

Cambridge Healthtech Institute's Third Annual

OPT Boston

Oligonucleotide & Peptide THERAPEUTICS

Advancing the Discovery, Development and Delivery of Oligonucleotide and Peptide Therapeutics



March 26-28, 2018

Boston Marriott Cambridge
Cambridge, MA

2018 CONFERENCES



**Oligonucleotide
Discovery and Delivery**



**Peptide Discovery
and Delivery**



Symposium: Drug Discovery for Rare Diseases

SHORT COURSES

- **Oligonucleotide Therapeutics: From Discovery to Manufacturing**
- **Overcoming Challenges with Peptide Delivery**
- **CRISPR-Based Gene Editing for Targeted Therapies**

FEATURED SPEAKERS



**Muthiah (Mano)
Manoharan, PhD**
Senior Vice President,
Drug Discovery, Alnylam
Pharmaceuticals, Inc.



Tomi Sawyer, PhD
Distinguished Scientist,
Discovery Chemistry
Modalities, Merck
Research Laboratories



Melissa J. Moore, PhD
CSO, mRNA Research
Platform, Moderna



Lex Van der Ploeg, PhD
CSO, Rhythm
Pharmaceuticals

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Event At-A-Glance

SUNDAY, MARCH 25	MONDAY, MARCH 26	TUESDAY, MARCH 27	WEDNESDAY, MARCH 28
Short Course*	Oligonucleotide Discovery and Delivery		
	Peptide Discovery and Delivery		Symposium: Drug Discovery for Rare Diseases
	Short Courses*		

*Separate registration required.

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HOTEL & TRAVEL INFORMATION

Conference Venue and Hotel:

Boston Marriott Cambridge Hotel
50 Broadway, Cambridge, MA 02142
Phone: 617-494-6600

Discounted Room Rate: \$199 s/d

Discounted Room Rate Cut-off Date: February 26, 2018

Top Reasons to Stay at the Boston Marriott Cambridge:

- No commute as conference takes place in the hotel
- Located within walking distance from the Kendall/MIT subway station
- 5 Miles from Boston Logan International Airport (BOS) via public transportation
- Nearby to wonderful restaurants and shopping

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Invitation-Only VIP Dinner/Hospitality Suite

Select specific delegates from the pre-registration list to attend a private function at an upscale restaurant or a reception at the hotel. From extending invitations, to venue to suggestions, CHI will deliver your prospects and help you make the most of this invaluable experience.

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For additional sponsorship, exhibit & lead generation information, please contact:

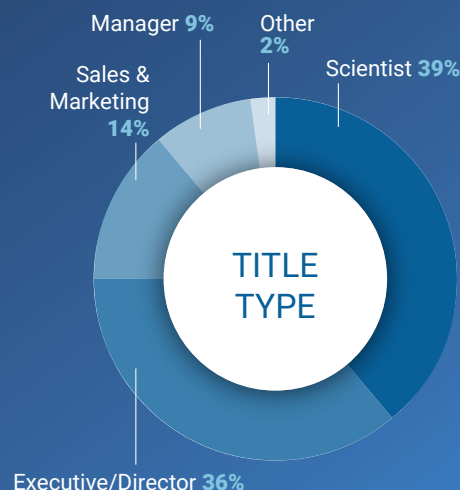
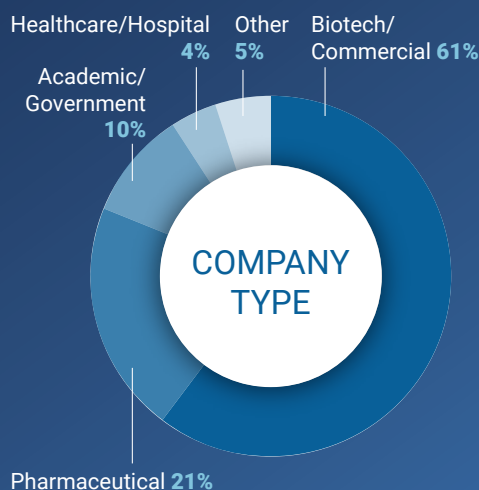
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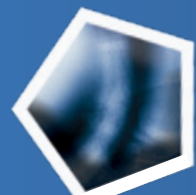
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2017 Attendee Demographics





Oligonucleotide Discovery and Delivery

March 26 - 28, 2018

Advances in the Development and Delivery of Aptamer, Antisense and RNA Therapeutics

Oligonucleotide-based therapeutics have long been considered as forming the third major drug development platform specifically focused on modulating gene expression by targeting RNA transcripts or the genome itself. A key distinguishing attribute of utilizing nucleic acids as therapeutic agents is their ability to access the “undruggable” space left by small molecules and biologics, allowing drug developers to address disease areas currently with limited or no therapeutics options. However, first- and second-generation molecules exhibiting potency and safety issues have hindered the potential of oligonucleotide therapies dramatically impacting the drug development landscape. Recent advances in nucleic acid medicinal chemistry and delivery have led to the creation of a new generation of oligonucleotide therapies harnessing chemical modifications and conjugations to improve their stability, bioavailability, specificity and potency. These advances, along with a robust development landscape, and several late-stage clinical products poised for approval, have led to a sharp resurgence of interest in the discovery of oligonucleotide-based therapeutics.

Due to the remarkable success of the event, Cambridge Healthtech Institute is delighted to host the Third Annual Oligonucleotide Discovery and Delivery conference, March 26-28, in Cambridge, MA. Join leading oligonucleotide developers and discovery scientists to discuss technological and scientific advances in nucleic acid synthesis, medicinal chemistry and delivery, as well as preclinical and clinical findings.

SUNDAY, MARCH 25

4:30 pm Dinner Short Course and Pre-Conference Registration

5:00-8:00 SC1: Oligonucleotide Therapeutics: From Discovery to Manufacturing*

* Separate registration required. See page 14 for details.

MONDAY, MARCH 26

7:00 am Registration and Morning Coffee

ADVANCES IN OLIGONUCLEOTIDE THERAPEUTICS AND DELIVERY

8:00 Welcome Remarks from Conference Director

Kip Harry, Senior Director, Conferences, Cambridge Healthtech Institute

8:10 Chairperson's Opening Remarks

Muthiah (Mano) Manoharan, PhD, Senior Vice President, Drug Discovery, Alnylam Pharmaceuticals, Inc.

8:15 GalNAc-Conjugated siRNAs as a New Paradigm in Oligonucleotide Therapeutics

Muthiah (Mano) Manoharan, PhD, Senior Vice President, Drug Discovery, Alnylam Pharmaceuticals, Inc.

During this presentation, I will discuss the progress in the advancement of RNAi therapeutics and review delivery of RNAi and where the field is going. I will also discuss conjugated delivery of oligonucleotides to the liver and combining novel chemical modifications with conjugation strategies.

8:45 Messenger RNA as a Novel Therapeutic Approach

Melissa J. Moore, PhD, CSO, mRNA Research Platform, Moderna

The contemplation of mRNA as a therapeutic platform has historically been shunned owing to challenges in oligonucleotide delivery and, maybe more importantly, the perceived shortcomings of mRNA with regard to stability and immunogenicity. Significant advances in oligonucleotide delivery have been realized over the past decade thereby enabling mRNA therapeutics. Recent discoveries in mRNA chemistry further enhance the attractiveness of this platform by eliminating innate immune activation and maximizing protein expression.

