DISCOVERY | DEVELOPMENT | DELIVERY

OPT Congress

10 CELEBRATING YEARS

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SAVE UP TO $300

MARCH 11 - 12, 2025 | Seaport Hotel Boston, MA & Virtual

Oligonucleotide & mRNA Therapeutics

Conference Programs

- Oligo Discovery & Delivery
- mRNA Design & Delivery
- Oligo CMC & Regulatory Strategies
- Emerging Oligo Modalities

In-Person Short Courses

- **Safety and Toxicity of Nucleic Acids**
- **Successful Regulatory Submission for a Complex Oligonucleotide**

PREMIER SPONSOR

Nitto Avecia

Plenary Speakers

Anastasia Khvorova, PhD
Professor, RNA Therapeutic Institute, University of Massachusetts Medical School

Edward Kaye, MD
CEO and Director, Stoke Therapeutics

Eric Swayze, PhD
Executive Vice President, Research, Ionis Pharmaceuticals

Rubina Parmar, PhD
Vice President, Chemistry & Delivery Sciences, Intellia Therapeutics

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Welcome to OPT Congress:
Oligonucleotides & mRNA Therapeutics

OPT Congress is the premier event for scientists and executive directors involved in discovering and developing oligonucleotide and mRNA therapeutics. For 2025, we are delighted to expand our content and offer a conference program dedicated to emerging oligo modalities, sharing cutting-edge research and technologies used in designing new targeted therapies. Now in its 10th year, this unique event brings together leading chemists, biologists, toxicologists, CMC experts, regulatory specialists, and technology providers to discuss advances in next-generation therapeutics. In addition to 2 days of inspiring keynotes, breakout discussions, and 95+ scientific presentations, we deliver two in-depth short courses to further add to the learning opportunities. We look forward to welcoming you to our community focused event, offering robust and customizable programming tailored to your specific needs.

EVENT-AT-A-GLANCE

TUESDAY, MARCH 11	WEDNESDAY, MARCH 12
Short Courses	Conference Programs
Safety & Toxicity of Nucleic Acids	Oligonucleotide Discovery & Delivery
	Oligonucleotide CMC & Regulatory Strategies
Successful Regulatory Submission for a Complex Oligonucleotide	mRNA Design & Delivery
	Emerging Oligonucleotide Modalities

WITH THANKS TO OUR EXECUTIVE ADVISORY BOARD

Mano Manoharan, PhD
Senior Vice President, Drug Discovery, Alnylam Pharmaceuticals

Dmitry Samarsky, PhD
Former CTO, Sirnaomics

Chandra Vargeese, PhD
CTO & Head, Platform Discovery Sciences, Wave Life Science

Arthur Levin, PhD
Executive Vice President, Research and Development, Avidity Biosciences

Lubo Nechev, PhD
Vice President Process and Analytical Sciences, Alnylam Pharmaceuticals

Ekkehard Leberer, PhD
Senior Life Sciences Consultant, ELBIOCON

Plenary Presentations

siRNA Chemical Engineering

Anastasia Khvorova, PhD
Professor, RNA Therapeutic Institute, University of Massachusetts Medical School

Delivery with Bicycles and Camelids: Targeted Delivery of Oligonucleotide Drugs to Muscle and the Central Nervous System via the Transferrin Receptor

Eric Swayze, PhD
Executive Vice President, Research, Ionis Pharmaceuticals

TANGO: An RNA Splicing Approach to Upregulate Proteins

Edward Kaye, MD
CEO and Director, Stoke Therapeutics

CRISPR Genome Editing for Therapeutic Applications: Advances in *in vivo* Editing

Rubina Parmar, PhD
Vice President, Chemistry & Delivery Sciences, Intellia Therapeutics

"My first OPT conference showed me that it is critical for the industry to meet with this type of focus. Happy to have been a part of it and looking forward to next year!"

-Randon Davis, Global Product Manager, WuXi TIDES

Featured Presentations

Biological Research with Thiomorpholino Oligonucleotides (TMOs)
Marvin Caruthers, PhD, Distinguished Professor, University of Colorado

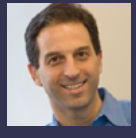
Characterization of Stereopure Chimeric PO/PS/PN Oligonucleotides
Pachamuthu Kandasamy, PhD, Vice President & Head, Medicinal Chemistry, Wave Life Sciences

Use of Poly(A) Tail Mimetics to Enhance mRNA Expression from Genes Associated with Haploinsufficiency Disorders
Jeffery M. Coller, PhD, Bloomberg Distinguished Professor of RNA Biology and Therapeutics, Johns Hopkins University

Design and Delivery of tRNA Therapeutics to Treat Stop Codon Disease
William Kiesman, PhD, CTO, Alltrna

Ways to Improve Antisense Oligonucleotide-Mediated Exon Skipping for Duchenne Muscular Dystrophy
Annemieke Aartsma-Rus, PhD, Professor of Translational Genetics, Leiden University Medical Center

Overcoming Common Regulatory Hurdles during siRNA Product Lifecycle Management
Arwa El Hagrasy, PhD, Director, Regulatory Affairs CMC, Alnylam Pharmaceuticals



miRNA-Based Logic Circuits Encoded on Self-Amplifying RNA for Highly Specific Cancer Cell Classification
Ron Weiss, PhD, Professor, Biological Engineering, Massachusetts Institute of Technology

OPT Congress Oligonucleotide & mRNA Therapeutics

Top Reasons to Attend

BE INSPIRED BY 4 PLENARY PRESENTATIONS delivered by leading industry and academic experts from Ionis Pharmaceuticals, University of Massachusetts Medical School, Intellia Therapeutics, and Stoke Therapeutics.

