells, spheroids, and organoids from a variety of cells, stimulate the secretion of *in vivo*-like extracellular vesicles (exosomes). Biologically formed stem cell spheroids in PGmatrix demonstrate high pluripotency and differentiation potential at molecular levels. PGmatrix system is affordable, scalable, injectable, bioprintable, microfluidable and beyond.

4:05 Networking Refreshment Break and Transition to Keynote

PLENARY KEYNOTE SESSION
4:25 - 6:05

Driving Entrepreneurial Innovation to Accelerate Therapeutic Discoveries

The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare.

Moderator: Nadeem Sarwar, President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai Inc.

Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV

Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer

John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council

See Plenary Keynotes Page for More Information.

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

7:10 Close of Day

Disease Modeling

3D Cellular Modeling • iPSCs • Bioengineered Models

WEDNESDAY, JUNE 3

iPSC-BASED MODELS

With advances in reprogramming and differentiation technologies, as well as with the recent availability of gene editing approaches, we are finally able to create more complex and phenotypically accurate cellular models based on pluripotent cell technology. This opens new and exciting opportunities for pluripotent stem cell utilization in early discovery, preclinical, and translational research. Day 2 of the Disease Modeling conference at World Pharma Week is designed to bring together experts and bench scientists working with induced pluripotent cells, end-users of their services, and researchers working on finding cures for specific diseases and disorders.

7:30 am Registration Open and Morning Coffee

UTILIZING iPSC TO MODEL DISEASES AND EXPLORE TOMORROW'S THERAPEUTICS

8:10 Chairperson's Remarks
Stefan Braam, PhD, CEO, Ncardia

8:15 FEATURED PRESENTATION: Generation, Validation & Application of iPSC Models in Early Discovery
Lisa Mohamet, PhD, Scientific Leader, Drug Design & Selection, GSK
This presentation will focus on the use of iPSC-derived platforms, complex *in vitro* models to improve disease relevance in phenotypic screening, and target engagement.

8:45 Using "Brains-in-a-Dish" to Investigate Developmental Features of Huntington Disease
*Mahmoud Pouladi, PhD, Principal Investigator, Agency for Science, Technology and Research (A*STAR) and National University of Singapore (NUS)*
Cerebral organoids grown from human embryonic and pluripotent stem cells can be used to perform detailed studies on brain development and to understand cellular mechanisms underlying Huntington's disease. Details of these findings and other possible applications will be discussed.

9:15 Development of Patient-Derived iPSC Models and Phenotypic Assays for Early Drug Discovery in Neuroscience
Yoshiyuki Tsujihata, PhD, Director, Phenotypic Reverse Translation Lab, Neuroscience Drug Discovery Unit, Takeda Pharmaceutical Company Limited
Phenotypic assay/screening, with patient iPSC-derived models and quantitative image analysis, is an attractive strategy to develop innovative drugs in neurological disorders. Our strategy is to create simple and complex assay systems comprised of iPSC-derived neurons and glial cells and quantitatively capture pathological events, such as synapse plasticity and mitochondrial dysfunction. Those are being developed with a robustness that not only supports initial screening, but also downstream pharmacological and mechanistic evaluations.

9:45 Talk Title to be Announced
Blake Anson, PhD, Vice President, Business Operations, StemoniX

Sponsored by StemoniX

10:00 Presentation to be Announced

Sponsored by maxwell BIOSYSTEMS

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

BIOENGINEERED BLOOD-BRAIN BARRIER MODELS

11:00 Reconstruction of the Human Blood-Brain Barrier *in vitro* Reveals the Pathogenic Mechanisms of APOE4 in Cerebral Amyloid Angiopathy
Joel Blanchard, PhD, Postdoctoral Fellow, Picower Institute for Learning and Memory, MIT
Alzheimer's disease leads to amyloid deposits along cerebral vasculature which impair the function of the blood-brain barrier (BBB) and accelerate cognitive degeneration. APOE4 is the strongest risk factor for cerebrovascular amyloid pathology (CAA) and Alzheimer's disease (AD); however, the underlying pathogenic mechanisms are unknown. We developed an *in vitro* model of the human BBB that revealed the mechanisms through which APOE4 predisposes amyloid deposition, and uncovered new therapeutic opportunities for CAA and AD.

11:30 3D Alzheimer's Disease (AD) Model for Studying the Blood-Brain Barrier Dysfunctions in AD
Yoojin Shin, PhD, Postdoctural Fellow, Mechanical Engineering, Roger Kamm's Lab, MIT
We have developed a physiologically relevant three-dimensional (3D) Alzheimer's disease (AD) model with a neurovascular unit (blood-brain barrier, BBB) including human neurons, astrocytes, pericytes, and brain endothelial cells in a microfluidic system. Using this model, we have investigated BBB dysfunction, such as the increase in permeability and abnormal angiogenesis in AD, and explored whether Aβ and/or toxic molecules disrupt normal BBB function.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 LUNCHEON PRESENTATION: Structural Maturation in the Development of hiPSC-Cardiomyocyte Models for Preclinical Safety, Efficacy, and Discovery

Sponsored by NANOSURFACE BIOMEDICAL

Nicholas Geisse, PhD, CSO, NanoSurface Biomedical
HiPSC-CM maturation is sensitive to structural cues from the extracellular matrix (ECM). Failure to reproduce these signals *in vitro* can hamper experimental reproducibility and fidelity. Engineering approaches to address this gap typically trade off complexity with throughput, making them difficult to deploy in the modern development paradigm. NanoSurface technology leverages scalable engineering approaches in a cell-, assay-, and instrument-agnostic manner. It can be employed non-disruptively in nearly any workflow to enhance an assay's predictive power.

1:05 Session Break

Disease Modeling

3D Cellular Modeling • iPSCs • Bioengineered Models

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease
Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras
Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine
See Plenary Keynotes Page for More Information.

3:15 Refreshment Break in the Exhibit Hall with Poster Viewing

iPSC FOR TISSUE-CHIPS

4:00 Chairperson's Remarks
Chairperson to be Announced, Maxwell Biosystems

4:05 HiPSC-Based Disease Modeling and Taking iPSC Derivatives to the Clinic
Dhruv Sareen, PhD, Executive Director, Cedars-Sinai Biomanufacturing Center, Director, iPSC Core and Assistant Professor, Departments of Biomedical Sciences and BOG Regenerative Medicine Institute, Cedars-Sinai
This presentation will discuss modeling neurological, metabolic, and pancreatic diseases using iPSCs in different formats *in vitro*, including Tissue-Chips. Then it will discuss a pathway for taking iPSC-derived cells to the clinic describing processes used for cGMP manufacturing, including Cedars-Sinai's new biomanufacturing center.

4:35 Neuromuscular Junction-on-a-Chip Model
Graham Marsh, PhD, Scientist II, Biogen
Modeling the complex physiology of the human NMJ is essential to building our understanding of the underlying biology of diseases. We have developed a 3D co-culture model of the NMJ, including iPSC-derived motor neurons and skeletal muscle cells with physiological and translatable readouts that recapitulate a patient phenotype *in vitro*.

5:05 Find Your Table, Meet Your Moderator

5:10 Roundtable Breakout Discussions

TABLE: Organoids – Is It a Fad or an Enduring Technology?
Moderator: Angela Zhang, PhD, Product Manager, Epithelial Cell Biology, Research & Development, Stemcell Technologies

TABLE: Developing Organs-on-a-Chip/Microphysiological Systems for Drug Discovery
Moderator to be Announced

5:45 Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

THURSDAY, JUNE 4

MPS, ORGANS-ON-A-CHIP, BIOPRINTING

Day 3 of the Disease Modeling conference at World Pharma Week will focus on cellular and tissue engineering and will explore a variety of approaches, including microfluidic engineering methods like organ-on-a-chip, as well as bioprinting. This day will also discuss the applications of such approaches for disease modeling and drug testing.

8:00 am Registration Open and Morning Coffee

PLENARY KEYNOTE SESSION
8:30 - 9:40

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility
Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics
See Plenary Keynotes Page for More Information.

9:40 Coffee Break in the Exhibit Hall with Poster Viewing

BIOENGINEERED MODELS FOR DRUG DISCOVERY AND DEVELOPMENT

10:25 Chairperson's Remarks
Roger Kamm, PhD, Cecil and Ida Green Distinguished Professor of Mechanical and Biological Engineering, Departments of Mechanical Engineering and Biological Engineering, Massachusetts Institute of Technology

10:30 KEYNOTE PRESENTATION: PhysioMimetics: Integration of Systems Biology with Organs-on-Chips for Drug Development
Linda Griffith, PhD, School of Engineering Professor of Teaching Innovation, Biological Engineering, and Mechanical Engineering, Massachusetts Institute of Technology

Disease Modeling

3D Cellular Modeling • iPSCs • Bioengineered Models

11:00 IQ MPS Consortium Update

Szczepan Baran, Head, Emerging Technologies, LAS, SO, Novartis

The International Consortium for Innovation and Quality in Pharmaceutical Development (IQ) is a technically-focused organization of pharmaceutical and biotechnology companies with a mission of advancing science and technology to augment the capability of member companies to develop transformational solutions that benefit patients, regulators, and the broader R&D community.

11:30 Biofabrication of 3D Tissues for Disease Modeling and Drug Screening

Marc Ferrer, PhD, Leader, Biomolecular Screening and Probe Development, Division of Pre-Clinical Innovation, National Center for Advancing Translational Sciences, National Institutes of Health (NIH)

The NCATS 3D Tissue Bioprinting Laboratory is using biofabrication techniques together with quantitative assay technologies to produce architecturally and physiologically validated normal and diseased 3D tissue models in multi-well plate format to create an in-tissue assay platform for drug discovery and development that will be more clinically predicative than current *in vitro* cellular models. The presentation will describe the approach used at NCATS to create a portfolio of biofabricated 3D tissue models of the retina, skin, ometum and brain, as in tissue assay platforms for disease modeling, including age-related macular degeneration, atopic dermatitis and several cancers, and for pharmacological testing of toxicity and efficacy effects.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

MODELS TO INFORM DRUG SAFETY AND TOXICITY

2:00 Chairperson's Remarks

Madhu Lal-Nag, PhD, Program Lead, Research Governance Council, Office of Translational Sciences, Center for Drug Evaluation & Research, U.S. Food and Drug Administration

2:05 Emerging Microphysiological Systems for Drug Safety Testing: A Regulatory Perspective

Madhu Lal-Nag, PhD, Program Lead, Research Governance Council, Office of Translational Sciences, Center for Drug Evaluation & Research, U.S. Food and Drug Administration

There is a great need to understand the synergy between the areas of translational and regulatory science research as they pertain to microphysiological systems and their application in evaluating safety and efficacy for therapeutic indications for different disease areas. My presentation will focus on identifying these areas of synergy and focus on the development of microphysiological systems that are a best fit for different applications.

2:35 Microphysiological Systems: Tissues on Chip for Safety, Toxicity, and Efficacy Tools in Precision Medicine

Danilo Tagle, PhD, Associate Director for Special Initiatives, National Center for Advancing Translational Sciences, National Institutes of Health

Microphysiological systems are bioengineered *in vitro* tools that mimic the 3D structure and function of human organ systems and have been developed to improve the predictive assessment of the safety and efficacy of promising therapeutics. The use of human-derived cells and tissues have increased the utility of tissue chips towards modeling diseases and for clinical trials on chips to inform human trial design. This presentation will focus on the latest advances in this promising technology.

3:05 Of Microtissues and Men: Applications of Advanced *in vitro* Systems in Toxicology

Matthew Wagoner, PhD, Director, Investigative Toxicology, Takeda Pharmaceutical

Advanced in vitro cell culture systems are transforming the way we design safer medicines. Here we share case studies of how neural, hepatic, and intestinal organoids are allowing us to more effectively detect and de-risk toxicity, while reducing a reliance on animal models.

3:35 Close of Conference

Preclinical Strategies Models and Tools in Oncology

Platforms and Combinations • Novel Therapeutics • Tumor Models

Recommended Short Course*

SC1: *In vitro* and *in vivo* Modeling for Cancer Research

Separate registration required; see page 8 for details.

TUESDAY, JUNE 2

PLATFORMS AND COMBINATIONS

Immunotherapeutic strategies have changed the way cancers are being treated, providing significant benefit to patients. Despite success, a large fraction of patients does not respond to single-agent therapy. Combination approaches may be the key to improving response rates in these patients. Preclinical immuno-oncology models provide tremendous value for shaping clinical strategies, given that countless potential combinations exist with other immunotherapies, radiation, and/or standard of care.