9:15 Talk Title to be Announced

Punit Seth, PhD, Vice President, Medicinal Chemistry, Ionis Pharmaceuticals

9:45 Sponsored Presentation (Opportunity Available)

10:15 Networking Coffee Break

ADVANCES IN OLIGONUCLEOTIDE THERAPEUTICS AND DELIVERY (CONT.)

10:30 siRNA Therapeutics for Extrahepatic Indications: Quark's Case Study

Elena Feinstein, MD, PhD, CSO, Quark Pharmaceuticals

Quark is active in the field of discovery and development of siRNA therapeutics focusing on acute or subacute indications involving organs other than the liver. An overview of advanced clinical (Phase III) and some of nonclinical programs will be provided.

11:00 Talk Title to be Announced

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

11:30 Development of Stereopure Nucleic Acid Therapeutics

Chandra Vargeese, PhD, Senior Vice President and Head, Drug Discovery, WAVE Life Sciences

WAVE Life Sciences is utilizing its innovative and proprietary synthetic chemistry drug development platform to design, develop and commercialize stereopure nucleic acid therapeutics that precisely target the underlying cause of rare genetic diseases, delivering exceptional treatment options for patients. Given the unique versatility of its chemistry platform, WAVE's pipeline will span multiple oligonucleotide modalities including antisense, exon-skipping and single-stranded RNAi.

12:00 pm Session Break

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

12:40 Session Break

SYNTHESIS AND MEDICINAL CHEMISTRY

1:25 Chairperson's Remarks

Gunnar J. Hanson, PhD, Senior Director, Research Chemistry, Sarepta Therapeutics, Inc.

1:30 Breakthrough Innovation in Phosphorodiamidate Morpholino Oligomer (PMO) Delivery Chemistry

Gunnar J. Hanson, PhD, Senior Director, Research Chemistry, Sarepta Therapeutics, Inc.

Phosphorodiamidate morpholino oligomers (PMOs) enable Watson-Crick binding to pre-mRNA in the nucleus and thereby enable the control of new definitions of intron-exon junctions within the spliceosome. Such splice alteration is limited by the efficiency of PMO delivery into the cytosol and nucleus. To solve this 40-year old delivery problem, new cell-penetrating peptides (CPPs) were designed, which by covalent attachment to PMOs, dramatically enhance the delivery of these macromolecules into the cytosol and nucleus.

2:00 Challenges in the Synthesis of Conjugated LNA Oligonucleotides

Nanna Albaek, PhD, Principal Scientist and Group Leader of New Chemistry, Roche Pharma Research and Early Development, Roche Innovation Center

Recently there has been considerable focus in the conjugation of oligonucleotides with non-nucleotide moieties which, for example, enable targeting of therapeutic oligonucleotides to specific organs and tissues *in vivo*. The conjugation of different chemical moieties to oligonucleotides is often achieved by post-synthetic amide bond formation. This approach requires the synthesis of LNA-oligonucleotides with a primary amine at the 5' end. During this work, we noticed a (to us) new impurity with M+28.

2:30 Approaches to Improve Potency of Antisense Oligonucleotides in Extrahepatic Tissues

Thazha P. Prakash, Director, Medicinal Chemistry, Ionis Pharmaceuticals

Antisense oligonucleotide (ASO)-based drug development is evolving as an effective therapeutic modality. In order to fully realize the potential of this technology, it is necessary to improve the potency of ASOs in extrahepatic tissues. We investigated the effect of conjugating hydrophobic ligand capable of interacting with plasma proteins on productive uptake of ASO into extrahepatic tissues. Our results suggest that conjugation of hydrophobic ligands improved potency of ASOs in extrahepatic tissues.

3:00 Refreshment Break in the Exhibit Hall with Poster Viewing

DELIVERY TO THE CNS

3:45 nOligos: A Cell Specific Oligonucleotide Delivery Platform: Application to MDD and PD Treatments

Andres Montefeltro, PhD, CEO, nLife Therapeutics, S.L.

nLife Therapeutics has developed different nucleic acid chemical modifications with the aim to optimize cell specific delivery capabilities to neurons. We have combined siRNAs and antisense oligonucleotides (ASOs) with some specific and potent small molecule ligands to neuronal receptors or transporters, named nOligos (neuronal specific oligonucleotides). These combinations proved to deliver the nucleic acid to the target neuron in an effective way. Also, the intranasal administration of the modified nucleic acids reached the targeted brain area and neurons in mice and monkeys.

4:15 Expanding the Chemical Diversity of Therapeutic Oligonucleotides

Maire Osborn, PhD, Research Scientist, Khvorova Lab, RNA Therapeutics Institute, University of Massachusetts Medical School

We have identified several novel chemical classes of conjugates that demonstrate markedly improved brain distribution and robust *in vivo* efficacy. Direct conjugation of a fully chemically modified siRNA to docosahexaenoic acid (DHA), the most abundant poly-unsaturated fatty acid in the brain, results in improved tissue retention with wide distribution and robust efficacy in the striatum and cortex after single injection. Most importantly, DHA-hsiRNA conjugates do not induce neural cell death or measurable innate immune activation following administration of concentrations 20-fold over the efficacious dose, establishing a new approach toward development of RNAi-based therapeutics for a wide range of neurodegenerative disorders.

4:45 Sponsored Presentation (Opportunity Available)

5:15 Welcome Reception in the Exhibit Hall with Poster Viewing

6:15 Dinner Short Course Registration

6:30-9:30 SC2: Overcoming Challenges with Peptide Delivery*

* Separate registration required. See page 14 for details.

7:30 am Breakfast Breakout Roundtable Discussions

Grab a cup of coffee and join a roundtable discussion. These are moderated discussions with brainstorming and interactive problem solving, allowing participants from diverse backgrounds to exchange ideas and experiences and develop future collaborations around a focused topic.

For more details, please visit OPTCongress.com

ADVANCES IN RNA THERAPEUTICS AND DELIVERY

8:25 Chairperson's Remarks

Balkrishen (Bal) Bhat, PhD, Vice President, Chemistry, RaNA Therapeutics, Inc.

8:30 Novel Strategies for Endogenous mRNA Upregulation

Balkrishen (Bal) Bhat, PhD, Vice President, Chemistry, RaNA Therapeutics, Inc.

We are developing two gene upregulation platforms. The first approach targets lncRNAs (long non-coding RNA) with chemically modified oligonucleotides to block recruitment of PRC2 to the target gene of interest which results in significant upregulation of mRNA and protein. In the second approach, we selectively upregulate target mRNA and the corresponding protein by stabilizing identified regions of mRNA with chemically modified oligonucleotides.

9:00 microRNA Targeted Therapies for Hematological Malignancies and Pathological Fibrosis: Translation from Basic Sciences to the Clinic

William S. Marshall, PhD, President and CEO, miRagen Therapeutics

9:30 Development of Novel Breakthrough Cancer Therapies Based on the Unique Functions of miRNAs

Roel Q.J. Schaapveld, PhD, MBA, CEO, InterRNA Technologies BV

To explore miRNAs as therapeutic agents for the treatment of cancer, InterRNA Technologies has performed functional screens in cell lines covering different types of cancer. Lead candidates are now advancing in preclinical development programs with a focus on hepatocellular cancer. This presentation will provide insights into the latest progress in the preclinical development of InterRNA's lead miRNA compounds.

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

EMERGING NUCLEIC ACID DEVELOPMENT PLATFORMS

10:30 Chairperson's Remarks

Balkrishen (Bal) Bhat, PhD, Vice President, Chemistry, RaNA Therapeutics, Inc.