TRACK-HOP BETWEEN FOUR CONCURRENT CONFERENCES dedicated to oligonucleotide & mRNA therapeutics—with on-demand access included in your conference registration, you can view the content you may have missed for one full year—it's like getting four conferences for the price of one.

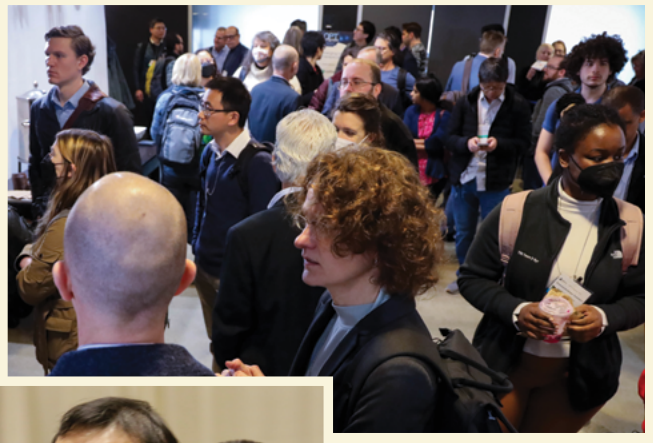
HEAR CASE STUDIES, INSIGHTS, AND NEW DEVELOPMENTS in oligo and mRNA discovery, design, delivery, performance, CMC, manufacturing, and regulatory strategies.

LEARN WHERE THE FIELD IS HEADING and address industry-wide challenges in efficacy, stability, and toxicity alongside KOLs and experts from biotech, pharma, and academia.

ATTEND OUR INTERACTIVE SHORT COURSES examining the safety and toxicity of nucleic acids and the successful regulatory submission of a complex oligonucleotide.

TAKE FULL ADVANTAGE OF NUMEROUS NETWORKING OPPORTUNITIES, small group discussions, and brainstorming sessions, and find your next collaboration in the Boston's historic Seaport.

VISIT THE EXHIBIT HALL to engage with technology and service providers, explore the latest research, and meet the poster presenters.



UNPARALLELED Networking Opportunities

In addition to many informal opportunities to collaborate, share insights, build networks, and solve shared challenges, OPT Congress has designed a dynamic program and invested in innovative technology to ensure attendees can connect with fellow participants.

- **NETWORK** onsite during the Welcome Reception, Refreshment Breaks, Luncheon, and Closing Reception.
- **CONTINUE** your discussions during our Breakout Sessions.
- **ENGAGE** with our industry-leading sponsors.
- **TAKE PART** in live Q&A with speakers and participants following each presentation.
- **PARTICIPATE** in 1-on-1 networking with an easy-to-navigate profile search, filter, and scheduling platform.
- **IDENTIFY** and establish meetings with participants who have similar initiatives and challenges within minutes.

"This is my fourth trip to OPT Congress. This is right-sized to be able to find people, to network, and to have the face-to-face conversations where we can really get into some of the details that we've discussed earlier in the day."

-Mike Webb, PhD, Founder and CEO, Mike Webb Pharma; Former Vice President, API Chemistry & Analysis, GSK

Short Courses*

TUESDAY, MARCH 11 | 8:00 – 10:00 AM | IN-PERSON ONLY
7:30am Short Course Registration and Morning Coffee

SC1: Safety & Toxicity of Nucleic Acids

Nucleic acid drugs continue to deliver on their promise to become a third therapeutic modality, in addition to small molecules and biologics. Several antisense oligonucleotide drugs have been on the market for some time, while the first RNAi approval was granted in 2018. Despite the common "nucleic acid" component, the mechanisms of action and of non-specific effects differ for each of these drug types.

TOPICS TO BE DISCUSSED INCLUDE:

- Different types of nucleic acid-based drugs
- Mechanisms of actions and non-specific effects
- Current approaches to address non-specific and potentially toxic effects
- Findings secondary to class-effect of oligonucleotides

INSTRUCTORS:

Xiao Shelley Hu, PhD
Vice President, Head of DMPK and Clinical Pharmacology, Wave Life Sciences

Sarah Lamore, PhD, DABT
Senior Director, Toxicology, PepGen

Kuldeep Singh, PhD
Senior Director & Head Pathology, Wave Life Sciences

Aimed at both novice and advanced nucleic drug developers, the course will:

- Introduce and explain the differences between various types of nucleic acid drugs
- Summarize our current understanding of the origins of non-specific and potentially toxic effects
- Provide direction on how to minimize the potential toxic effects of nucleic acid drugs
- Provide an overview of DMPK considerations from a safety evaluation perspective

SC2: Successful Regulatory Submission for a Complex Oligonucleotide

ICH guidelines have established clear expectations for the control strategy for synthetically manufactured medicines. Oligonucleotides fall into the synthetic category and yet their manufacture and control are very different compared to small molecules. In this short course, we will look at the requirements for a control strategy combining starting material control, process understanding, and final drug substance specifications and methods. With a common understanding in mind, we will discuss how to apply the control principles to therapeutic oligonucleotides from early development to registration.