10:00 am Main Conference Registration Open

MULTI-TARGETED PLATFORMS AND EXTERNAL COLLABORATIONS

11:15 Chairperson's Remarks

Michael Woo, PharmD, Head, Search & Evaluation, Immuno-Oncology, Business Development & Licensing, Novartis Institutes for BioMedical Research, Inc

11:25 KEYNOTE PRESENTATION: Leveraging Multi-Targeting for More Effective Cancer Immunotherapy

Dmitri Wiederschain, PhD, Global Head, Immuno-Oncology Research Therapeutic Area, Sanofi

Cancer immunotherapies with anti-PD-1/PD-L1 checkpoint blockers have revolutionized the treatment of a wide variety of malignancies. However, immunotherapy is ineffective in a significant subset of cancer patients or eventually results in the development of resistance with relapsed disease. Therefore, the future of immuno-oncology is identification of new multi-targeted agents that can elicit robust anti-tumor immunity as single agents and/or be combined with PD1/PDL1 inhibitors to increase the duration and durability of clinical responses. Sanofi is leveraging its rich internal toolbox of therapeutic modalities, including multispecific antibodies, nanobodies and ADCs, to reduce the concept of multi-targeting to practice and convert "cold" non-immunogenic tumors into "hot" tumors with rich and functionally active immune infiltrate.

11:55 Exploring Novel Immunotherapy Combinations to Overcome Resistance to PD-1 Blockade

Russell Jenkins, MD, PhD, Assistant Professor, Medicine, Center for Cancer Research, Massachusetts General Hospital

Cancer immunotherapy with immune checkpoint blockade has transformed the treatment of patients with advanced melanoma, but strategies to overcome resistance are limited. Using molecular and pharmacologic tools, we have confirmed TANK-binding kinase 1 (TBK1) as a novel target to overcome resistance to PD-1 blockade, further supporting the preclinical and clinical development of this novel combination strategy.

12:25 pm External Collaboration in Immuno-Oncology: New Approaches and Business Models

Michael Woo, PharmD, Head, Search & Evaluation, Immuno-Oncology, Business Development & Licensing, Novartis Institutes for BioMedical Research, Inc

The rapid expansion of the field of immune-oncology provoked a spike of venture capital activity and increased the level of external collaboration among pharmaceutical and biotechnology companies. This presentation will focus on strategic consequences of the IO wave for pharma, biotech, and the venture ecosystem.

12:55 Transition to Lunch

1:00 Advances in Patient Derived *in vitro* and *in vivo* Models for Hematology, Solid Tumors and Immuno-Oncology

Sponsored by CHAMPIONS ONCOLOGY

Amy Wesa, PhD, Director of Immuno-Oncology Research, Champions Oncology

Patient-derived models that can be used both *in vivo* and *ex vivo* represent a new mechanism for streamlining testing of therapeutic agents through preclinical development. Innovative translationally relevant models for Immuno-Oncology and hematology that span both *in vitro* and *in vivo* applications will be presented to highlight advances beyond traditional cancer models.

1:30 Session Break

TRANSLATIONAL APPROACHES AND NOVEL TARGETS

2:00 Chairperson's Remarks

Viviana Cremasco, PhD, Investigator III, Exploratory Immuno-Oncology, Novartis

2:05 *In vivo* Imaging Techniques for Model Characterization and Guiding Combination Strategies

Tapan Nayak, PhD, Director, Translational Imaging Biomarkers, Merck & Co., Inc.

The success rate of experimental therapy is difficult to predict, as its efficacy often depends upon the characteristics of the preclinical animal models. The presentation will cover different non-invasive imaging techniques to characterize animal models and the information used to guide combination therapies in animal models.

2:25 TGFβ-Blockade Uncovers Stromal Plasticity in Tumors by Revealing the Existence of a Novel Subset of Interferon-Licensed Fibroblasts

Viviana Cremasco, PhD, Investigator III, Exploratory Immuno-Oncology, Novartis

By performing an unbiased interrogation of tumor mesenchymal cells, our study shows that TGFβ-neutralization leads to a profound

remodeling of CAF dynamics, greatly reducing the frequency and activity of myofibroblasts, while promoting the formation of a novel fibroblast population characterized by strong response to interferon and heightened immunomodulatory properties. These changes are sufficient to drive productive anti-tumor immunity, laying the foundation for future investigations aimed at defining strategies to reprogram CAF composition for cancer therapy.

2:45 Driving Clinical Decisions about Indications and Combination Partners Using Patient-Derived Xenograft Models
Anderson Clark, PhD, Director, Translational in vivo Pharmacology, Translational Innovation Platform, Oncology, EMD Serono
Preclinical tumor models can provide data to drive clinical decisions about responsive indications, biomarkers, suitable combination partners (both standard-of-care and novel agents), and dosing strategies. In this talk, I will present the preclinical strategy that was used to support early clinical development of M2698, a dual inhibitor of p70S6K/AKT, at EMD Serono.

3:05 TAC Development for the Treatment of Solid and Liquid Tumors
Christopher Helsen, PhD, Director, R&D and Head, Platform Development, Triumvira Immunologics Inc.
Triumvira is a clinical-stage company developing T-cell therapies engineered with the proprietary T-cell antigen coupler (TAC). TAC is designed to co-opt the natural TCR independent of MHC showing safe and effective tumor rejection in mouse models of solid and liquid tumors. Triumvira successfully cleared IND/CTA submission for TAC01-CD19 to treat LBCL with a second solid tumor program in preclinical development.

3:35 Presentation to be Announced

Sponsored by OcellO

3:50 Using Quantitative Super-Resolution Imaging to Design Safe and Effective Therapies
Valerio Pereno, Business Development, ONI

Sponsored by ONi

4:05 Networking Refreshment Break and Transition to Keynote

PLENARY KEYNOTE SESSION
4:25 - 6:05

Driving Entrepreneurial Innovation to Accelerate Therapeutic Discoveries
The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare.
Moderator: Nadeem Sarwar, President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai Inc.
Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV
Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer
John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council
See Plenary Keynotes Page for More Information.

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

7:10 Close of Day

WEDNESDAY, JUNE 3

NOVEL THERAPEUTICS

Cancer immunotherapy remains the fastest growing field in oncology, with immune checkpoint inhibitors and T cell therapy as the backbone of current advances in oncology. However, in the form of monotherapy, none of the therapies work as a magic bullet; the quest for effective combination regimens and novel therapies is underway.

7:30 am Registration Open and Morning Coffee

COMBINATION REGIMENS AND NOVEL THERAPEUTICS

8:10 Chairperson's Remarks
Benno Rattel, PhD, Executive Director Research Amgen, CBSS, Amgen

8:15 KEYNOTE PRESENTATION: Rational Development of Immuno-Therapy Combination Regimens
Roy Baynes, MD, PhD, Senior Vice President and Head, Global Clinical Development, CMO, Merck Research Laboratories
After initially defining the breadth and depth of PD-1 antibody (pembrolizumab) monotherapy activity and deploying precision medicine tools across the program, certain biological leads led to the exploration of many combination therapeutic approaches. These included company-owned products, as well as a broad array of external collaborations. Broadly, the approach has encompassed combinations with anti-proliferative agents, targeted therapies, other immuno-therapeutic agents and those addressing specific resistance biology.

8:45 Development of a T-Cell Redirecting CD3 Bispecific Antibody for the Treatment of Gastrointestinal Tumors

Lindsay King, PhD, Associate Research Fellow, Biomedicines Design, Pfizer

PF-07062119 is a novel T-cell redirecting bispecific against tumors expressing Guanylate Cyclase 2C (GUCY2C), a target expressed in more than 90% of CRC, and in other gastrointestinal cancers. We demonstrate tumor selective and potent *in vitro* and *in vivo* efficacy with PF-07062119 in human xenograft models with T-cell adoptive transfer, as well as in an immunocompetent syngeneic model. PF-07062119 shows combination benefits with checkpoint inhibitors and with chemo- and anti-VEGF-therapy.

9:15 Bispecific T Cell Engagers: Overview of Amgen's BiTE® Pipeline

Benno Rattel, PhD, Executive Director Research Amgen, CBSS, Amgen

Bispecific T cell engagers, commonly referred to as BiTE® antibody constructs, can transiently link tumor cells with resting polyclonal T cells for induction of a surface target antigen-dependent redirected lysis of tumor cells. Blinatumomab (BLINCYTO®) is directed against CD19 and is the first approved T cell engaging antibody. The nonclinical characterizations of blinatumomab, as well as of various BiTE® antibody constructs, and their translation into the clinic will be presented.

9:45 Presentation to be Announced

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10:15 Coffee Break in the Exhibit Hall with Poster Viewing

TARGETING INFLAMMATORY MICROENVIRONMENTS AND INFLAMMASOMES

11:00 Friends & Enemies: Spatial Mapping of Regulatory T Lymphocytes in Inflammatory Microenvironments

Shawn O'Neill, DVM, PhD, Senior Director, Global Pathology & Investigative Toxicology, Global Microscopic Imaging Lead, Drug Safety Research & Development, Pfizer Worldwide Research & Development

Tregs are CD4+ T lymphocytes that are central to peripheral immune tolerance, actively inhibiting inflammation upon antigenic stimulation. Tregs thus play a conflicting dual role: as endogenous suppressors of inflammation in autoimmune diseases, while also inhibiting effector CTL from killing tumor cells. In this presentation. we will localize Tregs and CTL by multiplex immunofluorescence and demonstrate spatial mapping of these cells in inflammatory microenvironments by digital pathology using artificial intelligence.

11:30 Targeting Tumor-Promoting Inflammation via the Inflammasome Pathway – Lessons Learned

Pushpa Jayaraman, PhD, Senior Investigator I, Exploratory Immuno Oncology, Novartis Institutes for Biomedical Research

Chronic inflammation via the inflammasome pathway plays a key role in carcinogenesis by accelerating tumor invasiveness, growth, and metastatic spread by promoting an immunosuppressive tumor microenvironment. Our work highlights the pathophysiological role of inflammasome mediator, IL-1b in tumor immunomodulation and that IL-1b blockade might have important consequences on T cell function and checkpoint blockade in cancer.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Session Break

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease

Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras

Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine

See Plenary Keynotes Page for More Information.

3:15 Refreshment Break in the Exhibit Hall with Poster Viewing

NEW MODALITIES

4:00 Chairperson's Remarks

Aaron Goldman, PhD, Faculty and Principal Investigator, Goldman Laboratory Drug Resistance Group, Harvard Medical School

4:05 Targeting Immune Checkpoint TIM-3 for Cancer Immunotherapy

Xiaomo Jiang, PhD, Principal Scientist II, Immuno-Oncology, Novartis Institutes for BioMedical Research

TIM-3 has critical roles in tumor-induced immune suppression. Blockade of TIM-3, alone or in combination with PD-1 pathway blockade, has shown anti-tumor efficacy in several preclinical cancer models and in clinical trials. TIM-3 blockade to activate immune response and control tumor growth could reflect the combined effects on modulating multiple cell types in the complex interactions between cancer and the immune system.

4:25 Novel Fully Synthetic Bicyclic Peptides as Tumor Targeted Immune Cell Modulators

Sailaja Battula, PhD, Associate Director, Immuno-Oncology, Bicycle Therapeutics

CD137 is a validated target for cancer immunotherapy, but antibody approaches targeting CD137 thus far had limited success, likely due to systemic immune activation. We demonstrated that Bicycle's tumor targeted immune cell agonists (TICATM) showed tumor target-dependent immune activation localized to tumor with superior anti-tumor activity in pre-clinical models.

4:45 'Smart' Release Therapeutics Target Multi-Drug Resistance in Solid Cancers

Aaron Goldman, PhD, Faculty and Principal Investigator, Goldman Laboratory Drug Resistance Group, Harvard Medical School

The ability for cancer cells to phenotypically switch and survive under drug pressure, referred to as drug-induced resistance or tolerance, is an emerging, yet poorly understood, mechanism of anticancer therapy

failure. We discovered a novel metabolic pathway induced by the first drug in a standard chemotherapy combination leads to multi-drug resistance. To target this mechanism, we engineered small molecule inhibitors of upstream glucose metabolism with anthracyclines using a 'smart' release mechanism, which improves response to therapy *in vivo*.