10:35 An RNA Aptamer Platform

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

11:05 ZATA's Novel Oligonucleotides (ZONs) with Self-Neutralizing Backbones

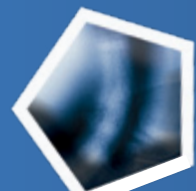
David Tabatadze, PhD, President and CEO, R&D, ZATA

We developed a nucleic acid platform enabling the new generation oligonucleotides (ZONs) comprising target number of branched charge-neutralizing groups (CNGs) on the internucleoside phosphates of ON by phosphotriester bonds. The CNGs are terminated with positively charged amino groups, and are optimized to form ion pairs with the neighboring phosphate groups. ZONs can be synthesized by standard automated phosphoramidite chemistry in good yield and purity.

11:35 Sponsored Presentation (Opportunity Available)

11:50 Session Break

TUESDAY, MARCH 27



Oligonucleotide Discovery and Delivery

March 26 - 28, 2018

Advances in the Development and Delivery of Aptamer, Antisense and RNA Therapeutics

12:00 pm Luncheon Presentation (*Sponsorship Opportunity Available*)
or Enjoy Lunch on Your Own

12:30 Dessert Break in the Exhibit Hall with Poster Viewing

ADVANCES IN OLIGONUCLEOTIDE DELIVERY

1:15 Chairperson's Remarks

Dmitry Samarsky, PhD, CSO, Silence Therapeutics

1:20 Development of Novel Therapies Using Advanced GalNAc-siRNA Technology

Dmitry Samarsky, PhD, CSO, Silence Therapeutics

Silence Therapeutics utilizes RNA interference (RNAi) technology to develop a new generation of drugs to treat serious human diseases with unmet needs. Attachment of the N-acetylgalactosamine (GalNAc) moieties to the RNAi triggers (siRNA) allows the resulting conjugates to travel to the liver and to downregulate genes specifically in hepatocytes. We will present our advances with the GalNAc-siRNA technology, as well progress with company's therapeutic programs.

1:50 A Novel Nano-Medicine Platform for Oligonucleotide Discovery and Delivery

Art Levin, PhD, Executive Vice President, Research and Development, Avidity NanoMedicines

Despite the considerable promise, delivery has proven to be one of the central challenges of oligonucleotide-based therapeutics. Oligonucleotides are large, hydrophilic and highly negatively charged, so they don't cross cell membranes. We have pioneered the development of Precision NanoMedicines, which are targeted, polymeric nanoparticles encapsulating siRNA drug payloads for delivery to specific tumor types. These self-assembling nanoparticles can be decorated with antibodies, proteins, peptides and small molecules to bind to extracellular receptors and facilitate cellular uptake.

2:20 Translation of Messenger RNA Therapeutics from Preclinical Research into Clinical Studies

Pad Chivukula, PhD, CSO & COO, Arcturus Therapeutics

Arcturus has developed a novel, potent and safe RNA therapeutics platform called LUNAR™, a proprietary lipid-enabled delivery system for RNA medicines including small interfering RNA, messenger RNA, antisense and microRNA oligotherapeutics. In addition, we incorporate Unlocked Nucleic Acid (UNA) chemistry into the oligonucleotide drug candidate enabling the targeting of any gene in the human genome. This presentation will provide an update on our lead asset, a UNA-modified, LUNAR-formulated siRNA targeting transthyretin (TTR) for the treatment of TTR-mediated amyloidosis.

2:50 Sponsored Presentation (*Opportunity Available*)

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

NOVEL AND EMERGING APPROACHES FOR IN VIVO DELIVERY

3:35 DsiRNA Applications for Oncology and Chronic Liver Diseases

Marc Abrams, PhD, Senior Director, Preclinical Development, Dicerna Pharmaceuticals, Inc.

Dicerna is advancing two platforms for delivery of Dicer-substrate siRNAs (DsiRNA): EnCore lipid nanoparticles for oncology, and GalNAc-DsiRNA-EX conjugates for liver indications. Lipid Nanoparticle (LNP) technology is an elegant solution for delivery of RNAi triggers, since it enables both bioavailability to target organs as well as the ability to transfect target cells.

4:05 Therapeutic Protein Expression in vivo Using Messenger RNA-Lipid Nanoparticles

Thomas D. Madden, PhD, President and CEO, Acuitas Therapeutics

Therapeutic applications of messenger RNA (mRNA) are currently being advanced into clinical development. However, mRNA is relatively labile and requires a delivery system to efficiently access the cytoplasmic compartment where the mRNA is translated. Acuitas is developing lipid nanoparticle systems (LNP) that allow the efficient delivery and expression of mRNA via different routes of administration. Biophysical characteristics that facilitate efficient mRNA delivery and provide a favorable safety profile will be discussed.

4:35 Development of Anti-Fibrosis siRNA Therapeutics Using HKP Polypeptide Nanoparticle Technology

Patrick Y. Lu, PhD, President & CSO, Sirnaomics, Inc.

Using a proprietary and optimized polypeptide-based delivery technology, we have developed the novel anti-fibrotic therapeutics with siRNAs targeting both TGFβ1 and Cox-2 simultaneously, for initial indication of skin hypertrophic scar followed with liver fibrosis and other fibrotic conditions. I will discuss the unique advantage of HKP polypeptide nanoparticle technology for efficient siRNA delivery, its pharmaceutical properties for manufacturing and its preclinical safety profile.

5:05 Dinner Short Course Registration

5:30-8:30 SC3: CRISPR-Based Gene Editing for Targeted Therapies*

* Separate registration required. See page 14 for details.

WEDNESDAY, MARCH 28

8:00 am Morning Coffee

TOLL-LIKE RECEPTOR (TLR) AGONISTS AND CHECKPOINT COMBINATIONS

8:25 Chairperson's Remarks

Art Krieg, MD, Founder and CEO, Checkmate Pharmaceuticals

8:30 Making "Cold" Tumors "Hot" with Intratumoral Injection of CpG-A Oligonucleotide

Art Krieg, MD, Founder and CEO, Checkmate Pharmaceuticals

CMP-001 is a formulation of a CpG-A oligonucleotide, G10, within a virus-like particle, Qb. We are performing a Phase Ib dose escalation study of intratumoral CMP-001 given in combination with systemic pembrolizumab in advanced melanoma patients whose cancer has previously progressed on an anti-PD-1 Ab, or who have failed to respond to at least 12 weeks of such therapy.

9:00 Creating a Beneficial Tumor Microenvironment for Effective Cancer Immunotherapy

Sudhir Agrawal, DPhil, FRSC, President, Research, Idera Pharmaceuticals

We are evaluating the role of endosomal Toll-like receptors 3, 7, 8, and 9, in the TME by administering intratumorally an agonist of these receptors. IMO-2125, a TLR9 agonist, has shown potent anti-tumor activity following i.t. administration and has led to an abscopal effect. These anti-tumor activities are associated with beneficial changes in the TME, which potentiated the anti-tumor activity of anti-CTLA4, anti-PD1, and IDO-1 inhibitor. A Phase I/II trial of intratumoral IMO-2125 in combination with ipilimumab in PD-1 refractory melanoma patients is in progress.



9:30 TLR9-Targeted Spherical Nucleic Acids for Cancer Immunotherapy

Ekambar Kandimalla, PhD, CSQ, R&D, Exicure

Spherical nucleic acids (SNAs) are dense and radially arranged synthetic oligonucleotides on a central nanoparticle core. The 3D structure of SNA provides enhanced cellular uptake, and nuclease stability, compared with linear oligonucleotides with advantages for local delivery. A novel TLR9-targeted SNA has shown greater antitumor activity as a monotherapy and in combination with an anti-PD-1 antibody compared with a linear oligo in syngeneic tumor models with the induction of innate immune responses and long-term tumor-specific memory responses to subsequent challenge with the same tumor cell line.