TOPICS TO BE DISCUSSED INCLUDE:

- The principles of a control strategy from ICH guidance and what this means in practice
- The challenges (and advantages) in applying the principles to oligonucleotides
- Where to start in early development of oligonucleotides
- How to get to a successful commercial control strategy for oligonucleotides

INSTRUCTOR:

Mike Webb, PhD
Founder and CEO, Mike Webb Pharma; Former Vice President, API Chemistry & Analysis, GSK

Benefits of attending include:

- Understand the activities required to carry out and fund in order to achieve regulatory success for a therapeutic oligonucleotide
- Understand when to plan relevant activities when initiating an oligonucleotide development project
- Support decision-making from early development onwards
- Support CDMO selection, development, and financial planning
- Understand the regulatory challenges and how to overcome them

Premium Registration or separate registration required for Short Courses.

Oligonucleotide Discovery & Delivery

Optimizing Design and Advances in the Clinic

TUESDAY, MARCH 11

8:00 am Recommended Short Course*
SC1: Safety & Toxicity of Nucleic Acids
*Premium Registration or separate registration required. See Short Courses page for details.

9:45 Registration and Morning Coffee

10:45 Welcome Remarks by Conference Organizer

OPTIMIZING DESIGN, DELIVERY, AND PERFORMANCE

10:55 Chairperson's Remarks
Dmitry Samarsky, PhD, Former CTO, Sirnaomics

11:00 KEYNOTE PRESENTATION: Biological Research with Thiomorpholino Oligonucleotides (TMOs)
Marvin Caruthers, PhD, Distinguished Professor, University of Colorado
Using genetically targeted mouse studies, TMOs have focused on DMD, NPC, DIPG, STAT3, and type II diabetes with results superior to other chemistries. In various cell culture experiments using exon skipping or RNase H, significant biological activity targeting genes such as FUS, SLC6A1, ITGA4, PKM, PEG10, Psoriasis, RDEB, and others has been demonstrated. Recently TMOs have shown activity as siRNAs and in CRISPER/CAS experiments.

11:30 Living in the World of RNA Therapeutics: Chemistry Has No Limits
Mano Manoharan, PhD, Distinguished Scientist & Senior Vice President, Innovation Chemistry, Alnylam Pharmaceuticals

12:00 pm Expanding Lipidated siRNAs Chemistry for Heart Delivery
Annabelle Biscans, PhD, Director, Oligonucleotides and Targeted Delivery, AstraZeneca
Lipophilic conjugation of fully chemically stabilized small-interfering RNA supports significant and effective delivery throughout the body. Therefore, chemically engineering lipid conjugates may be a strategy to improve siRNA delivery to extrahepatic tissues. In this talk, I will describe recent progress in understanding the relationship between conjugate chemical structure and siRNA pharmacokinetic/pharmacodynamic behavior. We will exemplify that modulating conjugate chemistry supports functional delivery to a range of tissues, including heart.

12:30 Transition to Lunch

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Session Break

1:50 Chairperson's Remarks
Renee Williams, Founder and Managing Partner, Williams Biotech Consulting and Executive Director, Woodside Capital Partners; Former VP of External Strategy, Genetic Medicines, Eli Lilly

1:55 FEATURED PRESENTATION: Ways to Improve Antisense Oligonucleotide-Mediated Exon Skipping for Duchenne Muscular Dystrophy
Annemieke Aartsma-Rus, PhD, Professor of Translational Genetics, Leiden University Medical Center
Exon skipping is a therapeutic approach that is approved for Duchenne muscular dystrophy. It utilizes antisense oligonucleotides to modulate the splicing of dystrophin pre-mRNA to allow Duchenne patients to produce a partially functional dystrophin protein. Approval was based on dystrophin restoration at very low levels and there is room for improvement, e.g., through increasing transcript levels, improving delivery to skeletal muscle, and improving muscle quality.

2:25 GalAhead muRNA: A Proprietary GalNAc-RNAi Therapeutic Platform for Simultaneous Downregulation of Multiple Genes
Jim Weterings, PhD, Vice President Research, RNA Therapeutics & Delivery, Sirnaomics
GalAhead muRNA allows for simultaneous downregulating of multiple genes in liver hepatocyte, providing treatment of liver associated diseases. The muRNA concept allows modulation of converging biological pathways while allowing a window to perform physiological function. muRNA can also simultaneously address two or more non-associated indications where patient populations have a considerable overlap. GalAhead muRNA offers an inspiring venue in the RNAi space providing safe and long-lasting effect in treating patients

2:55 Presentation to be Announced

3:10 Sponsored Presentation *(Opportunity Available)*

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

PLENARY SESSION

4:10 Organizer's Welcome Remarks
Gemma Smith, Senior Conference Director, Production, Cambridge Healthtech Institute

4:15 Plenary Chairperson's Remarks
Dmitry Samarsky, PhD, Former CTO, Sirnaomics

4:20 siRNA Chemical Engineering
Anastasia Khvorova, PhD, Professor, RNA Therapeutic Institute, University of Massachusetts Medical School
The focus of our lab is to identify, characterize, and develop novel chemistries that promote simple, efficient, and non-toxic delivery of oligonucleotides and potent silencing of therapeutic targets *in vivo*. Some examples will be highlighted in this talk.