5:05 **Find Your Table, Meet Your Moderator**

5:10 **Roundtable Breakout Discussions**

TABLE: Preclinical Strategies for T Cell Therapy
Moderator to be Announced

TABLE: Targeting Inflammasome in Cancer & Beyond
Moderator: Pushpa Jayaraman, PhD, Senior Investigator I, Exploratory Immuno Oncology, Novartis Institutes for Biomedical Research

5:45 **Reception in the Exhibit Hall with Poster Viewing**

6:45 **Close of Day**

THURSDAY, JUNE 4

TUMOR MODELS

Preclinical tumor models are key tools to evaluate the activity of cancer therapies. They are instrumental to understanding the mechanism of action of tested compounds and help with identifying rational combination partners for best anti-tumor efficacy. Next-generation tumor models, preclinical imaging, and translational strategies will be featured at Day 3 of this conference.

8:00 am **Registration Open and Morning Coffee**

PLENARY KEYNOTE SESSION
8:30 - 9:40

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility
Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics
See Plenary Keynotes Page for More Information.

9:40 **Coffee Break in the Exhibit Hall with Poster Viewing**

NEXT-GENERATION MODELING SYSTEMS AND WHAT WE CAN LEARN WITH THEIR HELP

10:25 **Chairperson's Remarks**
Christopher Kemball, PhD, Scientist, Biochemical & Cellular Pharmacology, Genentech

10:30 **Preclinical Modeling Using Human Cancer Xenografts Grown in Immune-Deficient Zebrafish**
David Langenau, PhD, Associate Chief of Research and Director of Molecular Pathology, Massachusetts General Hospital; Associate Professor, Pathology, Harvard Medical School
We have generated immune-compromised zebrafish that lack T-, B- and NK-cells that robustly engraft human cancers. Capitalizing on the optical clarity of zebrafish and facile imaging approaches, we have documented small-molecule therapy responses and dynamic cell killing by CAR T cell- and bispecific T cell-engager antibodies (BITES) at single-cell resolution. Our studies credential the immune-deficient zebrafish as a new platform for preclinical drug studies.

11:00 **CD34+ Stem Cell-Derived Human Dendritic Cells Provide a Physiologically Relevant System to Evaluate the Pharmacology of Therapeutic Molecules**
Christopher Kemball, PhD, Scientist, Biochemical & Cellular Pharmacology, Genentech
Anti-tumor immunity may be enhanced by therapeutic agents that promote dendritic cell expansion and differentiation. To better characterize the pharmacology of these therapies, *in vitro* models are needed that recapitulate physiologically relevant human DC subsets. DCs generated *in vitro* from human CD34+ progenitor cells closely resemble primary blood DCs. We show that CD34-derived DCs can be used to characterize the potency of a therapeutic molecule to drive cDC1 differentiation.

11:30 **Imaging Biomarkers to Guide Development of Cancer Immunotherapeutics**
Tapan Nayak, PhD, Director, Translational Imaging Biomarkers, Merck & Co., Inc.
The success rate of cancer immunotherapy is difficult to predict, as its efficacy often depends not only upon characteristics of the tumor lesions, but also of the tumor microenvironment involving immune cells and soluble mediators. Molecular imaging with Positron Emission Tomography (PET) allows repeated noninvasive *in vivo* measurement of many critical molecular features of tumor lesions and microenvironment, such as metabolism, hypoxia, and immune cell infiltrate, which can assist the knowledge of how cancer immunotherapy works and also facilitates decision making in development of novel cancer immunotherapeutics.

12:00 pm **Sponsored Presentation** *(Opportunity Available)*

12:30 **Transition to Lunch**

12:35 **Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

2:00 Chairperson's Remarks

Virna Cortez-Retamozo, PhD, Lab Head, Senior Scientist, Oncology-Pharmacology, Sanofi

2:05 CRISPR-Based Models in Drug Discovery: Developments, Caveats, and Future Perspectives

Danilo Maddalo, PhD, PharmD, Laboratory Head, Oncology, Novartis

The development and the application of genome-editing techniques *in vivo* has expanded the toolkit of preclinical models to assess drug efficacy and toxicology, as well as the effect of compounds on tumour-microenvironment interaction. Cost- and time-efficient, the talk will give an overview of CRISPR models, how they impacted significantly the workflow of preclinical drug discovery, and their limitations and caveats.

2:35 Transplanted Syngeneic Metastasis Models for Preclinical Applications

Viswanathan Muthusamy, PhD, Research Scientist; Executive Director, Center for Precision Cancer Modeling, Yale School of Medicine

There is a great need for robust *in vivo* preclinical models for evaluation of drugs interfering with metastasis. We have developed several transplantable, syngeneic metastasis models and used these to assess: 1) interventions to prevent colonization and growth in distant organs; and 2) treatment-induced abscopal effects on distant metastases. In preliminary studies, an immune-targeting, intratumorally injected drug candidate reduced metastatic burden and improved survival in one such model.

3:05 Using Humanized Mouse Models to Evaluate IO Therapeutics

Virna Cortez-Retamozo, PhD, Lab Head, Senior Scientist, Oncology-Pharmacology, Sanofi

The success of early cancer immunotherapies has led to the development of several new therapeutic approaches, including T cell engagers. T cell engagers are typically bispecific Abs directed against the T cell and a tumor-associated antigen, whose therapeutic strategy is to: 1) engage T cells; 2) activate the T cells; and 3) engage tumor cells and induce tumor cell killing. Preclinical evaluation relies on development of models that mirror some properties of a human setting to assess the therapeutic properties of T cell engagers.

3:35 Close of Conference

Advances in Drug Metabolism & Safety Testing

Lead Optimization • Predicting Toxicity • Safety for New Modalities

Recommended Short Course*

SC4: Optimizing Drug Metabolism, Drug Clearance and Drug-Drug Interactions

Separate registration required; see page 8 for details.

TUESDAY, JUNE 2

OPTIMIZING DRUG METABOLISM

Lead compounds need to be optimized for metabolism and safety early in the drug development process. Day 1 in the Advances in Drug Metabolism & Safety Testing conference looks at some innovative tools and strategies that are being utilized for lead optimization, particularly for drug metabolism, dosing, and drug-drug interactions. How to utilize these tools for evaluating and optimizing new drug modalities will also be discussed.

10:00 am Main Conference Registration Open

EARLY METABOLISM & SAFETY ASSESSMENTS

11:15 Chairperson's Remarks

Li Di, PhD, Research Fellow, Pharmacokinetics, Dynamics and Metabolism, Pfizer

11:25 The Impact of Intracellular Free-Drug Concentration on Prediction of Clearance and Drug-Drug Interaction

Li Di, PhD, Research Fellow, Pharmacokinetics, Dynamics and Metabolism, Pfizer

A novel *in vitro* method has been developed to estimate *in vivo* live-to-plasma unbound partition coefficient (Kpuu). The method uses hepatocytes in 4% bovine serum albumin (BSA). BSA plays an important role in maintaining transporter functional activities, similar to *in vivo*. *In vitro-in vivo* correlation (IVIVE) has been established for liver Kpuu and clearance-mediated by both enzymes and transporters. Applications of the method to predict human clearance and drug-drug interaction (DDI) will be discussed.

11:55 Incorporating Complex *in vitro* Models in Drug Safety Assessment

Terry Van Vleet, PhD, DABT, Director, Investigative Toxicology, Department of Preclinical Safety, AbbVie

This talk will discuss some example applications of complex *in vitro* models in early drug safety assessments. A comparison of 2D and 3D model outcomes will be presented as well for perspective.

12:25 pm Complex *In vitro* Models for ADME Applications: Current Status and Future Perspectives

Jinping Gan, PhD, Senior Principal Scientist, Pharmaceutical Candidate Optimization, Research & Early Development, Bristol-Myers Squibb

The evolving landscape of biopharmaceutical R&D demands more predictive and flexible models for many aspects of preclinical sciences, including ADME applications. Complex *in vitro* models, typically of more physiological nature, hold promise to improve translation from preclinical to clinical or from *in vitro* to *in vivo*. In this talk, key gaps in ADME translation will be reviewed, examples of progress will be shared, along with future perspectives.

12:55 Transition to Lunch

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:30 Session Break

ASSESSING NEW DRUG MODALITIES

2:00 Chairperson's Remarks

Donglu Zhang, PhD, Principal Scientist, Drug Metabolism and Pharmacokinetics, Genentech, Inc.

2:05 Local Metabolism Leads to Better Understanding of Tissue Drug Concentration for New Modalities

Donglu Zhang, PhD, Principal Scientist, Drug Metabolism and Pharmacokinetics, Genentech, Inc.

For small-molecule drugs, the liver is the major organ for drug clearance. Liver *in vitro* systems can be used to predict *in vivo* PK. Plasma drug concentration is a good surrogate for tissue concentrations. For new modalities, especially drug conjugates, there is a universal lysosomal degradation of proteins for clearance and generation of active drugs. The efficacy and toxicity is supported by the drug that is released locally in the right form and concentration from a conjugate. This talk discusses the importance of tissue metabolism.

2:35 CRISPR Screens Identify Regulators of Antibody-Drug Conjugate Toxicity

Kimberly Tsui, PhD, Postdoctoral Fellow, Laboratory of Dr. Andrew Dillin, Department of Molecular and Cell Biology, University of California, Berkeley

Using CRISPR-Cas9 screens, we have uncovered many known and novel endolysosomal regulators as modulators of Antibody-drug conjugate (ADC) toxicity. Through comparative analysis of screens with ADCs bearing different linkers, we show that a subset of late endolysosomal regulators selectively influence toxicity of non-cleavable linker ADCs. These results reveal new regulators of endolysosomal trafficking, provide important insights for ADC design and identify candidate combination therapy targets.

3:05 Developing and Embedding an *in vitro* Capability to De-Risk Translational *in vivo* Attributes of Therapeutic Antibody Panels
Daniel Rycroft, Antibody Pharmacology Team Leader and GSK Associate Fellow, Biopharm Molecular Discovery, GSK
While it is well established that small sequence differences between therapeutic monoclonal antibodies cause a range of biophysical attributes which can affect the manufacturability potential of drug candidates, it is now becoming increasingly understood that these same properties can impact *in vivo* suitability. By using a panel of orthogonal *in vitro* methods, it is however possible to de-risk antibody panels for *in vivo* properties without the need for iterative *in vivo* studies.

3:35 Sponsored Presentation *(Opportunity Available)*

4:05 Networking Refreshment Break and Transition to Keynote

PLENARY KEYNOTE SESSION
4:25 - 6:05

Driving Entrepreneurial Innovation to Accelerate Therapeutic Discoveries
The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare.
Moderator: Nadeem Sarwar, President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai Inc.
Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV
Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer
John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council
See Plenary Keynotes Page for More Information.

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

7:10 Close of Day

WEDNESDAY, JUNE 3

PREDICTING DRUG TOXICITY

Day 2 in the Advances in Drug Metabolism & Safety Testing conference focuses on innovative use of screening assays, computational and machine learning tools for better assessing and predicting drug-related toxicities. The talks highlight ways to use CRISPR screening, quantitative modeling, AI/ML algorithms, and high-performance computing to make better and more accurate drug safety predictions early in the drug development process.

7:30 am Registration Open and Morning Coffee

IDENTIFYING OFF-TARGET DRUG TOXICITY

8:10 Chairperson's Remarks
Jason Sheltzer, PhD, Principal Investigator, Cold Spring Harbor Laboratory

8:15 Off-Target Toxicity is a Common Mechanism of Action of Cancer Drugs Undergoing Clinical Trials
Jason Sheltzer, PhD, Principal Investigator, Cold Spring Harbor Laboratory
We have recently applied CRISPR mutagenesis to demonstrate that many putative targeted inhibitors in clinical trials kill cancer cells independently of their reported targets. This off-target toxicity raises significant safety concerns and may contribute to the frequent failure of new anti-cancer drugs. We discuss multiple genetic strategies to ensure on-target drug activity and to minimize potentially harmful off-target interactions.