10:00 Networking Coffee Break

10:30 Development of Pluripotent Stem Cell-Based Therapies for Neurologic and Oncologic Disorders

Kevin Nishimoto, PhD, Scientist, Asterias Biotherapeutics

Our group has established protocols to produce oligodendrocyte progenitors that upon transplantation into animals with spinal cord injuries can remyelinate denuded axons, induce axonal sprouting, and improve locomotor activity. Extensive preclinical studies have been completed to examine the activity, biodistribution, dosing, delivery, and potential toxicity and tumorigenicity of the oligodendrocyte progenitors. In collaboration with Cancer Research UK, Asterias is preparing for a clinical trial using these hESC derived dendritic cells as a cancer immunotherapy in non-small cell lung carcinoma in the neoadjuvant setting.

11:00 Bi-Functional Oligonucleotides to Unleash TLR9-Driven Antitumor Immune Responses

Marcin Kortylewski, PhD, Associate Professor, Department of Immunology, City of Hope

Here we demonstrate a strategy based on type A CpG ODN (D19) can be employed for the delivery of functional miR146a mimics as well as anti-miR146a oligonucleotides (146AMO). Both CpG-miR146a mimic and CpG-146AMO conjugates were quickly internalized by target human and mouse non-malignant myeloid cells, as well as by AML cells. Unexpectedly, the CpG/TLR9 activation to accelerate endosomal escape, was not indispensable for the inhibitory effect of the CpG-146AMO.

11:30 Sponsored Presentation (Opportunity Available)

11:45 Session Break

11:55 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:25 pm Session Break

NOVEL IMMUNOMODULATORY NUCLEIC ACIDS

1:15 Chairperson's Remarks

R.P. (Kris) Iyer, PhD, Co-Founder & CSO, Spring Bank Pharmaceuticals

1:20 Selective Stimulation of RIG-1 with Novel Synthetic RNA Induces Strong Anti-Tumor Immunity in Mouse Tumor Models

Jim Barsoum, PhD, Chair, Scientific Advisory Board, Rigontec GmbH

We describe a novel immunotherapy approach in which a natural viral defense system is harnessed to stimulate anti-tumor immunity. The cytosolic RNA receptor RIG-I recognizes double-stranded RNA bearing a 5'-triphosphate. RIG-I activation induces apoptosis preferentially in tumor cells and activates the immune system via type I interferon signaling. We developed an optimized, synthetic oligonucleotide, RGT100, as a RIG-I selective ligand. RGT100 activates RIG-I leading to the induction of cytokines, including interferons.

1:50 CureVac's Sequence-Optimized mRNA – En Route to the Next Generation Biologicals

Mariola Fotin-Mleczek, PhD, CSQ, CureVac

Recent advances strongly suggest that mRNA is the basis for a new class of vaccines and drugs. RActive®, one of CureVac's technologies has been developed on this basis and provides potent prophylactic vaccines and novel immunotherapies against cancer. These successes could be extended preclinically to mRNA protein and gene replacement therapy.

2:20 RNAi-Mediated β -Catenin Inhibition Promotes T Cell Infiltration and Potentiates Immune Checkpoint Blockade

Shanthi Ganesh, PhD, Associate Director, Preclinical Oncology, Dicerna Pharmaceuticals, Inc.

Recent research implicates Wnt/ β -catenin signaling as a mechanism of resistance to cancer immunotherapy. DCR-BCAT is an RNAi-based experimental drug targeting β -catenin, formulated in a tumor-selective nanoparticle. In preclinical models, systemic administration of DCR-BCAT induced rapid increases in tumor T cells and dramatically improved responses to immunotherapy agents. In this presentation, we explore the mechanism of synergistic efficacy and suggest clinical evaluation of this first-in-class RNAi agent.

2:50 SB 11285, a Novel STING Agonist for Immunotherapy of Cancer

R.P. (Kris) Iyer, PhD, Co-Founder & CSO, Spring Bank Pharmaceuticals

Immunotherapy has emerged as a transformative approach for the treatment of cancer. Evidence suggests that the activation of Stimulator of Interferon Genes (STING) pathway in tumor cells and/or immune cells induce type I Interferon production leading to apoptosis of tumor cells, as well as induction of adaptive immune response, thereby providing a powerful anti-cancer strategy. Herein, we describe the discovery and preclinical studies of SB 11285, a novel STING agonist for application in immuno-oncology.

3:20 Networking Refreshment Break

3:35 Targeting hID01, CD39 and CD73 with 3rd Generation Antisense Oligonucleotides

Frank Jaschinski, PhD, CSO, Secarna Pharmaceuticals

4:05 Identification of LAG3 High Affinity Aptamers by HT-SELEX and Conserved Motif Accumulation (CMA)

Fernando Pastor Rodríguez, PhD, Principal Investigator, Aptamers, Molecular Therapy, CIMA

4:35 Cancer Immunotherapy: Charting a Course in the Rough Seas of Intellectual Property

Konstantin M. Linnik, PhD, Partner, Intellectual Property, Nutter, McClennen & Fish, LLP; former Lead Patent Counsel for Oligonucleotide Therapeutics at Pfizer, Inc.

Both immuno-oncology and oligonucleotide IP spaces are crowded – the number of drugs in R&D far exceeds the number of targets. Navigating the IP around major targets is critical but, more importantly, every drug developer faces challenges in protecting its own intellectual property. What are the patenting strategies that allow entry into this crowded IP space, while preserving the broadest scope of protection and commercialization opportunities?

5:05 Close of Conference



Peptide Discovery and Delivery

March 26 - 27, 2018

Developing the Next Generation of Targeted Peptide Therapeutics

CHI's Peptide Discovery and Delivery conference reveals the latest strategies at the forefront of peptide discovery, chemistry and delivery with in-depth sessions on new chemistries, novel delivery mechanisms and the most important preclinical and clinical updates, helping you develop the next generation of peptides therapeutics, including latest developments in antimicrobial peptides, peptide vaccines and macrocyclic and constrained peptides.

SUNDAY, MARCH 25

4:30 pm Dinner Short Course and Pre-Conference Registration

5:00-8:00 SC1: Oligonucleotide Therapeutics: From Discovery to Manufacturing*

* Separate registration required. See page 14 for details.

MONDAY, MARCH 26

7:00 am Registration and Morning Coffee

NEW PEPTIDE DISCOVERIES AND CHEMISTRIES

8:00 Welcome Remarks from Conference Director

Daniel Barry, Senior Conference Director, Cambridge Healthtech Institute

8:10 Chairperson's Opening Remarks

Waleed Danho, PhD, Distinguished Research Leader and Consultant for Peptides, Danho Associates, Inc.

8:15 KEYNOTE PRESENTATION: Peptide Drug Hunter: An Extraordinary Trek into Intracellular Target Space

Tomi Sawyer, PhD, Distinguished Scientist, Discovery Chemistry Modalities, Merck Research Laboratories

A deeper understanding of peptide science and technology is driving a renaissance in peptide drug discovery. This presentation will highlight past achievements and future opportunities to advance novel peptide therapeutics in tackling intracellular target space and complex diseases thereof.

8:45 High-Throughput Selection of Peptides with Biological Function

Alex Batchelor, PhD, CEO, Orbit Discovery

Peptide therapeutics has been greatly enhanced by the evolution of display technologies. These technologies enable the move from peptide discovery which uses endogenous peptides as a starting point to discovery which uses large, random libraries to identify novel structures. This means we can address targets for which there are no known peptide binder. Phage display is used to present natural peptides to both purified and cell-surface targets.