5:00 TANGO: An RNA Splicing Approach to Upregulate Proteins
Edward Kaye, MD, CEO and Director, Stoke Therapeutics
Targeted Augmentation of Nuclear Gene Output (TANGO) is an RNA splicing approach that enables the upregulation of many proteins. Specifically designed Anti-sense Oligonucleotides (ASOs) splice out retained naturally occurring "poison exons" or NMD exons from pre-mRNA, thus enabling an increase of full length message and full length protein. We are targeting autosomal dominant diseases which are missing 50% of an essential protein to correct the underlying genetic defect.

5:40 10th Annual Welcome Reception in the Exhibit Hall with Poster Viewing

6:50 Close of Day

WEDNESDAY, MARCH 12

7:30 am Registration and Morning Coffee

ADVANCES IN THE CLINIC

8:00 Chairperson's Remarks
Ekkehard Leberer, PhD, Professor of Biochemistry, Technical University of Munich; Senior Consultant, ELBIOCON; Advisor, Neuway Pharma

8:05 Improving the Pharmacological Properties of Oligonucleotides through Stereopure Design
Chandra Vargeese, PhD, CTO & Head, Platform Discovery Sciences, Wave Life Sciences

Oligonucleotide Discovery & Delivery

Optimizing Design and Advances in the Clinic

Wave's PRISM platform enables the generation of chimeric backbone-containing stereopure oligonucleotides with position-controlled chemistry and stereochemical configuration. Here, we will describe how incorporating phosphoryl guanidine (PN) backbone linkages can improve the pharmacological properties of oligonucleotides designed for distinct high priority genetic targets, modalities, and tissues. Early data from our ongoing clinical trials suggests that the improved pharmacological properties of investigational PN-containing oligonucleotides are translating into the clinic.

8:35 Targeting Tumor-Associated Immune Cells with RNAi-Lipid Conjugates

Shanthi Ganesh, PhD Director, Pharmacology, Global Nucleic Acid Therapies, Novo Nordisk

Refractory malignant solid tumors create an immunosuppressive tumor microenvironment, which renders them resistant to standard-of-care immune checkpoint inhibitors. We developed RNAi agents to silence PD-L1 targets in tumor-associated immune cells, which mediates immune suppression in the TME. Silencing PD-L1 in antigen presenting cells remodeled the TME and increased cytotoxic T cell infiltration into the tumor. Human active PDL1 RNAi conjugate is currently in Phase 1 clinical trials for immunotherapy-refractory cancers.

9:05 Sponsored Presentation *(Opportunity Available)*

9:35 Coffee Break in the Exhibit Hall with Poster Viewing

ECLIPSEBIO

10:15 Clinical Translation of Targeted Oligonucleotide Delivery via FORCE Platform in Neuromuscular Disease Creates an Opportunity for the Treatment of FSHD

Nicholas Yoder, PhD, Executive Director, Dyne Therapeutics

The FORCE platform demonstrates targeted, neuromuscular delivery of oligonucleotides and achieved clinical translation in ACHIEVE trial for DM1 and DELIVER trial for DMD to open an opportunity for the treatment of FSHD. In preclinical models of FSHD, DYNE-302, a Fab-siRNA conjugate, achieved robust muscle delivery and target engagement, leading to appreciable benefit on muscle function and myofiber pathology.

DEVELOPING EDITING THERAPIES

10:45 New Directions in the Chemistry of Guides for Gene Editing

Jonathan Watts, PhD, Professor, RNA Therapeutics Institute, University of Massachusetts Chan Medical School

Chemical modification has been a key enabler of clinical success for all previous classes of oligonucleotide therapeutics. As genome editing increases its clinical reach, we describe progress in modification of guides for Cas9 nuclease, base editing and prime editing approaches, including split prime editing systems. We measure changes in both specificity and *in vivo* efficacy (LNP delivery co-formulated with mRNA).

11:15 Transition to Lunch

11:25 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

11:55 Session Break

PLENARY SESSION

12:40 pm Plenary Chairperson's Remarks

Chandra Vargeese, PhD, CTO & Head, Platform Discovery Sciences, Wave Life Sciences

12:45 Delivery with Bicycles and Camelids: Targeted Delivery of Oligonucleotide Drugs to Muscle and the Central Nervous System via the Transferrin Receptor

Eric Swayze, PhD, Executive Vice President, Research, Ionis Pharmaceuticals

Ligands for transferrin receptor can potentially provide solutions to the delivery of oligonucleotides to skeletal and cardiac muscle, as well as across the blood brain barrier. We have optimized oligonucleotide conjugates to TfR1 ligands including Bicycle peptides and camelid nanobodies to reduce the total dose of the administered drug. These constructs have achieved successful delivery to the target tissues, offering the potential for treatment of cardiovascular and neurological diseases.