8:45 Novel Microbiome-Targeting Drugs to Improve the Therapeutic Window of Prescription Medicines
Ward Peterson, PhD, President & CEO, Symberix Inc.
The use of various classes of prescription medicines are frequently associated with dose-limiting intestinal sequelae. These drugs undergo glucuronidation by liver UDP-glucuronosyltransferases and subsequent de-glucuronidation by gut bacterial b-glucuronidases (GUS), resulting in the production of toxic drug catabolites in the intestinal lumen. Symberix's approach for ameliorating these toxicities is to selectively inhibit bacterial GUS with microbiome-targeting "symbiotic drugs" that do not damage the endogenous microbiota.

9:15 Application of Tox21 qHTS Data in Predicting Drug Toxicity
Ruili Huang, PhD, Group Leader, Tox21 Informatics, National Center for Advancing Translational Sciences, National Institutes of Health
Target-specific, mechanism-oriented *in vitro* assays post a promising alternative to traditional animal toxicology studies. The Tox21 program, a large-scale *in vitro* chemical toxicity screening effort, has tested ~10K drugs and environmental chemicals in quantitative high-throughput screening (qHTS) format against a panel of ~70 assays, producing more than 100 million data points to date. Strategies will be discussed on applying this rich set of *in vitro* activity profiles to assess potential drug toxicity.

9:45 Sponsored Presentation *(Opportunity Available)*

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

Advances in Drug Metabolism & Safety Testing

Lead Optimization • Predicting Toxicity • Safety for New Modalities

STRATEGIES FOR EARLY RISK ASSESSMENTS

11:00 Using DILIsym to Predict Hepatotoxicity Risk during Preclinical Development

Paul Michalski, PhD, Investigator, Systems Modeling and Translational Biology, GlaxoSmithKline

DILIsym is a quantitative systems toxicology (QST) model of drug-induced liver injury (DILI) developed primarily to provide mechanistic understanding of clinically observed hepatotoxicity. We recently evaluated DILIsym as a screening tool for preclinical development. Here we will give an overview of DILIsym and discuss the results of our evaluation, highlighting where DILIsym can provide value in early development. We also provide practical advice on the steps required to industrialize DILIsym as an in-house screening tool.

11:30 Accelerating Drug Discovery through Accurate Safety Predictions: One Goal of The ATOM Consortium

Sarine Markossian, PhD, Specialist, Department of Pharmaceutical Chemistry, University of California San Francisco

The Accelerating Therapeutics for Opportunities in Medicine (ATOM) consortium is an academia, industry, and government partnership with the goal of rapidly accelerating drug discovery by integrating high-performance computing and diverse biological data. One of our goals in ATOM is to optimize preclinical safety predictions, so we can incorporate predictive toxicology early in the drug discovery process. Here we present our strategy and efforts towards reliably measuring and predicting drug-induced liver injury (DILI).

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Session Break

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease

Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras

Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine

See Plenary Keynotes Page for More Information.

3:15 Refreshment Break in the Exhibit Hall with Poster Viewing

USE OF AI/ML FOR ADME/Tox PREDICTIONS

4:00 Chairperson's Remarks

Barun Bhhatarai, PhD, Investigator, Novartis Institute for Biomedical Research

4:05 ML and AI on ADME/Tox Accelerating Drug Discovery

Barun Bhhatarai, PhD, Investigator, Novartis Institute for Biomedical Research

ML- and AI-related approaches have been tested and applied in various areas within Novartis. In ADMETox, ML approaches are serving intended purposes and complementing experimental methods. With the advent of AI, ingenious deep learning algorithms, and powerful micro-processors, we have explored its anticipated benefit in preclinical and clinical programs. Our various efforts on data digitization, ML and AI implementation, and collaborations will be discussed with specific examples from ADMETox.

4:35 Artificial Intelligence and Small-Molecule Drug Metabolism

Joshua Swamidass, MD, PhD, Assistant Professor, Immunology and Pathology, Laboratory and Genomic Medicine; Faculty Lead, Translational Informatics, Institute for Informatics, Washington University

We have been building artificial intelligence (AI) models of metabolism and reactivity. Metabolism can both render toxic molecules safe and safe molecules toxic. The AI models we use quantitatively summarize the knowledge from thousands of published studies. The hope is that we could more accurately model the properties of medicines to determine whether metabolism renders drugs toxic or safe. This is one of many places where artificial intelligence could give traction on the difficult questions facing the industry.

5:05 Find Your Table, Meet Your Moderator

5:10 Roundtable Breakout Discussions

TABLE: Impact of Artificial Intelligence and Machine Learning on Drug Safety Assessments

Moderators: Barun Bhhatarai, PhD, Investigator, Novartis Institute for Biomedical Research

Joshua Swamidass, MD, PhD, Assistant Professor, Immunology and Pathology, Laboratory and Genomic Medicine; Faculty Lead, Translational Informatics, Institute for Informatics, Washington University

TABLE: Traditional and Advanced Models and Strategies for Early Risk Assessments

Moderators: Terry Van Vleet, PhD, DABT, Director, Investigative Toxicology, Department of Preclinical Safety, AbbVie

Paul Michalski, PhD, Investigator, Systems Modeling and Translational Biology, GlaxoSmithKline

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5:45 Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

Advances in Drug Metabolism & Safety Testing

Lead Optimization • Predicting Toxicity • Safety for New Modalities

THURSDAY, JUNE 4

IMPROVING TRANSLATION INTO CLINIC

Translation of preclinical findings to the clinical setting remains a formidable challenge in drug development. Day 3 in the Advances in Drug Metabolism & Safety Testing conference focuses on attempts being made to reduce those gaps in translation and to find better ways to accurately predict clinical outcomes. The talks will highlight scientific and technical innovations and applications that are making this possible.

8:00 am Registration Open and Morning Coffee

PLENARY KEYNOTE SESSION
8:30 - 9:40

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility
Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics
See Plenary Keynotes Page for More Information.

9:40 Coffee Break in the Exhibit Hall with Poster Viewing

OVERCOMING TRANSLATIONAL CHALLENGES

10:25 Chairperson's Remarks
James Hickman, PhD, Founding Director, NanoScience Technology Center and Professor, Nanoscience Technology, Chemistry, Biomolecular Science, Material Science and Electrical Engineering, University of Central Florida

10:30 Lost in Translation: Challenges in Interpreting *in vitro* Studies Using Human-Derived Tissues
Gary Gintant, PhD, Senior Research Fellow, Department of Integrative Pharmacology, Integrated Science and Technology, AbbVie
With the advent of human-derived cells and tissues has come newfound challenges for the translation of *in vitro* study findings to guide drug development. This presentation will focus on biological and platform-related challenges (and potential solutions) for nonclinical safety studies with human-derived tissues.

11:00 Human Heart Slices as a Reliable Platform for Predicting Cardiotoxicity
Tamer Mohamed, PhD, Assistant Professor of Medicine, Institute of Molecular Cardiology, University of Louisville
Culturing human heart slices is a promising model of intact human myocardium. This technology provides access to the complete 3D multicellular system that is similar to the human heart tissue that reflects the human myocardium in physiological or pathological conditions, both functionally and structurally. Recently, we have developed a novel biomimetic culture system that maintains full viability and functionality of human and pig heart slices (300 µm thickness) for 6 days in culture.

11:30 Human-on-a-Chip Applications in ADME/Tox to Predict Clinical Outcomes
James Hickman, PhD, Founding Director, NanoScience Technology Center and Professor, Nanoscience Technology, Chemistry, Biomolecular Science, Material Science and Electrical Engineering, University of Central Florida
Multi-organ human-on-a-chip platforms have been used to demonstrate concurrent measurement of efficacy and toxicity for therapeutic index estimation. Evaluation of drugs and compounds has shown similar responses to results seen from clinical data, as well as demonstrated long-term (28-day) function. Applications for ALS, Alzheimer's, rare diseases, diabetes, and cardiac mechanistic toxicity will be reviewed. The development of *in vitro* PDPK models that are being used to predict *in vivo* results will also be presented.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

2:00 Chairperson's Remarks
Madhu Lal-Nag, PhD, Program Lead, Research Governance Council, Office of Translational Sciences, Center for Drug Evaluation & Research, U.S. Food and Drug Administration

2:05 Emerging Microphysiological Systems for Drug Safety Testing: A Regulatory Perspective
Madhu Lal-Nag, PhD, Program Lead, Research Governance Council, Office of Translational Sciences, Center for Drug Evaluation & Research, U.S. Food and Drug Administration
There is a great need to understand the synergy between the areas of translational and regulatory science research as they pertain to microphysiological systems and their application in evaluating safety and efficacy for therapeutic indications for different disease areas. My presentation will focus on identifying these areas of synergy and focus on the development of microphysiological systems that are a best fit for different applications.

2:35 Microphysiological Systems: Tissues on Chip for Safety, Toxicity, and Efficacy Tools in Precision Medicine

Danilo Tagle, PhD, Associate Director, Special Initiatives, National Center for Advancing Translational Sciences, National Institutes of Health

Microphysiological systems are bioengineered *in vitro* tools that mimic the 3D structure and function of human organ systems and have been developed to improve the predictive assessment of the safety and efficacy of promising therapeutics. The use of human-derived cells and tissues have increased the utility of tissue chips towards modeling diseases and for clinical trials on chips to inform human trial design. The presentation will focus on the latest advances in this promising technology.

3:05 Of Microtissues and Men: Applications of Advanced *in vitro* Systems in Toxicology

Matthew Wagoner, PhD, Director, Investigative Toxicology, Takeda Pharmaceutical

Advanced *in vitro* cell culture systems are transforming the way we design safer medicines. Here we share case studies of how neural, hepatic, and intestinal organoids are allowing us to more effectively detect and de-risk toxicity, while reducing a reliance on animal models.

3:35 Close of Conference

Immuno-Oncology Biomarkers

Patient Selection • Companion Diagnostics • Immune Profiling

Recommended Short Course*

SC3: Fit-for-Purpose Biomarker Assay Development – Performance Characterization and Validation to "Context of Use"

**Separate registration required; see page 8 for details.*

TUESDAY, JUNE 2

PATIENT SELECTION

Integration of precision medicine into clinical trials will provide better patient selection to maximize benefit to the trial participant and provide valuable information for the study sponsor. These sessions will cover novel trial designs, biomarker development strategies, and predicting response and resistance to treatment.

10:00 am Main Conference Registration Open

PRECISION MEDICINE IN ONCOLOGY

11:15 Chairperson's Remarks

Tracy Lively, PhD, Chief, Diagnostics Evaluation Branch; Deputy Associate Director, Cancer Diagnosis Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute

11:25 Precision Medicine Initiatives at the NCI

Tracy Lively, PhD, Chief, Diagnostics Evaluation Branch; Deputy Associate Director, Cancer Diagnosis Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute

The development of predictive markers to guide the use of emerging therapeutic agents requires new approaches to both clinical trials and correlative laboratory science. This talk will present NCI's experience with novel trial designs, including lessons learned from NCI MATCH, and additional approaches to more effective integration of biomarker development into cancer therapy trials.

11:55 Oncology Biomarker Development Strategies in Precision Therapies

Yan Li, PhD, Director, Oncology Biomarkers, Bayer U.S.

This presentation will discuss combining tissue and liquid biopsy to follow the patient's tumor evolution and adding RNA gene expression profiling to DNA to expand clinical options for patients.

12:25 pm How to Catch Them All: Genomic Panels Big and Small

Jennifer Morrissette, PhD, Director, Clinical CytoGenomics Laboratory, Associate Professor, Pathology, University of Pennsylvania

High volume clinical laboratories need to accommodate a variety of specimen types, qualities and quantities. This typically cannot be accomplished using a single method; we have validated a large hybrid-capture based panel and a small amplicon-based companion panel for low-input and/or low-quality DNA. This talk will discuss the decision making process for panel design, both inter- and intra-laboratory. The large panel includes content shared across multiple institutions which have decided to utilize similar methodologies allowing for cross-validation.

12:55 Transition to Lunch

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:30 Session Break

PREDICTIVE BIOMARKERS OF RESPONSE AND RESISTANCE

2:00 Chairperson's Remarks

Hua Eleanor Yu, PhD, Billy and Audrey Wilder Endowed Professor; Co-Leader, Cancer Immunotherapeutics Program, City of Hope Comprehensive Cancer Center

2:05 PD-L1 Immunohistochemistry (IHC) as a Predictive Marker for the PD-1/PD-L1 Axis Blockade

Mari Mino-Kenudson, MD, Professor, Pathology, Harvard Medical School

PD-L1 IHC is a globally accepted predictive biomarker for the PD-1/PD-L1 axis blockade and is now deployed in the most pathology laboratories. Although its appropriate implementation and interpretation are critical, it can be challenging due to the multiple antibody clones/platforms available and given the typically small samples provided. Thus, I will discuss important considerations on pre-analytical, analytical, and post-analytical aspects of PD-L1 IHC for lung cancer and other solid tumors.