9:15 Genetic Encoded Peptide Libraries, 48 Hours Hits Identification

Ratmir Derda, PhD, Assistant Professor, University of Alberta

Genetically-encoded (GE) libraries of peptides are one of the major sources of discovery of biological drugs and development of ligands. We use GE libraries as starting materials for multi-step organic synthesis. Examples are N-terminal conjugation and cyclization of linear peptides with simultaneous introduction of glycan entities. We developed the Genetically-Encoded Fragment-Based Discovery (GE-FBD) platform, which combines >109 peptides with GE-modifications. The talk will describe the progress and challenges in application of GE-FBD platform.

9:45 Sponsored Presentation (Opportunity Available)

10:15 Networking Coffee Break

NEW DEVELOPMENTS

10:30 Is Glucagon a Suitable Drug Target?

Thomas Kruse, PhD, Senior Principle Scientist, Novo Nordisk

The pharmaceutical industry has pursued glucagon as a drug target for years with no clear consensus on the way forward. Agonists or antagonists? Long-acting or short-acting? This talk summarizes the literature and the Novo Nordisk efforts to understand glucagon pharmacology in greater depth.

11:00 Identification of Long Acting GIP/GLP-1 Dual-Acting Peptide Hormones

Pernille Tofteng Shelton, PhD, Senior Scientist, Medicinal Chemistry, Zealand Pharma

Research showing beneficial metabolic effects of GIPR and GLP-1R co-activation in T2D patients has led to a renewed interest in GIP biology. Here we present the design and characterization of long acting novel balanced GLP-1-GIP receptor dual agonists. We will describe optimization of enzymatic stability, chemical and physical stability, and half-life extension through albumin binding with a Lys17 acylation. These novel potent dual-agonists have a significantly increased half-life and demonstrate pharmacodynamic effects in mice.

11:30 FEATURED PRESENTATION: Setmelanotide for the Treatment of Severe Obesity Resulting from MC4-Pathway Deficiency

Lex Van der Ploeg, PhD, CSO, Rhythm Pharmaceuticals

Setmelanotide is a once daily injectable cyclic octapeptide MC4R agonist that acts as a precision medicine 'replacement' therapy to compensate for the lack/reduction of endogenous MC4R-pathway activation, leading to re-establishing weight and appetite control. Setmelanotide is currently in Phase III trials for the treatment of POMC, PCSK1 and LEPR deficiency related obesity. Our epidemiological studies have unveiled the predicted prevalence of MC4R-pathway genetic deficiencies. We are currently addressing the position of other MC4R-pathway genes to identify additional at-need patient populations that could benefit from setmelanotide therapy.

12:00 pm Session Break

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

12:40 Session Break

MACROCYCLIC AND CONSTRAINED PEPTIDES

1:25 Chairperson's Remarks

Waleed Danho, PhD, Distinguished Research Leader and Consultant for Peptides, Danho Associates, Inc.

1:30 Properties of Orally Bioavailable Peptide Macrocycles beyond the Rule-of-5

Alan Mathiowetz, PhD, Director, Discovery Network, Pfizer, Inc.

Peptidic macrocycles with properties beyond the Rule-of-5 (BRo5) have the

potential to be effective modulators of difficult targets. Oral delivery of BRo5 molecules is challenging and requires a balance of competing properties such as permeability, clearance, and potency; macrocyclization has the potential to impact all of these properties. This talk provides an overview of structure/property trends we have found spanning multiple series of BRo5 peptidic macrocycles.

2:00 Macrocyclic Peptide Inhibitors of the Hedgehog Signaling Pathway

Rudi Fasan, PhD, Associate Professor, Department of Chemistry, University of Rochester

The Hedgehog signaling pathway plays a central role during embryonic development and its aberrant activation has been implicated in the development and progression of several human cancers. This talk will describe the design and optimization of macrocyclic peptides capable of inhibiting the Hedgehog pathway by targeting and disrupting the Hedgehog protein/Patched interaction, the most upstream event in the ligand-induced activation of this cell signaling pathway.

2:30 Turning Full Circle from Linear to Cyclic Azapeptide Modulators of the Cluster of Differentiation 36 Receptor

William D. Lubell, PhD, Département de Chimie, Université de Montréal

Azacyclopeptides were identified that exhibited unprecedented CD36 binding affinity and ability to reduce the overproduction of nitric oxide, an important marker of inflammation produced by macrophages when stimulated by the Toll-like receptor-2 agonist fibroblast-stimulating lipopeptide. Our presentation will describe synthetic methods, structure-activity relationships and conformational analyses to provide understanding of the requirements for azacyclopeptide CD36 modulator activity.

3:00 Refreshment Break in the Exhibit Hall with Poster Viewing

3:45 Discovery and Development of Novel Macrocyclic Drugs: Outer Membrane Protein Targeting Antibiotics (OMPTA), a New Class with a Novel Mode of Action

Daniel Obrecht, PhD, CSO & Co-Founder, Pharma, Polyphor Ltd

We have recently shown exceptional *in vitro* activity on the most recently emerging antibiotic-resistant strains, and in animal model studies we have shown excellent *in vivo* efficacy against relevant bacterial strains, including resistant strains. We will also give an update on our lead antibiotic Murepavadin (POL7080), which is a narrow-spectrum, targeted therapy for Pseudomonas infections in critically ill patients in the ICU. POL7080 has successfully completed Phase II and we are preparing the path forward for a Phase III registration trial.

4:15 Targeting Intracellular Protein-Protein Interactions with Structure-Based Designed Macrocyclic Peptides

David Spellmeyer, CSO, Circle Pharma

Circle Pharma deploys a structure-based design/synthetic chemistry platform for macrocycle therapeutic discovery that incorporates prediction of intrinsic cell permeability as a key step in the design workflow. While this platform is target-agnostic, Circle's internal pipeline is directed to intracellular protein-protein interactions that are key drivers in oncology pathways, including p53:MDM2/4, MCL1:BH3, cyclinA:cdk2 and beta-catenin:TCF4. Examples of Circle's development work will be presented.

4:45 Sponsored Presentation (Opportunity Available)

5:15 Welcome Reception in the Exhibit Hall with Poster Viewing

6:15 Dinner Short Course Registration

6:30-9:30 SC2: Overcoming Challenges with Peptide Delivery*

* Separate registration required. See page 14 for details.

TUESDAY, MARCH 27

7:30 am Breakfast Breakout Roundtable Discussions

Grab a cup of coffee and join a roundtable discussion. These are moderated discussions with brainstorming and interactive problem solving, allowing participants from diverse backgrounds to exchange ideas and experiences and develop future collaborations around a focused topic.

For more details, please visit OPTCongress.com

PEPTIDES FOR CANCER

8:25 Chairperson's Remarks

Jesse Dong, PhD, Vice President, Peptide Chemistry, Neon Therapeutics

8:30 Engineering Potent NaV1.7 Inhibitory Peptide-Antibody Conjugates

Justin Murray, PhD, Senior Scientist, Hybrid Modality Engineering, Amgen

We describe NaV1.7 inhibitory peptide-antibody conjugates for potential prolonged channel blockade. A GpTx-1 peptide was conjugated to a carrier monoclonal antibody, and variations in attachment site, linker, and peptide loading established design parameters for potency optimization. Antibody conjugation led to *in vivo* half-life extension by 130-fold relative to a nonconjugated GpTx-1 peptide. Further improvements in potency have been achieved through the conjugation of selective analogs of JzTx-V.