1:25 CRISPR Genome Editing for Therapeutic Applications: Advances in *in vivo* Editing

Rubina Parmar, PhD, Vice President, Chemistry & Delivery Sciences, Intellia Therapeutics

At Intellia, we are advancing a full-spectrum genome editing company. We are deploying the industry's broadest and deepest toolbox, including novel editing and delivery solutions, to harness the immense power of CRISPR-based technologies for *in vivo* and *ex vivo* therapeutic applications. In this presentation, we will share the advances in the therapeutic applications of CRISPR/Cas9 for *in vivo* genome editing.

2:05 Refreshment Break in the Exhibit Hall with Last chance for Poster Viewing

IN-PERSON BREAKOUT DISCUSSIONS

2:40 In-Person Breakout Discussions

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

IN-PERSON BREAKOUT DISCUSSION: Trending: How Companies Get Acquired

Renee Williams, Founder and Managing Partner, Williams Biotech Consulting and Executive Director, Woodside Capital Partners; Former VP of External Strategy, Genetic Medicines, Eli Lilly

DEVELOPING EDITING THERAPIES

3:25 Chairperson's Remarks

Jonathan Watts, PhD, Professor, RNA Therapeutics Institute, University of Massachusetts Chan Medical School

3:30 Therapeutic Applications for Hepatic and Extrahepatic RNA Editing via Endogenous ADAR Enzymes

Ian Harding, PhD, Senior Scientist I, Wave Life Sciences

AIMers are oligonucleotides that engage endogenous ADAR enzymes to induce highly efficient and specific A-to-I RNA base editing. Our recently optimized AIMer design increases the potency, target space, and tissue-targeting capabilities of RNA editing. Optimized AIMers support efficient RNA editing in both hepatic and extrahepatic tissues, including the central nervous system, kidney, and lung. We will show that AIMers support RNA editing of disease-relevant targets in multiple tissues.

Oligonucleotide Discovery & Delivery

Optimizing Design and Advances in the Clinic

4:00 Developing Novel RNA-Editing Therapies to Address Unmet Needs for Rare and Highly Prevalent Diseases

Venkat Krishnamurthy, PhD, Senior Vice President & Head of Platform, Korro Bio

This talk will focus on creating transformative genetic medicines for diseases of the liver, CNS, and beyond. At Korro, we use the "OPERA" (Oligonucleotide Promoted Editing of RNA) platform as a differentiated approach to identifying highly potent RNA editing therapeutics. This talk will also discuss Korro's lead program, KRRO-110, which is potentially a best-in-class therapeutic for the treatment of Alpha-1 Antitrypsin Deficiency (AATD).

4:30 Approaches to Optimize Safety and Potency of LNP-Based CRISPR-Based Medicines Delivered *In Vivo*

Steven Wolk, PhD, Vice President, Analytical Chemistry, Editas Medicine

The goal for the next generation of CRISPR-based medicines is the development of potent and safe therapeutics that can be delivered *in vivo* specifically to the target cells of interest. The mRNA/LNP format is currently showing the most promise to achieve this challenging goal, and various factors can be optimized to enhance performance, including vehicle (lipid composition and targeting elements), cargo (mRNA and gRNA), and analytical method development.

NOVEL PHOSPHORAMIDITES

5:00 Novel Phosphoramidites Enabling a Cationization of The Selective Segments of Oligonucleotides

David Tabatadze, PhD, President, ZATA Pharmaceuticals, Inc.

ZATA's amidites enable incorporation of ON backbone modifying (cationization) groups by direct automated synthesis. Such groups can be incorporated at any number and location enabled by size of ONs. Incorporated groups do not compromise any key properties, such as hybridization, solubility, stability, and others.

5:30 Close of Conference

5:30 Close of Conference

Oligonucleotide CMC & Regulatory Strategies

Enhancing Analytical Methods and Accelerating Time to Market

TUESDAY, MARCH 11

8:00 am Recommended Short Courses*
SC1: Safety & Toxicity of Nucleic Acids OR SC2: Successful Regulatory Submission for a Complex Oligonucleotide
*Premium Registration or separate registration required. See Short Courses page for details.

9:45 Registration and Morning Coffee

10:45 Welcome Remarks by Conference Organizer

ADVANCES IN CMC & ANALYTICAL CHARACTERIZATION

10:55 Chairperson's Remarks
Lori Troup, Director, Analytical Development, Novo Nordisk

11:00 KEYNOTE PRESENTATION: Characterization of Stereopure Chimeric PO/PS/PN Oligonucleotides
Pachamuthu Kandasamy, PhD, Vice President & Head, Medicinal Chemistry, Wave Life Sciences
Wave Life Sciences is advancing new chemistries to generate stereopure chimeric backbone-containing oligonucleotides—those in which the chirality of each backbone linkage has been precisely controlled during chemical synthesis. We will provide an overview of the methods we have developed to synthesize, manufacture, and quality control stereopure chimeric oligonucleotides containing phosphoryl guanidine (PN) backbone linkages in combination with more traditional phosphodiester (PO) and phosphorothioate (PS) backbone linkages.

11:30 Getting VO659 into the Clinic—CMC Lessons Learned
Bas Groenendaal, PhD, Director CMC, Vico Therapeutics
VO659 is an antisense oligonucleotide currently being developed to treat patients with polyglutamine diseases including HD, SCA1, and SCA3. This presentation will focus on the work performed within the CMC department at VICO Therapeutics to prepare for the first-in-human clinical trial, and will summarize our lessons learned from the interactions with various European regulatory agencies on the submission of the Investigational Medicinal Product Dossier for VO659.