2:35 Fatty Acid Oxidation Is a Biomarker for Breast Cancer Chemo-Resistance and CD8 T Cell Suppression

Hua Eleanor Yu, PhD, Billy and Audrey Wilder Endowed Professor; Co-Leader, Cancer Immunotherapeutics Program, City of Hope Comprehensive Cancer Center

We recently demonstrated a critical role of STAT3 in regulating lipid metabolism/fatty acid β-oxidation (FAO) to promote breast CSCs and cancer chemo-resistance. We further show that FAO in tumor CD8+ T effector cells is important for obesity-associated breast tumor progression. Moreover, PD-1 ligation in CD8+ T cells activates STAT3 to increase FAO, inhibiting CD8+ T effector cell functions. Therefore, FAO is a biomarker for breast cancer chemo-resistance and immunosuppression.

3:05 How to "Read" Immune Responses with Exosomes and Other EVs

Jennifer Jones, MD, PhD, Investigator, Laboratory of Pathology; Head, Translational Nanobiology Section, Center for Cancer Research, NCI, NIH

Extracellular vesicles (EVs) are an area of substantial interest in the area of liquid biopsies. However, EV analyses are a frontier with few well-established roadmaps or guides. The pitfalls and potentials of EV studies will be discussed, and a framework for safely proceeding in this area will be presented.

3:35 Using Single-Molecule Imaging of Biomarkers as a Tool to Predict Therapy Response
Ricardo Bastos, Head, Applications, ONI

Sponsored by ONi

4:05 Networking Refreshment Break and Transition to Keynote

PLENARY KEYNOTE SESSION
4:25 - 6:05

Driving Entrepreneurial Innovation to Accelerate Therapeutic Discoveries
The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare.
Moderator: Nadeem Sarwar, President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai Inc.
Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV
Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer
John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council
See Plenary Keynotes Page for More Information.

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

7:10 Close of Day

WEDNESDAY, JUNE 3

IMMUNE PROFILING

Immune profiling promises to identify biomarkers that predict response to immunotherapy and to help monitor its progress. Understanding the tumor microenvironment and mechanisms of tumor immune evasion are the goal of this session.

7:30 am Registration Open and Morning Coffee

INTEGRATED IMMUNE PROFILING AND TUMOR MICROENVIRONMENT

8:10 Chairperson's Remarks
Samir Hanash, MD, PhD, Director, McCombs Institute for Cancer Early Detection and Treatment, MD Anderson Cancer Center

8:15 Integrative Analyses of Environment, Microbiome, Immunity, and Tumor for Precision Oncology
Shuji Ogino, MD, PhD, MS, Professor of Pathology, Brigham & Women's Hospital, Harvard Medical School; Professor, Epidemiology, Harvard T.H. Chan School of Public Health; Chief of Molecular Pathological Epidemiology (MPE) Program, Brigham & Women's Hospital; Associate Member, Broad Institute of MIT and Harvard
The integrative field of immunology-MPE (molecular pathological epidemiology) is an emerging paradigm and can investigate influences of the exposome on tumor-immune interactions, thereby informing immunotherapy research. Using over 1500 colorectal cancer cases with rich data on immune response, whole exome sequencing, RNA-sequencing, tumor neoantigens, and clinical outcomes, proof-of-principle immunology-MPE studies have shown great promise for precision prevention and immuno-oncology.

8:45 The Tumor Immune Microenvironment of Pre-Malignant Lesion in the Pancreas
Elizabeth Thompson, MD, PhD, Assistant Professor, Pathology and Oncology, The Johns Hopkins Hospital
While much work has focused on the tumor immune microenvironment of established cancers, little is known about the immune response to the earliest stages of tumor development. This talk will explore the immune microenvironment of neoplastic precursor lesions in the pancreas, focusing on pancreatic intraepithelial neoplasia and intraductal papillary mucinous neoplasms (IPMN) with emphasis on features predicting grade of dysplastic change and recurrence/progression to malignancies.

9:15 Immune Profiling
Veena Kandaswamy, PhD, Immuno-Oncology Biomarkers, Eli Lilly

9:45 How Biospecimen Sourcing Can Impact Your R&D Results
Vanessa Tumilasci, PhD, Commercial Director, Trans-Hit Bio

Sponsored by TRANS-HIT BIO

Biospecimen sourcing is becoming a challenge for many scientists who need to respect timelines for R&D plans as well as regulatory and ethical constraints. Are the scientists working with the samples aware of all the imperatives to obtain them; quality, respect of laws, ethics and regulations?

10:00 Sponsored Presentation *(Opportunity Available)*

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

INTEGRATED IMMUNE PROFILING AND TUMOR MICROENVIRONMENT (CONT.)

11:00 Molecular Signatures of Tumor Immune Evasion
Samir Hanash, MD, PhD, Director, McCombs Institute for Cancer Early Detection and Treatment, MD Anderson Cancer Center
A wide world of mechanisms leading to tumor immune evasion have emerged. Assessment of these mechanisms has relevance to immunotherapy applications.

11:30 Multiplex Immunofluorescence Tyramide Signal Amplification and Multispectral Imaging Assay to Support Translational Oncology Studies
Edwin Roger Parra Cuentas, MD, PhD, Assistant Professor, Translational

Molecular Pathology; Director of the Multiplex Immunofluorescence and Image Analysis Laboratory, MD Anderson Cancer Center

Multiplex immunofluorescence (mIF) has emerged in the last years as a very powerful tool to study tumor tissues. This revolutionary technology provides important visual techniques for tumor examination in formalin-fixed paraffin-embedded specimens to improve the understanding of the tumor microenvironment, promote new treatment discoveries, aid in cancer prevention, as well as allowing translational studies to be carried out.

12:00 pm **Sponsored Presentation** *(Opportunity Available)*

12:30 **Transition to Lunch**

12:35 **Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 **Session Break**

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease
Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras
Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine

See Plenary Keynotes Page for More Information.

3:15 **Refreshment Break in the Exhibit Hall with Poster Viewing**

BIOMARKERS FOR ONCOLOGY CLINICAL TRIALS

4:00 **Chairperson's Remarks**
Samir Hanash, MD, PhD, Director, McCombs Institute for Cancer Early Detection and Treatment, MD Anderson Cancer Center

4:05 **Pharmacodynamic Profiling of Patients Treated with BLZ945 Demonstrates On-Target Peripheral and Tumor Immune Microenvironment Modulation**
Jennifer Mataraza, PhD, Head, Translational Immuno-Oncology, Novartis Institutes for BioMedical Research

BLZ945 is an oral, highly selective and potent kinase inhibitor of CSF-1R. Both preclinical and clinical evidence demonstrates that blocking (CSF-1R) signaling may lead to depletion of TAMs and increased T cell activation. BLZ945X2101 is an ongoing clinical trial investigating the use of BLZ945 as single agent and in combination with spartalizumab (anti-PD-1) in advanced solid tumors. Biomarker analyses will be discussed as evidence of on-target pharmacodynamic effects of BLZ945 in treated patients.

4:35 **Overview of Genomic Biomarkers in Clinical Trials**
Chetan Deshpande, Clinical Biomarker Assay Lead, Pfizer

Genomics biomarkers have been implemented routinely in clinical trials, especially in oncology, for exploratory endpoints. Over the last few years, molecular testing by NGS has been applied not only to understand the molecular mechanism of the underlying disease but also to gain insights into resistance mechanism. This presentation will review the current trends in implementing genomic biomarkers in oncology clinical trials.

5:05 **Find Your Table, Meet Your Moderator**

5:10 **Roundtable Breakout Discussions**

TABLE: Tumor Immune Microenvironment
Moderator: Elizabeth Thompson, MD, PhD, Assistant Professor, Pathology and Oncology, The Johns Hopkins Hospital

TABLE: Theranostics in Immuno-Oncology
Moderator: Michael Roehrl, MD, PhD, Director, Precision Pathology Center, Memorial Sloan Kettering Cancer Center; Associate Professor, Pathology and Laboratory Medicine, Weill Cornell Medicine

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5:45 **Reception in the Exhibit Hall with Poster Viewing**

6:45 **Close of Day**

THURSDAY, JUNE 4

COMPANION DIAGNOSTICS

The companion diagnostics session will cover biomarker discovery and assay development, patient selection strategies, and identifying biomarkers to monitor patients during treatment.

8:00 am **Registration Open and Morning Coffee**

PLENARY KEYNOTE SESSION
8:30 - 9:40

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility
Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics

See Plenary Keynotes Page for More Information.

9:40 **Coffee Break in the Exhibit Hall with Poster Viewing**

IO BIOMARKERS FOR PATIENT SELECTION AND CLINICAL TRIALS

10:25 **Chairperson's Remarks**
Michael Roehrl, MD, PhD, Director, Precision Pathology Center, Memorial Sloan Kettering Cancer Center; Associate Professor, Pathology and Laboratory Medicine, Weill Cornell Medicine

10:30 Deep Proteome-Based Theranostics in Immuno-Oncology

Michael Roehrl, MD, PhD, Director, Precision Pathology Center, Memorial Sloan Kettering Cancer Center; Associate Professor, Pathology and Laboratory Medicine, Weill Cornell Medicine

Steering the patient's own immune system to fight cancer is a promising direction. However, identifying which patients benefit from such therapies and distinguishing which tumors may be more or less susceptible to immunological attack remain great challenges. We describe deep proteomic approaches to identify novel biomarkers that risk-stratify patients and that could be used to monitor patients before, during, and after IO therapy.

11:00 Patient Selection Strategies during Early Clinical Development – The Use of Big Data to Select Patient Populations

Dirk Brockstedt, PhD, CSO, RAPT Therapeutics

11:30 Biomarkers for Cancer Immunotherapy and Cellular Therapy Selection and Treatment Monitoring

Glen Weiss, MD, MBA, Senior Medical Director, Unum Therapeutics

While several monoclonal antibody immunotherapies and cellular therapies are clinically available to treat advanced cancers, only a minority of patients treated with these agents experience impressive durable responses. How are these therapies selected and how is efficacy monitored? This presentation will highlight current data on biomarkers being used and evaluated for treatment selection and monitoring.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

BIOMARKER DISCOVERY AND ASSAY DEVELOPMENT FOR ONCOLOGY AND IMMUNO-ONCOLOGY

2:00 Chairperson's Remarks

Michael Roehrl, MD, PhD, Director, Precision Pathology Center, Memorial Sloan Kettering Cancer Center; Associate Professor, Pathology and Laboratory Medicine, Weill Cornell Medicine

2:05 Maximizing the Return on Clinical Samples: Considerations for IO Discovery Biomarker Analysis

Amber Donahue, PhD, Senior Manager, Biomarker Clinical Assay Lead, Oncology Clinical Assay Group, Pfizer

Clinical samples are precious and generally limited. There are ways to stretch specimens further, such as aliquoting, or provision of extracted nucleic acid or even data rather than FFPE sections to analyzing laboratories. However, there are considerations necessary to this approach, including careful specimen tracking, freeze/thaw stability, fit-for-purpose cross-validation, and assay limitations.

2:35 Molecular Cytometry: Application to Immuno-Oncology and Possibilities for Precision Oncology

Pratip Chattopadhyay, PhD, Associate Professor, Pathology, Isaac and Laura Perlmutter Cancer Center, NYU-Langone Medical Center

3:05 PANEL DISCUSSION: Integrated Biomarker Approaches

Coverage includes:

- Integrating genomics, genetics, proteomics, post-translational modifications, molecular histology and other data for biomarker discovery
- Informatics tools and data requirements for biomarker identification
- Translational approaches for biomarker discovery, qualification and clinical development
- High-throughput biomarker analysis and data generation
- Integrated biomarker approaches for disease progression monitoring and predicting response to therapy

Moderator: Katherine Call, PhD, Senior Director, Head, Proteogenomics, Sanofi Translational Sciences

Panelists:

Michael Baratta, BA/MCAHPM, Scientific Director and Chief of Staff, Clinical Biomarker Development Innovation, Takeda

Pratip Chattopadhyay, PhD, Associate Professor, Pathology, Isaac and Laura Perlmutter Cancer Center, NYU-Langone Medical Center

Additional panelists to be announced

3:35 Close of Conference

Clinical and Translational Biomarkers

Precision Medicine • Liquid Biopsy • Clinical Trials

Recommended Short Course*

SC3: Fit-for-Purpose Biomarker Assay Development – Performance Characterization and Validation to "Context of Use"

Separate registration required; see page 8 for details.