9:00 Development Strategies of Neo-Antigen-Based Personalized Cancer Vaccines

Jesse Dong, PhD, Vice President, Peptide Chemistry, Neon Therapeutics

Neon Therapeutics is pursuing an exciting clinical development program of a personalized cancer vaccine, NEO-PV-01, which targets patient-specific tumor neoantigens to engage the immune system to precisely and selectively attack tumors. Our objective is to create and deepen anti-tumor immune responses and broaden the range of cancers treatable via immuno-oncology approaches.

9:30 Nanofitin-Drug Conjugates for Solid Tumors: From Imaging to Treatment

Olivier Kitten, PhD, Founder & CEO, Afflogic

The putative advantage of small targeting scaffolds in comparison with antibodies lies in their small size, at the expense of a short plasma half-life. The 7 kDa, highly specific Nanofitins are protein scaffolds that exhibit high tumor invasion capability. This feature is conserved after addition of cytotoxic payloads and radiotracers. Combined with Nanofitin-based half-life extension moieties, these assemblies constitute a novel set of therapeutically relevant modalities that will be illustrated.

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

PEPTIDE DEVELOPMENTS

10:30 Chairperson's Remarks

Jesse Dong, PhD, Vice President, Peptide Chemistry, Neon Therapeutics

10:35 The Development of Stapled Peptide Therapeutics

Loren D. Walensky, MD, PhD, Professor of Pediatrics, Investigator, Linde Program in Cancer Chemical Biology, Dana-Farber Cancer Institute – Boston Children's Hospital, Harvard Medical School





Peptide Discovery and Delivery | March 26 - 27, 2018

Developing the Next Generation of Targeted Peptide Therapeutics

11:05 Preclinical Studies on P8, a Novel Disease-Modifying Peptide Drug Candidate for the Treatment of Alzheimer's Disease

Nazneen Dewji, PhD, Associate Adjunct Professor of Medicine, UCSD and President and CEO, Cenna Biosciences, Inc., USA

We previously demonstrated that two small, non-overlapping peptides, P4 and P8, from the PS-1 NH₂-terminal domain, can substantially and specifically inhibit the production of total A β as well as A β 40 and 42 in model systems of AD without affecting the catalytic activities of β - or γ -secretase, or the level of APP. These peptides and their derivatives offer new disease-modifying drug candidates for the treatment of AD. We now provide data on the preclinical development of the lead peptide drug candidate P8.

11:35 Sponsored Presentation (Opportunity Available)

11:50 Session Break

12:00 pm Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:30 Dessert Break in the Exhibit Hall with Poster Viewing

PEPTIDE DELIVERY

1:15 Chairperson's Remarks

Steve Prezstelski, PhD, CSO, Xeris Pharmaceuticals

1:20 How Can Nanosystems Help Address Present and Future Challenges in Peptide Delivery?

Joël Richard, PhD, Senior Vice President, Peptides Development, Ipsen

Peptides, which have become very attractive drugs in the last decades, remain difficult-to-administer molecules, because they have a short plasma half-life and are very sensitive to enzymatic and pH-driven degradation. Moreover, they show a poor cellular membrane permeability. Then, nanodelivery systems (e.g., nanotubes, nanoparticles) can provide appropriate solutions to address present and future challenges of peptide delivery, especially for sustained release, or to cross cellular membranes and target intracellular receptors.

1:50 Cell Penetration Profiling for Biotherapeutics

Joshua Kritzer, PhD, Associate Professor, Department of Chemistry, Tufts University

Several classes of biomolecules have emerged as exciting potential therapies, but their development has been impeded by imprecise measurements of intracellular delivery. The Kritzer lab has devised a new method for quantitating cell penetration, the ChloroAlkane Penetration Assay (CAPA). CAPA is inexpensive and high-throughput, and it can quantitate penetration to individual cellular compartments. We are using CAPA to comprehensively profile cell penetration for diverse biomolecules and drug delivery systems.

2:20 Update on Xeris Peptide Development and Delivery

Steve Prezstelski, PhD, CSO, Xeris Pharmaceuticals

2:50 Sponsored Presentation (Opportunity Available)

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing

PEPTIDE STABILITY AND LATE-STAGE DEVELOPMENT

3:35 Stable and Effective Formulations of Peptide Drugs in Phospholipid Micelles

Hayat Onyuksek, PhD, Professor, Department of Biopharmaceutical Sciences, University of Illinois, Chicago

Poor stability of peptide drugs causes a major problem during manufacturing, storage and *in vivo* use. Stability of peptide drugs can significantly be improved when delivered in sterically stabilized phospholipid micelles (SSM). In this talk, using vasoactive intestinal peptide (VIP) as a model drug, data obtained with free peptide or in SSM on two disease models, RA and IBD, will be compared. Reasons for significant improvements in peptide drug stability, efficacy and safety when used as a nanomedicine (VIP-SSM) will be explained.

4:05 Transitioning Manufacturing Processes from Clinical Trial Supply to Registration and Pre-Commercial Readiness

Dave Garman, PhD, CTO, NoNO, Inc.

There are vast differences in the manufacturing and testing requirements between supplying a drug for clinical trials and registering a drug for market access. For small to midsize companies, these development expenses are often pushed to late stages when the risk of failure in clinical studies is lower. We examine the transition to commercial development of drug substance and drug product manufacturing processes to mitigate risks of a FDA refusal to file in the context of our Phase III peptide therapeutic NA-1.

4:35 Stalking Elusive Pathogenic Bacteria with Cationic Amphiphilic Polyproline Helices: Diving into Human Cells to Treat Infections

Jean Chmielewski, PhD, AW Kramer Distinguished Professor, Department of Chemistry, Purdue University

A number of pathogenic bacteria invade and reside within mammalian host cells. However, most commonly used antibiotics are unable to achieve therapeutic concentrations within these same cells. There is a great need, therefore, to develop antibiotics that enter mammalian cells and target intracellular pathogens. In this work we have developed cationic amphiphilic polyproline helical (CAPHs) peptides containing unnatural proline amino acids.

5:05 Close of Conference



SUBMIT A POSTER WHEN REGISTERING AND BECOME A STUDENT FELLOW

****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 and will be recognized as a Student Fellow of the event.**

Student rates cannot be combined with any other discount offers. Students must present a valid/current student ID to qualify for the student rate. Limited to the first 25 students that apply.

Student Fellows must register and submit a poster abstract by February 9, 2018

“ This three-day meeting combines frontier works from both academic and industry which truly illustrated the current status of oligonucleotides therapeutics. ”

- Patrick L., PhD, President & CEO, Sirnaomics, Inc.



Rare diseases, or diseases that affect only a small percentage of the population, have been growing in significance and prominence in recent years. According to the National Institutes of Health, there are nearly 7,000 rare diseases and more than 25 million Americans who are affected. Approximately 80% of these rare diseases are genetic in origin. Cambridge Healthtech Institute's symposium on Drug Discovery for Rare Diseases will bring together leading scientists, clinicians, executives and experts who are deeply involved in bringing to market the treatments for such rare disorders. This symposium will bring to light some of the new drug targets, and peptide and oligonucleotide-based drug modalities that are being pursued. This unique one-day event will bring together people from diverse backgrounds to tackle translational challenges and to discuss potential opportunities in this field. The goal is to help attendees and sponsors meet scientific and technical experts who are involved in rare disease research to exchange ideas and set up collaborations.