12:00 pm Differentiation of N-1 Positional Isomers in Antisense Oligonucleotides with Orthogonal Mass Spectrometry Methods
Xiaoqing (Sherry) Kong, PhD, Scientist II, Analytical Development, Biogen
Investigating the origins of n-1 impurities during solid-phase synthesis is crucial for enhancing therapeutic oligonucleotide quality. In producing 2'-O-[2-(methylamino)-2-oxoethyl] modified phosphorothioate antisense oligonucleotide (NMA PS ASO), we identified n-NMA 5-methylcytosine (n-NMA MeC) as a key impurity caused by deletions of any of five MeC residues. Employing desulfurization for chromatographic separation and direct fragmentation for MS2-based quantitation, we differentiated five isomeric impurities. Incorporating targeted capping steps reduced n-1 levels to <1%.

12:30 Transition to Lunch

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Session Break

1:50 Chairperson's Remarks
Michael Hellerstein, Head of Operations, Vaxxinity Inc

1:55 Advances in Antibody Oligonucleotide Conjugates (AOCs)
Juhi Firdos, Scientist II, Avidity Biosciences
Avidity Biosciences is developing Antibody Oligonucleotide Conjugates (AOCs), combining monoclonal antibodies with oligonucleotide therapies to treat rare genetic diseases, such as Myotonic Dystrophy Type 1 and Duchenne Muscular Dystrophy. This talk will review siRNA and PMO modalities, focusing on differences in analytical methods for the oligos and their conjugates. Key challenges include analytical methods for AOCs with high drug-to-antibody ratios (DAR) and peak identification through CE-SDS.

2:25 Adoption and Implementation of Innovative Technologies in CMC
Robert Dream, PhD, Managing Director, HDR Co. LLC
CMC has an opportunity to reimagine its innovation to improve drug development. It's a complex multidisciplinary function critical to the successful development of any drug. Its purpose is to develop processes and methods for producing safe and effective medicines. In the shadows of clinical development, it drives important advances to accelerate drug development, devise new forms of drug delivery that make conditions "druggable," optimize development cost, and increase patient adherence.

2:55 Sponsored Presentation *(Opportunity Available)*

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

PLENARY SESSION

4:10 Organizer's Welcome Remarks
Gemma Smith, Senior Conference Director, Production, Cambridge Healthtech Institute

4:15 Plenary Chairperson's Remarks
Dmitry Samarsky, PhD, Former CTO, Sirnaomics

4:20 siRNA Chemical Engineering
Anastasia Khvorova, PhD, Professor, RNA Therapeutic Institute, University of Massachusetts Medical School
The focus of our lab is to identify, characterize, and develop novel chemistries that promote simple, efficient, and non-toxic delivery of oligonucleotides and potent silencing of therapeutic targets *in vivo*. Some examples will be highlighted in this talk.

5:00 TANGO: An RNA Splicing Approach to Upregulate Proteins
Edward Kaye, MD, CEO and Director, Stoke Therapeutics
Targeted Augmentation of Nuclear Gene Output (TANGO) is an RNA splicing approach that enables the upregulation of many proteins. Specifically designed Anti-sense Oligonucleotides (ASOs) splice out retained naturally occurring "poison exons" or NMD exons from pre-mRNA, thus enabling an increase of full length message and full length protein. We are targeting autosomal dominant diseases which are missing 50% of an essential protein to correct the underlying genetic defect.

5:40 10th Annual Welcome Reception in the Exhibit Hall with Poster Viewing

6:50 Close of Day

Oligonucleotide CMC & Regulatory Strategies

Enhancing Analytical Methods and Accelerating Time to Market

WEDNESDAY, MARCH 12

7:30 am Registration and Morning Coffee

REGULATORY STRATEGIES

8:00 Chairperson's Remarks
Robert Dream, PhD, Managing Director, HDR Co. LLC

8:05 FEATURED PRESENTATION: Overcoming Common Regulatory Hurdles during siRNA Product Lifecycle Management
Arwa El Hagrasy, PhD, Director, Regulatory Affairs CMC, Alnylam Pharmaceuticals

siRNA therapeutics are a growing class of products, with novel manufacturing processes and controls. Managing regulatory requirements in different regions during initial marketing applications and lifecycle management becomes increasingly important in this rapidly growing field. Alnylam has multiple siRNA products on the market at various stages of market expansion and lifecycle management. This talk will identify some of those hurdles and provide strategies for managing regulatory requirements in different regions.

8:35 Developing an Impurity Control Strategy in Light of Emerging Regulatory Guidelines
Mike Webb, PhD, Founder and CEO, Mike Webb Pharma; Former Vice President, API Chemistry & Analysis, GSK

The EMA have recently published draft CMC guidelines for oligonucleotides. We will discuss the implications of these guidelines for the control strategy of therapeutic oligonucleotides from early development to registration. With the guidelines in mind, we will discuss the evolution of a control strategy for impurities in double-stranded oligonucleotides with typical 2' chemical modifications and a limited number of phosphorothioate linkages.