TUESDAY, JUNE 2

PRECISION MEDICINE

Breakthroughs in precision medicine for oncology lead to targeted therapies based on genetic information about tumor pathogenesis. Presentations in this session will cover recent advances in the development of predictive markers to guide therapy, integration of biomarkers into clinical trials, and tissue and liquid biopsy to understand tumor evolution.

10:00 am Main Conference Registration Open

PRECISION MEDICINE IN ONCOLOGY

11:15 Chairperson's Remarks

Tracy Lively, PhD, Chief, Diagnostics Evaluation Branch; Deputy Associate Director, Cancer Diagnosis Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute

11:25 Precision Medicine Initiatives at the NCI

Tracy Lively, PhD, Chief, Diagnostics Evaluation Branch; Deputy Associate Director, Cancer Diagnosis Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute

The development of predictive markers to guide the use of emerging therapeutic agents requires new approaches to both clinical trials and correlative laboratory science. This talk will present NCI's experience with novel trial designs, including lessons learned from NCI MATCH, and additional approaches to more effective integration of biomarker development into cancer therapy trials.

11:55 Oncology Biomarker Development Strategies in Precision Therapies

Yan Li, PhD, Director, Oncology Biomarkers, Bayer U.S.

This presentation will discuss combining tissue and liquid biopsy to follow the patient's tumor evolution and adding RNA gene expression profiling to DNA to expand clinical options for patients.

12:25 pm How to Catch Them All: Genomic Panels Big and Small

Jennifer Morrissette, PhD, Director, Clinical CytoGenomics Laboratory, Associate Professor, Pathology, University of Pennsylvania

High volume clinical laboratories need to accommodate a variety of specimen types, qualities and quantities. This typically cannot be accomplished using a single method; we have validated a large hybrid-capture based panel and a small amplicon-based companion panel for low-input and/or low quality DNA. This talk will discuss the decision making process for panel design, both inter- and intra-laboratory. The large panel includes content shared across multiple institutions which have decided to utilize similar methodologies allowing for cross-validation.

12:55 Transition to Lunch

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:30 Session Break

BIOMARKERS FOR PATIENT SELECTION

2:00 Chairperson's Remarks

Hua Gong, MD, PhD, Senior Director, Head of Genomics Biomarker Development, Navigate Biopharma, a Novartis company

2:05 Accelerating Oncology Drug Development by Patient Stratification

Hua Gong, MD, PhD, Senior Director, Head of Genomics Biomarker Development, Navigate Biopharma, a Novartis company

This presentation will cover: 1) validation and implementation of "fit-for-purpose" CTA/IUO assays for patient selection; 2) bridging IUO assay to CDx to enable drug approval; 3) emerging technologies for future biomarker assays.

2:35 Predictive Molecular Marker for *C. Difficile* Infection Recurrence

Xuemei Zhao, PhD, Senior Principal Scientist, Merck

This presentation will discuss endogenous serum IgG antibodies to *clostridium difficile* toxin B which are associated with protection against *C. difficile* infection recurrence.

3:05 Cytogenetic and Genomic Correlates Within AML Prognostic Stratification Strategies

Robyn Sussman, PhD, Assistant Director, Molecular Development, Pathology, University of Pennsylvania

Newly diagnosed AML can be stratified into prognostic groups using cytogenetic and genomic findings. We have identified 152 *de novo* AMLs that received both a karyotype and next-generation sequencing study at the time of diagnosis. We compared mutations and cytogenetic abnormalities within prognostic categorizations defined by the European Leukemia Net (ELN) and Medical Research Council (MRC) and found that the functional characterization of a mutation can predict the prognostic category of AMLs.

3:35 Phenotyping the Tumor Microenvironment with Advanced Tissue-

Sponsored by ULTIVUE

Based Multiplexing Assays
Katir Patel, PhD, Field Applications Manager, Ultivue, Inc.
Next-generation multiplex fluorescence immunohistochemistry methods offer new capabilities for scientists to explore the biology of disease within patient tissues. These methods have the potential to enable in-depth cell phenotype characterization and spatial context for more accurate co-expression analysis of the TME through a streamlined multiplex assay.

3:50 **Sponsored Presentation** *(Opportunity Available)*

4:05 **Networking Refreshment Break and Transition to Keynote**

PLENARY KEYNOTE SESSION
4:25 - 6:05

Driving Entrepreneurial Innovation to Accelerate Therapeutic Discoveries
The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare.
Moderator: Nadeem Sarwar, President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai Inc.
Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV
Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer
John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council
See Plenary Keynotes Page for More Information.

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

7:10 **Close of Day**

WEDNESDAY, JUNE 3

LIQUID BIOPSY

Liquid biopsy is an important innovation in precision medicine. While minimally invasive, it allows the early detection of disease and the monitoring of response to therapy. These sessions will consider the application of ctDNA and extracellular vesicles in liquid biopsy, including high-resolution analysis, ultradeep sequencing, and NGS assays sensitivities.

7:30 am **Registration Open and Morning Coffee**

LIQUID BIOPSY IN PRECISION MEDICINE

8:10 **Chairperson's Remarks**
Christian Klose, PhD, Head, R&D, Lipotype GmbH

8:15 **Liquid Biopsies Enabling Precision Medicine**
Jonathan Beer, Director, FPM Lead of Disruptive Technologies, Novartis Precision Medicine
Liquid biopsies are a minimally invasive source of biomarker data with clear benefits in monitoring response to therapy and early detection of disease progression. The US FDA has approved the detection of CTCs as a prognostic marker for several cancer types and has now approved two CDx assays to detect variants in ctDNA. Further technology advances are required in order to deliver on the promise of liquid biopsies utility in precision medicine.

8:45 **High-Resolution, High-Throughput Single Vesicle Analysis**
John Nolan, PhD, Professor, The Scintillon Institute
Extracellular vesicles (EVs, aka exosomes, microvesicles, etc.) are released by all cells and can carry molecular cargo to nearby or distant cells to affect their function. I will review the current state of EV analytics, highlight new minimum information (MI) guidelines for methods and reporting, and present new high-resolution analysis methods for single EV analysis that shed new light on the origins and composition of EVs in biofluids.

9:15 **Personalized Serial Detection of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients with Pediatric Cancers**
Rachel Nga Wan Tam, PhD, Senior Scientific Researcher, Oncology Biomarker Development, Genentech
We have utilized a novel highly sensitive and specific approach (Signetera RUO assay) for the detection and quantification of circulating tumor DNA (ctDNA) by tracking personalized cancer signatures in plasma. By targeting 16 somatic mutations present in the tumor, we can detect ctDNA presence longitudinally in pediatric CNS and solid tumor patients with an estimated LOD of 0.01% tumor DNA in a patient's plasma. It has the potential for the diagnosis and therapeutic monitoring to improve clinical outcomes for children.

9:45 **The Lipidomics BMI: A Clinical Index for Classification, Stratification and Monitoring of Systemic Lipid Metabolism** *Sponsored by* lipotype Lipidomics for a better life
Christian Klose, PhD, Head, Research & Development, Lipotype GmbH
Machine learning was used to predict the BMI of more than 1000 subjects based on plasma lipidomics data. The lipidomics BMI was designed to be integrated into routine clinical trial workflows, holds further information on body fat distribution and revealed a clinically relevant BMI misclassification of 15% of test subjects.

10:00 **Sponsored Presentation** *(Opportunity Available)*

10:15 **Coffee Break in the Exhibit Hall with Poster Viewing**

LIQUID BIOPSY IN PRECISION MEDICINE (CONT.)

11:00 Evaluation of NGS Assay Sensitivities in Liquid Biopsies for MRD
Amelia Raymond, Scientist, Translational Medicine, AstraZeneca

11:30 Liquid Biopsy for Brain Tumors
Brian Nahed, MD, MSc, Associate Professor, Neurosurgery, Harvard Medical School; Associate Director, Neurosurgery Residency Program, Massachusetts General Hospital
Advances in liquid biopsy modalities in cancer have created the pathway for similar analyses in brain tumor patients; however, until recently this has been unsuccessful. Circulating tumor cells, extracellular vesicles, and circulating DNA may provide the long-awaited ability to diagnose and monitor brain tumors.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Session Break

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease
Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras
Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine
See Plenary Keynotes Page for More Information.

3:15 Refreshment Break in the Exhibit Hall with Poster Viewing

BIOMARKERS FOR ONCOLOGY CLINICAL TRIALS

4:00 Chairperson's Remarks
Samir Hanash, MD, PhD, Director, McCombs Institute for Cancer Early Detection and Treatment, MD Anderson Cancer Center

4:05 Pharmacodynamic Profiling of Patients Treated with BLZ945 Demonstrates On-Target Peripheral and Tumor Immune Microenvironment Modulation
Jennifer Mataraza, PhD, Head, Translational Immuno-Oncology, Novartis Institutes for BioMedical Research
BLZ945 is an oral, highly selective and potent kinase inhibitor of CSF-1R. Both preclinical and clinical evidence demonstrate that blocking (CSF-1R) signaling may lead to depletion of TAMs and increased T cell activation. BLZ945X2101 is an ongoing clinical trial investigating the use of BLZ945 as single agent and in combination with spartalizumab (anti-PD-1) in advanced solid tumors. Biomarker analyses will be discussed as evidence of on-target pharmacodynamic effects of BLZ945 in treated patients.

4:35 Overview of Genomic Biomarkers in Clinical Trials
Chetan Deshpande, Clinical Biomarker Assay Lead, Pfizer
Genomics biomarkers have been implemented routinely in clinical trials especially in oncology for exploratory endpoints. Over the last few years, molecular testing by NGS has been applied not only to understand the molecular mechanism of the underlying disease but also to gain insights into resistance mechanisms. This presentation will review the current trends in implementing genomic biomarkers in oncology clinical trials.

5:05 Find your Table, Meet your Moderator

5:10 Roundtable Breakout Discussions

TABLE: Genomics and Biomarker Data Analysis
Moderator: Viswanath Devanarayan, PhD, Global Health of Statistics & Data Sciences, Charles River Laboratories

TABLE: Big Data to Select Patient Populations
Moderator: Dirk Brockstedt, PhD, CSO, RAPT Therapeutics

5:45 Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

THURSDAY, JUNE 4

CLINICAL AND TRANSLATIONAL BIOMARKERS

Clinical and translational biomarkers will address integrated approaches to the discovery and qualification of biomarkers, leveraging technologies for biomarker discovery, fit-for-purpose validation, and translational research strategies.

8:00 am Registration Open and Morning Coffee

8:30 - 9:40
PLENARY KEYNOTE SESSION

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility
Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics
See Plenary Keynotes Page for More Information.

9:40 Coffee Break in the Exhibit Hall with Poster Viewing

Clinical and Translational Biomarkers

Precision Medicine • Liquid Biopsy • Clinical Trials

INTEGRATED APPROACH TO TRANSLATIONAL BIOMARKERS

10:25 Chairperson's Remarks

10:30 Translational Biomarkers – From Discovery to the Clinic

Katherine Call, PhD, Senior Director, Head, Proteogenomics, Sanofi Translational Sciences

Biomarkers are a critical component to advance therapeutic programs and to make informed decisions along the value chain. In Sanofi Translational Sciences, we utilize genomics, genetics, proteomics, molecular histology and informatics approaches to identify candidate biomarkers. This presentation will illustrate multi-pronged and integrated approaches to discover and qualify biomarkers for hand-off for use in development and in the clinic. Several biomarker case studies will be presented.

11:00 Utility of Biomarker Post-Translational Modifications Enabling Patient Stratification

Michael Baratta, BA/MCAHPM, Scientific Director and Chief of Staff, Clinical Biomarker Development Innovation, Takeda

Advances in analytical instrumentation and reagents have afforded researchers the opportunity to interrogate post-translational modifications (PTMs) of protein biomarkers. Analysis of Tau and p181 Tau levels in CSF has been utilized in clinical trials to gain insight as a diagnostic compliment to PET scans, monitoring disease progression and response to therapeutic intervention. Incorporation of expanded Tau PTM analysis as part of a translational research strategy will be presented.