WEDNESDAY, MARCH 28

7:30 am Registration and Morning Coffee

EXPLOITING DIVERSE DRUG MODALITIES & TARGETS

8:15 Welcome Remarks from Conference Director

Tanuja Koppal, PhD, Conference Director, Cambridge Healthtech Institute

8:25 Chairperson's Opening Remarks

Eric B. Kmiec, PhD, Director, Gene Editing Institute; Senior Research Scientist, Center for Translational Cancer Research, Helen F. Graham Cancer Center & Research Institute, Christiana Care Health System

8:30 Targeting microRNA-155 as a Therapeutic Strategy for Rare Hematological Malignancies

William Marshall, PhD, President and CEO, miRagen Therapeutics

microRNA-155 is an important control point for regulation of pathways implicated in oncology and inflammatory disease. Its overexpression has been shown to be an indicator of poor prognosis in a variety of rare hematological malignancies. MRG-106, an inhibitor of miR-155, is currently being evaluated in Phase I in patients with Cutaneous T-cell Lymphoma (CTCL). An overview of our latest clinical observations will be presented.

9:00 Chemistry and Biology of Rare Diseases Treatable with Hepatocyte Targeted RNAi Therapeutics

Muthiah (Mano) Manoharan, PhD, Senior Vice President, Drug Discovery, Alnylam Pharmaceuticals

9:30 The Natural History of Alpha-1 Antitrypsin Storage Disease and RNAi Intervention in PiZ Transgenic Mice and Implications for Treatment in Humans

Bruce D. Given, MD, COO, Arrowhead Pharmaceuticals

A large majority of patients with alpha-1 antitrypsin deficiency produce a mutant protein that mis-folds in the hepatocyte leading to deficiency in the plasma, but a storage disease in the liver. The PiZ transgenic mouse expresses the human mutant Z protein and recapitulates most of the human natural history in the liver. We have intervened throughout this natural history with RNAi trigger compounds and showing beneficial effects and are now entering the clinic with a second-generation RNAi compound.

10:00 Networking Coffee Break

10:30 Targeting the Pulmonary Vasculature with Oligonucleotide Therapy: Fact or Fiction?

Hyung Chun, MD, FAHA, Associate Professor of Medicine, Section of Cardiovascular Medicine, Yale School of Medicine

Pulmonary arterial hypertension is a rare disease that leads to right heart failure and ultimately death. While many studies have implicated the potential

therapeutic role of oligonucleotides (including microRNAs, microRNA inhibitors, and short interfering RNAs), challenges have surrounded the efficient delivery of such oligonucleotides to the pulmonary vasculature. Current state of technology and future directions will be discussed.

11:00 PANEL DISCUSSION: Tackling Rare Diseases: From Conviction to Cure

Moderator: Michael Liebman, PhD, Managing Director, Strategic Medicine, Inc.

Panelists:

Iris Melendez, President and Founder, The Nathaniel Adamczyk Foundation

Torsten Hoffmann, PhD, COO, Silence Therapeutics

Nicholas Sarlis, MD, PhD, CMO and Senior Vice President, Sellas Life Science Group Ltd.

11:30 Sponsored Presentation (Opportunity Available)

11:45 Session Break

11:55 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:25 pm Session Break

EXPLORING INNOVATIVE STRATEGIES

1:15 Chairperson's Remarks

James J. Hickman, PhD, Founding Director, NanoScience Technology Center; Professor, Nanoscience Technology, Chemistry, Biomolecular Science, Material Science and Electrical Engineering, University of Central Florida

1:20 From Rare to Common: Targeting Gaucher Defects for the Treatment of Parkinson's Disease

S. Pablo Sardi, PharmD, PhD, R&D Director, Sanofi Genzyme

Clinical, genetic and experimental evidence underlies the relevance of lysosomal dysfunction in Parkinson's disease. Stimulation of the lysosomal GBA pathway in the CNS can improve the pathological and behavioral abnormalities in animal models of disease. Modulation of this lysosomal pathway may represent a new disease-modifying treatment for GBA-related Parkinson's disease. This research underscores the study of rare diseases as a new paradigm for drug discovery.

1:50 Orphan Indications as a Step to Developing Therapeutics for Major Unmet Medical Needs

Elena Feinstein, MD, PhD, CSO, Quark Pharmaceuticals

This talk will present Quark's strategy of drug development from proof-of-concept in orphan indications to major ones with similar underlying pathogenesis. A case study of development of QPI-1002, an siRNA targeting p53, from an orphan indication such as delayed graft function following kidney transplantation towards acute kidney injury following cardiac surgery will be discussed.

2:20 Preclinical Development of a CRISPR Medicine for the Treatment of Leber Congenital Amaurosis Type 10

Gerry Cox, MD, CMO, Editas Medicine

A common mutation in intron 26 of the CEP290 gene, c.2991+1655A>G, leads to retinal degeneration and infantile-onset blindness known as Leber congenital amaurosis type 10 (LCA10). A therapeutic approach involving subretinal delivery of AAV5 encoding CRISPR components is being developed to remove the mutation and potentially restore vision. Opportunities and preclinical challenges of developing human genome-based medicines for LCA10 will be discussed.

2:50 Efficient Delivery and Nuclear Uptake for Gene Editing in CD34+ Cells Directed by a CRISPR/Cas9 Ribonucleoprotein Complex

Eric. B. Kmiec, PhD, Director, Gene Editing Institute; Senior Research Scientist, Center for Translational Cancer Research, Helen F. Graham Cancer Center & Research Institute, Christiana Care Health System

Successful editing of the beta globin gene in CD34+ cells is a milestone for ex vivo cell therapy. While dramatic advances have been reported in the literature, by and large, the experimental protocols and conditions have been less than robust. We began a systematic evaluation of the relationship among cellular delivery, nuclear uptake and gene editing activity and defined the critical parameters for CRISPR/Cas9 RNP and ssODNs delivery into CD34+ cells.

3:20 Networking Refreshment Break

3:35 Developing a First-in-Class Drug for Familial Amyloid Polyneuropathy: A Case Study

Christine Bulawa, PhD, Senior Director, Rare Disease Research Unit, Pfizer

This talk will present a case study of drug development for familial amyloid polyneuropathy (FAP), a disease caused by mutations in the circulating protein transthyretin. Insights gleaned from biophysical studies of transthyretin and clinical observations of FAP patients led to the therapeutic strategy of native state stabilization and ultimately to development of tafamidis, the first disease modifying therapy for an amyloid disease.

4:05 Application of Genome Editing to Develop HTS Assays for Rare and Neglected Disease Drug Discovery

James Inglese, PhD, Head, Assay Development & Screening Technologies, National Center for Advancing Translational Sciences, NIH

Genome editing was used in combination with reporter gene technology to modify the genetic loci of neurologic target genes to create HTS assays for compound library interrogation. Assay design explored cases of gene duplication, haploinsufficiency, or genes with implied protective properties, associated with Charcot-Marie-Tooth type 1A, Dravet syndrome, or Parkinson's disease, respectively. Our goal was to identify transcriptionally active pharmacological agents acting by a variety of mechanisms, including through chromatin coregulators accessible by our assay design.

4:35 Human-on-a-Chip Systems Applied to Rare Disease Investigations for Efficacy and Toxicity

James J. Hickman, PhD, Founding Director, NanoScience Technology Center; Professor, Nanoscience Technology, Chemistry, Biomolecular Science, Material Science and Electrical Engineering, University of Central Florida

Our focus is on establishing functional *in vitro* systems where we seek to create organs and subsystems to model motor control, muscle function, myelination and cognitive function, as well as cardiac and hepatocyte subsystems for neurodegenerative diseases such as ALS as well as other rare diseases. Functional 2 and 4-organ systems where multi-organ toxicity as well as efficacy are evaluated will be discussed.