9:05 Technological Advancements in Oligonucleotide Synthesis CMC
Balasubramanian Arumugam, Director - Technical Research , Asymchem, Inc.

The oligonucleotide CMC faces numerous challenges due to the lack of guidelines from the ICH or FDA. Additionally, its CMC processes present complexities because the unique preparation steps require specialized equipment, differing from those used for small molecules due to their complex structures and higher molecular weights. Key issues include managing impurities and developing and validating analytical methods. Asymchem stands at the forefront, leveraging its expertise, technologies, and capacity to overcome the challenges and ensure the successful development and manufacturing.

9:35 Coffee Break in the Exhibit Hall with Poster Viewing

10:15 Mass Spectrometry of Oligonucleotides for the Development of NIST Reference Materials
Mark Lowenthal, PhD, Research Chemist, Analytical Chemistry, National Institute of Standards and Technology (NIST)

Mass spectrometry proves useful for quality assurance of therapeutic mRNA due to its unique ability to measure base modifications, capping, stability, and impurities. NIST is developing measurement capabilities and oligonucleotide-based reference materials to support measurements of critical quality attributes (CQAs) for therapeutic drug products. A new NIST Test Material (RG 10202 FLuc mRNA) serves as a system suitability standard, a primary quantitative standard, or QC/QA material for comparability assays.

10:45 PANEL DISCUSSION: The Confluence of Innovation in Therapeutics and Regulation: CMC Considerations for mRNA and Oligonucleotides
Moderator: Robert Dream, PhD, Managing Director, HDR Co. LLC

- Novel modalities and new developments in drug delivery technology for mRNA and oligonucleotides
- Understanding the regulatory framework to evaluate these modalities with an emphasis on CMC
- Specific forward-looking trends in regulatory science that could potentially ameliorate the aforementioned challenges, including the development of accelerated regulatory approvals and the harmonization of guidelines for international regulatory authorities
- Regulatory recommendations and guidance that address issues and describe some of the long-term manufacturing developments

Panelists:
Bas Groenendaal, PhD, Director CMC, Vico Therapeutics
Juhi Firdos, Scientist II, Avidity Biosciences
Arwa El Hagrasy, PhD, Director, Regulatory Affairs CMC, Alnylam Pharmaceuticals
Mahender Gurram, PhD, Senior Director, Entrada Therapeutics

11:15 Transition to Lunch

11:25 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

11:55 Session Break

PLENARY SESSION

12:40 pm Plenary Chairperson's Remarks
Chandra Vargeese, PhD, CTO & Head, Platform Discovery Sciences, Wave Life Sciences

12:45 Delivery with Bicycles and Camelids: Targeted Delivery of Oligonucleotide Drugs to Muscle and the Central Nervous System via the Transferrin Receptor
Eric Swayze, PhD, Executive Vice President, Research, Ionis Pharmaceuticals

Ligands for transferrin receptor can potentially provide solutions to the delivery of oligonucleotides to skeletal and cardiac muscle, as well as across the blood brain barrier. We have optimized oligonucleotide conjugates to TfR1 ligands including Bicycle peptides and camelid nanobodies to reduce the total dose of the administered drug. These constructs have achieved successful delivery to the target tissues, offering the potential for treatment of cardiovascular and neurological diseases.

1:25 CRISPR Genome Editing for Therapeutic Applications: Advances in *in vivo* Editing
Rubina Parmar, PhD, Vice President, Chemistry & Delivery Sciences, Intellia Therapeutics

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2:05 Refreshment Break in the Exhibit Hall with Last chance for Poster Viewing

Oligonucleotide CMC & Regulatory Strategies

Enhancing Analytical Methods and Accelerating Time to Market

IN-PERSON BREAKOUT DISCUSSIONS

2:40 In-Person Breakout Discussions
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BREAKOUT DISCUSSION: Laying the Groundwork for a Successful IND or CTA
Michael Hellerstein, Head of Operations, Vaxxinity Inc
• Phase-appropriate development: Planning for evolution and improvement of CMC systems to meet regulatory requirements
• Planning for success: Design of process and analytical development programs to meet regulatory requirements
• How much is too much? How to balance the need for control against the need for flexibility
• The expected unexpected: Proactively dealing with gaps in the data

BREAKOUT DISCUSSION: Analytical Characterization and Quantitation of Impurities in Single- and Double-Stranded Oligonucleotides
Mike Webb, PhD, Founder and CEO, Mike Webb Pharma; Former Vice President, API Chemistry & Analysis, GSK
• How to control impurity families with different 2' chemistries and limited chromatographic separation
• Orthogonal chromatographic methods versus orthogonal detection (UV and MS)
• Data requirements for controlling CQA's for batch analysis versus measuring CQA outputs during process characterization experiments
• How to leverage prior knowledge for process characterization

SAFETY CHALLENGES AND RISK-MITIGATION STRATEGIES

3:25 Chairperson's Remarks
Robert Dream, PhD, Managing Director, HDR Co. LLC

3:30 Safety and Pharmacokinetics Challenges with Nucleic Acid Therapeutics
Rakesh Dixit, PhD, DABT, President & Founder, Bionavigen Oncology, LLC and Regio Biosciences
Nucleic acid therapeutics (NATs) have revolutionized the potential to treat many debilitating diseases and life-threatening infections by targeting their genetic fingerprints *in vivo*. This presentation will provide a comprehensive review of safety challenges and risk mitigation strategies for NATs, including antisense oligonucleotides, ligand-modified small interfering RNA conjugates, lipid nanoparticles, adeno-associated virus vectors, and CRISPR.