11:30 Leveraging CyTOF Technology for Biomarker Discovery in a Clinical Setting

Emily Thrash, PhD, Scientist, Center for Immuno-Oncology Immune Assessment Laboratory, Dana-Farber Cancer Institute

Biomarker discovery in the clinical immuno-oncology setting is limited by the inherent complexity of the disease and immune response, as well as a lack of developed validated immunophenotyping methodology. With the capability to measure up to 50 parameters from a single cell, mass cytometry (CyTOF) is well poised to overcome these constraints and provide greater breadth and depth of cellular analyses within a sample compared to traditional assays like flow cytometry. Here, I will present our optimized clinical sample CyTOF workflow for high-throughput data generation and biomarker analysis pipeline.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

BIOMARKER DISCOVERY AND ASSAY DEVELOPMENT FOR ONCOLOGY AND IMMUNO-ONCOLOGY

2:00 Chairperson's Remarks

Michael Roehrl, MD, PhD, Director, Precision Pathology Center, Memorial Sloan Kettering Cancer Center; Associate Professor, Pathology and Laboratory Medicine, Weill Cornell Medicine

2:05 Maximizing the Return on Clinical Samples: Considerations for IO Discovery Biomarker Analysis

Amber Donahue, PhD, Senior Manager, Biomarker Clinical Assay Lead, Oncology Clinical Assay Group, Pfizer

Clinical samples are precious and generally limited. There are ways to stretch specimens further, such as aliquoting, or provision of extracted nucleic acid or even data rather than FFPE sections to analyzing laboratories. However, there are considerations necessary to this approach, including careful specimen tracking, freeze/thaw stability, fit-for-purpose cross-validation, and assay limitations.

2:35 Molecular Cytometry: Application to Immuno-Oncology and Possibilities for Precision Oncology

Pratip Chattopadhyay, PhD, Associate Professor, Pathology, Isaac and Laura Perlmutter Cancer Center, NYU-Langone Medical Center

3:05 PANEL DISCUSSION: Integrated Biomarker Approaches

Coverage includes:

- Integrating genomics, genetics, proteomics, post-translational modifications, molecular histology and other data for biomarker discovery
- Informatics tools and data requirements for biomarker identification
- Translational approaches for biomarker discovery, qualification and clinical development
- High-throughput biomarker analysis and data generation
- Integrated biomarker approaches for disease progression monitoring and predicting response to therapy

Moderator: Katherine Call, PhD, Senior Director, Head, Proteogenomics, Sanofi Translational Sciences

Panelists:

Michael Baratta, BA/MCAHPM, Scientific Director and Chief of Staff, Clinical Biomarker Development Innovation, Takeda

Pratip Chattopadhyay, PhD, Associate Professor, Pathology, Isaac and Laura Perlmutter Cancer Center, NYU-Langone Medical Center

Additional panelists to be announced

3:35 Close of Conference

AI for Drug Discovery & Development

Accelerating Drug Discovery - One Use Case At a Time

Recommended Short Course*

SC6: An ML/AI Tutorial: From Basics to Advanced

Separate registration required; see page 8 for details.

TUESDAY, JUNE 2

AI IN DRUG DESIGN AND DRUG DISCOVERY

Artificial Intelligence (AI), especially deep learning and machine learning, is coming out as disruptive technology for the faster discovery and development of innovative therapies. There is a lot of excitement about the opportunities associated with the application of AI. Day 1 of the conference will discuss the challenges and opportunities in applying AI to drug discovery processes, drug design, virtual screening, and *in silico* prediction of therapeutic targets using several use cases.

10:00 am **Main Conference Registration Open**

CHALLENGES AND OPPORTUNITIES

11:15 **Chairperson's Remarks**

Amol Jadhav, PhD, Industry Consultant, Transformational Health, Frost & Sullivan

11:25 **KEYNOTE PRESENTATION: Using AI Tools to Accelerate Drug Discovery**

Cornelis Hop, Vice President, Drug Metabolism & Pharmacokinetics, Genentech

This presentation will delve into the use of Machine Learning- and Artificial Intelligence-based applications in discovery and development projects. A sampling of what will be discussed: a retrospective analysis on predicting potency in drug discovery, use case data from current and past ADMET projects, and external collaborations to establish the benefits of these approaches.

11:55 **Human Genetics-Based Drug Discovery: Challenges and Opportunities**

Narender Gavva, PhD, Director, Early Target Discovery, Takeda California, Inc.

The drug discovery industry adapted patient genetics target identification and validation (TIDVAL) approaches last decade to increase success rates in the clinic. There remain many challenges for human genetics TIDVAL in finding large effect size targets that can prevent or reverse disease progression. The presentation will cover opportunities for longitudinal studies that couple AI for drug discovery.

12:25 pm **Artificial Intelligence Approach to Ligand and Structure-Based Design**

Istvan Enyedy, PhD, Principal Scientist, Medicinal Chemistry, Biogen

Ligand and structure-based methods in combination with machine learning models are necessary components of a drug discovery campaign. We can increase the efficiency of optimizing compounds by combining these methods into a multiparameter optimization platform that combines all three approaches. Preliminary results of this approach will be presented.

12:55 **Transition to Lunch**

1:00 **Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:30 **Session Break**

USE CASES

2:00 **Chairperson's Remarks**

Narender Gavva, PhD, Director, Early Target Discovery, Takeda California, Inc.

2:05 **AI and the Cloud: Novel Ways to Accelerate Innovation**

Todd Neuville, Leader, Worldwide Business Development, LeaderLife Sciences, Amazon Web Services (AWS)

Learn how pharma companies are working with artificial intelligence and machine learning (AI/ML) to accelerate research, enhance their clinical trials, improve manufacturing, and better understand real-world data. Hear how cloud technology is helping to expand the use of AI along the life sciences value chain to accelerate time to market for new products and increase operational efficiency.

2:35 **A Deep Learning Approach to Antibiotic Discovery**

Jonathan Stokes, PhD, Banting Fellow, Collins Lab, Broad Institute of MIT & Harvard

To address the antibiotic-resistance crisis, we trained a deep neural network to predict new antibiotics. We performed predictions on multiple chemical libraries and discovered a molecule from the Drug Repurposing Hub – halicin – that is structurally divergent from conventional antibiotics and displays activity against a wide spectrum of pathogens. Halicin also effectively treated *Clostridioides difficile* and *Acinetobacter baumannii* infections in mice. Deep learning approaches have utility in expanding our antibiotic arsenal.

3:05 **Fringing – Or, How to Best Search for Gold Nuggets**

Clayton Springer, PhD, Computational Chemist, Global Discovery Chemistry, Novartis Institutes for BioMedical Research, Inc.

The Fringing approach is inspired by Kriging. Kriging is a method from geostatistics which estimates the most likely distribution of gold based on samples from a few boreholes. Fringing translates this approach to chemical space and allows algorithmic exploitation and exploration of the chemical space.

3:35 **Sponsored Presentation** *(Opportunity Available)*

4:05 **Networking Refreshment Break and Transition to Keynote**

PLENARY KEYNOTE SESSION
4:25 - 6:05

Driving Entrepreneurial Innovation to Accelerate Therapeutic Discoveries

The life sciences community has an unprecedented scientific arsenal to discovery, develop and implement treatments, cures and preventions that enhance human healthcare.

Moderator: Nadeem Sarwar, President, Eisai Center for Genetics Guided Dementia Discovery (G2D2), Eisai Inc.

Panelists: Anthony Philippakis, Chief Data Officer, Broad Institute; Venture Partner, GV
Barbara Sosnowski, Vice President and Global Head, Emerging Science & Innovation Leads, WWRDM, Pfizer
John Hallinan, Chief Business Officer, Massachusetts Biotechnology Council

See Plenary Keynotes Page for More Information.

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

7:10 Close of Day

WEDNESDAY, JUNE 3

AI IN TRANSLATIONAL RESEARCH AND DEVELOPMENT

On Day 2 of the conference, we will take a deep dive into the preclinical, translational and clinical topics. The conference will examine the role of AI in making sense of clinical data, predicting clinical trial outcomes, finding correct patients for clinical trials, analyzing real-world evidence, making sense of complex medical data, and data integrity. The conference will also explore opportunities through use cases in the preclinical stage such as preformulation studies as well as safety and tox evaluation.

7:30 am Registration Open and Morning Coffee

AI STRATEGIES IN CLINICAL TRIALS

8:10 Chairperson's Remarks

Sean Ekins, PhD, DSc, CEO, Collaborations Pharmaceuticals, Inc.

8:15 KEYNOTE PRESENTATION: AI for Acceleration of Drug Development

Bino John, PhD, Associate Director, Data Science, Clinical Pharmacology and Safety Sciences – Data Science and AI, AstraZeneca

Drug development is an expensive and costly endeavor, costing an average of 2.6 billion dollars to bring a drug to market. Artificial Intelligence is essential in reducing the costs and time to bring these to the clinic. This talk will highlight some of the current AI initiatives at AstraZeneca, spanning chemical and biological data use cases that seek to improve drug design and develop safer medicines.

8:45 AI and ML Approaches to Healthcare Data Integration and Analysis

Shruthi Bharadwaj, PhD, Senior Scientist, Novartis Oncology Precision Medicine

With the increase in availability of clinical trial data, AI and Machine Learning Approaches are becoming imperative in mining and finding clinically significant insights. In this talk, I will provide an overview of the various approaches currently used to tackle the big-data problem in pharma.

9:15 Boosting Clinical Trial Success Rates with AI Strategies

Janaki Iyer, Team Lead/Senior Medical Writer, INVIVO Communications, Inc.

The typical drug discovery and development process, commonly termed as "bench to bedside", lasts about 10-15 years and costs over a billion dollars. Failed clinical trials can lead to tremendous losses in terms of both time and money. This talk will discuss AI strategies as a viable option to enhance trial designs, improve patient recruitment strategies, and advance patient monitoring with the aim of maximizing overall clinical trial success rates.

9:45 Sponsored Presentation *(Opportunity Available)*

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

11:00 Strategies for Building AI-Ready Data Sources and (Semi) Autonomous Reasoning Agents Operating on Top of Them

Marcin von Grotthuss, PhD, Senior Computational Scientist, Broad Institute of Massachusetts Institute of Technology and Harvard

Here, we present a prototype Translator framework and architecture, which we have developed for integrating semantically, annotated Knowledge Sources (over 40) and for creating a data platform to support automated reasoning and serendipitous discovery of new 'facts' or interesting and testable hypotheses. We also discuss the strategies of how to integrate and provide high-value AI-ready data sources as well as how to develop (semi) autonomous reasoning agents that would advance reasoning through innovative uses of these knowledge sources.

AI IN PREFORMULATION STUDIES

11:30 Segmentation and Classification of Crystalline Structures from 3D X-Ray Microscopy Images in Pharmaceutical Tablets

Pradeep Babburi, MS, Data Scientist, R&D, AbbVie, Inc.

Here we present ongoing work using image analysis and machine/deep learning techniques to segment and differentiate the crystalline and amorphous phases of the drug as well as other crystalline substances like silicon dioxide (SiO_2) from 3D x-ray microscopy (XRM) scans. Our work demonstrates the results of basic image analyses, geometric feature extraction, as well as unsupervised and supervised learning models trained to identify the crystalline structures based on their morphology.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Session Break

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease
Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras
Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine
See Plenary Keynotes Page for More Information.

3:15 Refreshment Break in the Exhibit Hall with Poster Viewing

USE OF AI/ML FOR ADME/Tox PREDICTIONS

4:00 Chairperson's Remarks
Barun Bhhatarai, PhD, Investigator, Novartis Institute for Biomedical Research

4:05 ML and AI on ADME/Tox Accelerating Drug Discovery
Barun Bhhatarai, PhD, Investigator, Novartis Institute for Biomedical Research
ML- and AI-related approaches have been tested and applied in various areas within Novartis. In ADMETox, ML approaches are serving intended purposes and complementing experimental methods. With the advent of AI, ingenious deep learning algorithms, and powerful micro-processors, we have explored its anticipated benefit in preclinical and clinical programs. Our various efforts on data digitization, ML and AI implementation, and collaborations will be discussed with specific examples from ADMETox.