5:05 Close of Symposium

PRESENT A POSTER AND SAVE \$50!

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by **February 9, 2018**.

Register online, or by phone, fax or mail. Please indicate that you would like to present a poster. Once your registration has been fully processed, we will send an email with a unique link and instructions for submitting your abstract using our online abstract submission tool. Please see below for more information.

Reasons you should present your research poster at this conference:

- Your poster will be seen by our international delegation, representing leaders from top pharmaceutical, biotech, academic and government institutions
- Receive \$50 off your registration
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Note: Posters should be portrait orientation, with maximum dimensions of 36 inches wide (3 feet) x 48 inches high (4 feet).

Please note, there are no posters Wednesday, March 28.

* We reserve the right to publish your poster title and abstract in various marketing materials and products.

Poster inquiries: jring@healthtech.com





SUNDAY, MARCH 25 | 5:00 - 8:00 PM

PRE-CONFERENCE DINNER SHORT COURSE

SC1: Oligonucleotide Therapeutics: From Discovery to Manufacturing

RNAi/antisense oligonucleotides can target virtually any disease-causing gene and promise to become a third major class of therapeutics (besides small molecules and biologics). For this to happen, however, several challenges have to be addressed. This course discusses considerations taken into account when selecting oligonucleotide therapeutic programs: from target and delivery selection to developmental and manufacturing particularities. Detailed discussion will focus on, but not be limited to, the tightly interconnected factors of therapeutic indication, delivery and targets, as well as chemistry manufacturing and controls (CMC), regulatory, cost, and intellectual property considerations. Developers who are seeking a comprehensive and up-to-date overview from recognized oligonucleotide development experts are highly encouraged to join.

Instructors:

Dmitry Samarsky, PhD, CSO, Silence Therapeutics

Muthiah (Mano) Manoharan, PhD, Senior Vice President, Drug Discovery, Alnylam Pharmaceuticals, Inc.

Thazha P. Prakash, Director, Medicinal Chemistry, Ionis Pharmaceuticals

Konstantin M. Linnik, PhD, Partner, Intellectual Property, Nutter, McClennen & Fish, LLP; former Lead Patent Counsel for Oligonucleotide Therapeutics, Pfizer, Inc.

MONDAY, MARCH 26 | 6:30 - 9:30 PM

DINNER SHORT COURSE

SC2: Overcoming Challenges with Peptide Delivery

Peptides make attractive drug candidates due to their specificity, potency and low toxicity, but present particular challenges for their delivery to the site of action, due to their short half-life and susceptibility to proteolytic degradation. This short course reviews the latest challenges in peptide drug delivery and the various options available, including oral, transdermal and nanosystems. We also look at challenges around half-life, bioavailability, stability and formulation.

Instructor:

Joël Richard, PhD, Senior Vice President, Peptides Development, Ipsen

TUESDAY, MARCH 27 | 5:30 - 8:30 PM

DINNER SHORT COURSE

SC3: CRISPR-Based Gene Editing for Targeted Therapies

While the challenges and risks associated with oligonucleotide therapies still remain, there is a new and better understanding of how genes can be effectively manipulated and delivered. With the rise of gene editing tools and enhanced knowledge of targeted delivery, these therapeutic modalities are once again being embraced with renewed hope and enthusiasm. This course helps you understand how gene editing – particularly the one enabled by the CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)/Cas9 system – works, and how it can be used to help develop targeted therapies with good efficacy and delivery.

Instructors:

Clifford Steer, MD, Professor of Medicine and Genetics, Cell Biology, and Development; Director, Molecular Gastroenterology Program, University of Minnesota Medical School

Ciro Bonetti, PhD, Scientist, Regeneron Pharmaceuticals

Eric B. Kmiec, PhD, Director, Gene Editing Institute; Senior Research Scientist, Center for Translational Cancer Research, Helen F. Graham Cancer Center & Research Institute, Christiana Care Health System

|| No events go without a hitch, but your crack team met all the obstacle[s] head on, to our complete satisfaction. We've already signed up for the next event. ||

- Rick N., President, Oligo Factory

|| It was my first time attending the show, and I was very impressed with the variety of speakers and content. ||

- Chris M., PhD, Director, Business Development, Bachem Americas, Inc.



Pricing and Registration Information

CONFERENCE PRICING

BEST VALUE REGISTRATION Includes access to entire 3-day Oligonucleotide and Peptide Discovery and Delivery programs, as well as 1-day Rare Diseases Symposium. (Does not include access to any short courses)

	Commercial	Academic, Government, Hospital-affiliated
Early Deadline until December 15, 2017	\$2,249	\$1,149
Advance Deadline until February 9, 2018	\$2,449	\$1,199
Registration after February 9, 2018, and on-site	\$2,599	\$1,299

BASIC PACKAGE Includes a 2-day access to any combination of Oligonucleotide Discovery and Delivery, Peptide Discovery and Delivery, or the Symposium on Rare Diseases. (Does not include access to any short courses)

	Commercial	Academic, Government, Hospital-affiliated
Early Deadline until December 15, 2017	\$1,699	\$879
Advance Deadline until February 9, 2018	\$1,849	\$899
Registration after February 9, 2018, and on-site	\$2,049	\$1,049

SYMPOSIUM REGISTRATION

Includes access to symposium. (Does not include access to other conference programs or short courses)

	Commercial	Academic, Government, Hospital-affiliated
Symposium: Rare Diseases	\$999	\$579

SHORT COURSE PRICING

	Commercial	Academic, Government, Hospital-affiliated
Single Short Course	\$699	\$399
Double Short Courses	\$999	\$699
Triple Short Courses	\$1,199	\$799

SUNDAY, MARCH 25 5:00 - 8:00 PM Pre-Conference Dinner Short Course	MONDAY, MARCH 26 6:30 - 9:30 PM Dinner Short Course	TUESDAY, MARCH 27 5:30 - 8:30 PM Dinner Short Course
SC1: Oligonucleotide Therapeutics: From Discovery to Manufacturing	SC2: Overcoming Challenges with Peptide Delivery	SC3: CRISPR-Based Gene Editing for Targeted Therapies

CONFERENCE DISCOUNTS

Attention Students: Become a Student Fellow to this event. Register online at a discount, submit a poster and be recognized as a Student Fellow.

Poster Submission - Discount (\$50 Off): Poster abstracts are due by February 9, 2018. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact jring@healthtech.com. *CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

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

Alumni Discount: Cambridge Healthtech Institute (CHI) appreciates your past participation at Oligonucleotide and Peptide Therapeutics Boston (OPT Boston). As a result of the great loyalty you have shown us, we are pleased to extend to you the exclusive opportunity to save an additional 20% off the registration rate.

Group Discounts: Discounts are available for multiple attendees from the same organization. For more information on group rates contact Jeff Knight (jknight@healthtech.com) at +1-781-247-6264.

If you are unable to attend but would like to purchase the Oligonucleotide and Peptide Therapeutics CD for \$750 (plus shipping), please visit OPTCongress.com. Massachusetts delivery will include sales tax.

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Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link.

Handicapped Equal Access: In accordance with the ADA, Cambridge Healthtech Institute is pleased to arrange special accommodations for attendees with special needs. All requests for such assistance must be submitted in writing to CHI at least 30 days prior to the start of the meeting.

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