4:35 Artificial Intelligence and Small-Molecule Drug Metabolism
Joshua Swamidass, MD, PhD, Assistant Professor, Immunology and Pathology, Laboratory and Genomic Medicine; Faculty Lead, Translational Informatics, Institute for Informatics, Washington University
We have been building artificial intelligence (AI) models of metabolism and reactivity. Metabolism can both render toxic molecules safe and safe molecules toxic. The AI models we use quantitatively summarize the knowledge from thousands of published studies. The hope is that we could more accurately model the properties of medicines to determine whether metabolism renders drugs toxic or safe. This is one of many places where artificial intelligence could give traction on the difficult questions facing the industry.

5:05 Find Your Table, Meet Your Moderator

5:10 Roundtable Breakout Discussions

TABLE: Decoding AI: Making the Case for Artificial Intelligence in the Pharma Industry
Moderator: Amol Jadhav, PhD, Industry Consultant, Transformational Health, Frost & Sullivan

TABLE: Machine Learning in Action: Moving Beyond Hype
Moderator: Sean Ekins, PhD, DSc, CEO, Collaborations Pharmaceuticals, Inc.

5:45 Reception in the Exhibit Hall with Poster Viewing

6:45 Close of Day

THURSDAY, JUNE 4

AI IN R&D STRATEGY AND BUSINESS DECISION

There is a lot of excitement about the opportunities associated with AI, but at the same time, a gap exists in understanding these possibilities. Day 3 gives strategic talks from a business perspective, allowing you to assess the value of investing in AI to supercharge pharma R&D. Also, we discuss the challenges in the adoption and implementation of AI in pharma. We discuss in detail through interactive talks, panels, and discussion issues such as separating the hype from reality, trust, privacy, explainable AI and more.

8:00 am Registration Open and Morning Coffee

PLENARY KEYNOTE SESSION
8:30 - 9:40

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility
Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics
See Plenary Keynotes Page for More Information.

9:40 Coffee Break in the Exhibit Hall with Poster Viewing

10:25 Chairperson's Remarks
Sean Ekins, PhD, DSc, CEO, Collaborations Pharmaceuticals, Inc.

10:30 PANEL DISCUSSION: Challenges in Adoption and Implementation: Hype, Trust, Privacy, and Explainable AI
Moderator: Sean Ekins, PhD, DSc, CEO, Collaborations Pharmaceuticals, Inc.
Panelists:
Joseph Lehar, PhD, Adjunct Professor, Bioengineering and Bioinformatics, Boston University
Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics
Amol Jadhav, PhD, Industry Consultant, Transformational Health, Frost & Sullivan
Jonathan Lefman, PhD, Developer Relations Manager, Healthcare and Life Sciences, Nvidia
Bino John, PhD, Associate Director, Data Science, Clinical Pharmacology and Safety Sciences – Data Science and AI, AstraZeneca
Narender Gavva, PhD, Director, Early Target Discovery, Takeda California, Inc.

AI IN R&D STRATEGY AND BUSINESS DECISION

11:30 Achieving Digital Disruption in Pharma through Artificial Intelligence – Status & Opportunities
Amol Jadhav, PhD, Industry Consultant, Transformational Health, Frost & Sullivan
This presentation will focus around the commercial aspects and call out major current application areas of AI in the pharmaceutical industry. Opportunity assessment within specific sub-segments, themes driving adoption, preview of successful business models and relevant case studies, expectation on returns, and global scenarios will be discussed.

12:00 pm Sponsored Presentation *(Opportunity Available)*

12:30 Transition to Lunch

12:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:05 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

2:00 Chairperson's Remarks
Jonathan Lefman, PhD, Developer Relations Manager, Healthcare and Life Sciences, Nvidia

2:05 Application of AI in Pharma R&D: Use Cases
Jonathan Lefman, PhD, Developer Relations Manager, Healthcare and Life Sciences, Nvidia

2:35 Building a Small Company to Apply Machine Learning for Rare and Neglected Disease Drug Discovery
Sean Ekins, PhD, DSc, CEO, Collaborations Pharmaceuticals, Inc.
Collaborations Pharmaceuticals, Inc. (CPI) aims to streamline the development of drugs for rare and neglected tropical diseases. Using our machine learning technology and combining forces with many academic collaborators, we have identified treatments for parasites (*T. cruzi*), bacteria (*M. tuberculosis*), and viruses (Ebola, HIV, etc.), progressing to *in vivo* models. I will describe how we can also apply this approach for rare diseases.

3:05 Application of DL Approaches for Non-Target-Based Drug Repurposing
Arash Keshavarzi Arshadi, MS, Research Fellow, College of Medicine, University of Central Florida
We talk about the use of DL approaches – especially transfer learning – for predicting the potency of already approved drugs for other diseases. Since the target of the known drugs would be completely different types of biomolecules in different cells, pursuing drug repositioning with target-based approaches would not be applicable. Also, many target molecules or mechanisms of their interactions are not discovered yet. Therefore, non-target approaches would be suitable for this manner. In the case of having low data, we will discuss how transfer learning would increase accuracy and recall.

3:35 Close of Conference

WEDNESDAY, JUNE 3

7:30 am Registration Open and Morning Coffee

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

STATE OF THE ART DISEASE MODELING

10:55 Chairperson Remarks

11:00 Applications of Organoid Technology
Sina Mohammadi, PhD, Associate Principal Scientist, Merck & Co., Inc.

11:15 Drug Discovery Using iPSC-Derived Cells and Phenotypic Screening
Hiroaki Nagai, PhD, Principal Scientist, Phenotypic Reverse Translation Labs, Neuroscience Drug Discovery Unit, Takeda Pharmaceutical Company, Japan

11:30 3D Models of Brain Cancer for Precision Medicine Therapeutic Profiling
Virneliz Fernández-Vega, Scientific Associate, Molecular Medicine, Scripps Florida

11:45 Human Heart Slices as a Reliable Platform for Predicting Cardiotoxicity
Tamer Mohamed, PhD, Assistant Professor of Medicine, Institute of Molecular Cardiology, University of Louisville

12:00 pm Animal Models of Cancer
Viswanathan Muthusamy, PhD, Research Scientist; Executive Director, Center for Precision Cancer Modeling, Yale School of Medicine

12:20 Tissue-Specific Extracellular Matrix Substrates to Accelerate Drug Development
Sponsored by
Evelyn Aranda, Senior Research Scientist, XYLYX BIO INC.
Introducing a standardized, commercial 3D cell culture platform for cancer research and discussing how this platform can reduce the dependence on animal models, and enable more relevant scientific results leading to improved drug discovery process.

12:35 Enjoy Lunch on Your Own

PLENARY KEYNOTE SESSION
1:45 - 3:15

Lgr5 Stem Cell-Based Organoids in Human Disease
Hans Clevers, MD, PhD, Principal Investigator of Hubrecht Institute and Princess Máxima Center, CSO of HUB Organoids Technology

Systematically Drugging Ras
Stephen Fesik, PhD, Professor of Biochemistry, Pharmacology, and Chemistry, Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University School of Medicine
See Plenary Keynotes Page for More Information.

3:15 Refreshment Break in the Exhibit Hall with Poster Viewing

Selected Poster Presentations

4:00 Chairperson Remarks

4:10 Selected Poster Presentations; 10 minutes each

4:40 Voting and Best Poster Award

5:05 Find your Table, Meet your Moderator

5:10 Roundtable Breakout Discussions

5:45 Reception in the Exhibit Hall with Poster Viewing

6:00 Innovation Station

6:45 Close of Day

Drug Discovery Technologies

Enabling Disruptive Innovation

THURSDAY, JUNE 4

8:00 am Registration Open

PLENARY KEYNOTE SESSION
8:30 - 9:40

Applications of Artificial Intelligence in Drug Discovery – Separating Hype from Utility
Patrick Walters, PhD, Senior Vice President, Computation, Relay Therapeutics
See Plenary Keynotes Page for More Information.

9:40 Coffee Break in the Exhibit Hall with Poster Viewing

DRUG TARGET SCREENING AND VALIDATION TECHNOLOGIES

10:25 Chairperson's Remarks

10:30 Ultra-High-Pressure Liquid Chromatography in Pharmaceutical Analysis: Benefits and Impact
Michael Dong, PhD, Principal Consultant, MWD Consulting

10:45 Sponsored Presentation *(Opportunity Available)*

11:00 Accelerating Drug Discovery and Development with an Emerging, Customizable Mode of Microfluidics
Anita Rogacs, PhD, Head of Life Sciences Strategy and R&D, HP Labs

11:15 DNA-Encoded Library Technology for Target-based Screening
Svetlana Belyanskaya, PhD, Encoded Library Technologies, R&D Platform Technology & Science, GSK Boston

11:30 Lipidomics for Pharmacodynamics: How Shotgun Lipidomics Unraveled the Mode-of-Action of the Anti-Tumor Drug Minerval®

Sponsored by lipotype

Christian Klose, PhD, Head, R&D, Lipotype GmbH
Pharmacodynamics studies research the biological effects of drugs and their modes-of-action. It is an integral part of drug discovery. Here, shotgun lipidomics was used to study the molecular effects of the anti-tumor drug Minerval®. The pharmacodynamics study revealed how the compound activates multiple signaling pathways and affects intracellular transport.

11:45 The State of the Art in Highly Multiplexed Multi *in situ* OMICs
Richie Kohman, PhD, Senior Research Scientist and Lead, Synthetic Biology Platform, Wyss Institute for Biologically Inspired Engineering, Harvard University

12:00 pm Women in Pharma Luncheon Panel Discussion
(Sponsorship Opportunity Available)

1:00 Dessert and Coffee Break in the Exhibit Hall with Poster Viewing

1:45 End of Drug Discovery Technologies Track

Hotel & Travel

Conference Venue:
Hynes Convention Center
900 Boylston Street
Boston, MA 02115

Host Hotel:
Sheraton Boston Hotel
39 Dalton Street
Boston, MA 02199
Phone: 1-617-236-2000

Visit PharmaWeek.com/Travel for additional information.

Discounted Room Rate: $329 s/d

Discounted Room Rate Cut-off Date: May 4, 2020

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Pricing and Registration Information

CONFERENCE PRICING

STANDARD PACKAGE (Includes access to 1 conference, excludes short courses)	**Commercial**	**Academic, Government, Hospital-affiliated**	**Student ***
Early - Registration Rate until March 20, 2020	$2,199	$1,149	$495
Advance - Registration Rate until April 24, 2020	$2,399	$1,199	$495
Registrations after April 24, 2020 and On-Site	$2,499	$1,299	$495

C1: Accelerating Target Discovery	C7: Preclinical Strategies, Models & Tools in Oncology
C2: Expanding Chemical & Druggable Space	C8: Advances in Drug Metabolism & Safety Testing
C3: New Small Molecule Drug Targets	C9: Immuno-Oncology Biomarkers
C4: Emerging Indications & Modalities	C10: Clinical and Translational Biomarkers
C5: Immuno-Oncology Advances	C11: AI for Drug Discovery & Development
C6: Disease Modeling	C12: Drug Discovery Technologies (Included with your complete registration)

PRE-CONFERENCE SHORT COURSES

One short course (Short courses run concurrently)	$549	$329	$149

SC1: In vitro and in vivo Modeling for Cancer Research	SC5: Chemoproteomics Enabling Drug Discovery
SC2: Immunology Basics: Focusing on Autoimmunity and Cancer	SC6: An ML/AI Tutorial: From Basics to Advanced
SC3: Fit-for-Purpose Biomarker Assay Development – Performance Characterization and Validation to "Context of Use"	SC7: Intro to OOAC and Bioprinting for Disease Modeling
SC4: Optimizing Drug Metabolism, Drug Clearance and Drug-Drug Interactions	

CONFERENCE DISCOUNTS

Poster Submission - **Discount ($50 Off)**: Poster abstracts are due by April 24, 2020. 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.*

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** Full time graduate students and PhD candidates qualify for the student rate. Students are encouraged to present a research poster and receive an additional $50 off their registration fee. Student rate cannot be combined with any other discount offers, except poster discount. Students must present a valid/current student ID to qualify for the student rate. Limited to the first 100 students that apply.*

If you are unable to attend but would like to purchase the World Pharma Week CD for $750 (plus shipping), please visit PharmaWeek.com. Massachusetts delivery will include sales tax.

ADDITIONAL REGISTRATION DETAILS

Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link.

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