EFFICIENT MANUFACTURING PROCESSES

4:00 How to Work with Your CMO for Successful Oligonucleotide Manufacturing
Hagen Cramer, PhD, CTO, QurAlis Corporation
QurAlis is developing precision therapies, targeting genetic drivers in sub-forms of ALS. Two of QurAlis's programs are in early-phase clinical trials. One of these programs is a splice modulator ASO delivered by intrathecal injection. The talk will focus on how to successfully work with your CMO to meet your timelines and regulatory expectations.

4:30 Strategies for Oligonucleotide Purification Applicable to Clinical Products Manufacture
Mahender Gurram, PhD, Senior Director, Entrada Therapeutics
Purification is probably the most time-consuming and critical step in the manufacture of oligos/modified oligos. The topic covers purification method selection criteria and strategies in minimizing the risk in the purification steps which are specifically applicable to clinical products manufacture.

5:00 Close of Conference

mRNA Design & Delivery

Increased Efficacy, Better Stability, Targeted Delivery, and Improved Safety

TUESDAY, MARCH 11

8:00 am Recommended Short Course*
SC1: Safety & Toxicity of Nucleic Acids
*Premium Registration or separate registration required. See Short Courses page for details.

9:45 Registration and Morning Coffee

10:45 Welcome Remarks by Conference Organizer

NOVEL TARGETED mRNA DELIVERY

10:55 Chairperson's Remarks
Dan Peer, PhD, Professor & Director, Laboratory of Precision Nanomedicine; Vice President for Research, Tel Aviv University

11:00 Delivery of Therapeutic RNAs into the Brain
Ekkehard Leberer, PhD, Professor of Biochemistry, Technical University of Munich; Senior Consultant, ELBIOCON; Advisor, Neuway Pharma
The presentation will describe the generation and use of protein-based nano-capsules to deliver therapeutic RNAs to the brain for the treatment of CNS diseases. This approach is making use of the brain tropism of a capsid protein derived from the John Cunningham virus. The therapeutic potential of this system will be illustrated by mRNA-based enzyme replacement to repair the genetic defect in metachromatic leukodystrophy, a monogenetic CNS lysosomal storage disorder.

11:30 DELiveri: High-Throughput Platform for the Discovery of Delivery Conjugates of Nucleic-Acid Therapeutics
Paloma Giangrande, PhD, CTO, Eleven Therapeutics
Advancing the frontier of RNA therapeutics demands innovative solutions for the precise, cell-selective delivery of nucleic acids—a challenge that has hindered progress for years. Notably, while liver-selective delivery has been achieved through GalNAc conjugation, extending this success to other tissues remains a formidable obstacle. Here, we introduce DELiveri, a massively parallel, hypothesis-free screening platform designed to discover novel delivery conjugates, coupled with state-of-the-art AI models to predict productive delivery.

12:00 pm Next-Generation Lipid Nanoparticles: From the Bench to the Clinic
Dan Peer, PhD, Professor & Director, Laboratory of Precision Nanomedicine; Vice President for Research, Tel Aviv University
In this presentation, I will detail the journey of NeoVac Ltd., a clinical-stage, Oxford-based company from an academic idea to the clinic with chemistry, formulation, analytics, biology, regulation, and clinical team—and how we generated the first UK mRNA-LNPs vaccine platform manufactured and clinically tested in the UK. I will also detail the mRNA-LNPs therapeutic platform with preclinical data in inflammatory bowel diseases and in cancer.

12:30 Transition to Lunch

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Session Break

ENHANCING mRNA EXPRESSION & TRANSLATION

1:50 Chairperson's Remarks
Vikram Agarwal, PhD, Head of mRNA Platform Design Data Science, mRNA Center of Excellence, Sanofi

1:55 Deep-Learning Guided Optimization of Translation Efficiency for mRNA Vaccine Development
Vikram Agarwal, PhD, Head of mRNA Platform Design Data Science, mRNA Center of Excellence, Sanofi
Delivered mRNA vaccines benefit from a high antigen yield to stimulate an effective immune response. Translational output is one mode of regulation that can be engineered to further optimize antigen yield; however, the degree to which translational control is specified by mRNA sequence is poorly understood. We developed RiboNN to address this question and propose it as a tool to guide the design of translation-optimized mRNA therapeutics for mRNA-based vaccines.

2:25 KEYNOTE PRESENTATION: Use of Poly(A) Tail Mimetics to Enhance mRNA Expression from Genes Associated with Haploinsufficiency Disorders
Jeffery M. Coller, PhD, Bloomberg Distinguished Professor of RNA Biology and Therapeutics, Johns Hopkins University
Poly(A) tails are crucial for mRNA stability and translation. We developed mRNA Boosters, a new therapy that attaches a poly(A) tail mimetic to targeted mRNAs, enhancing their expression. This approach is effective for haploinsufficiency disorders and has shown promise in increasing expression of genes related to autism spectrum disorders in both cell cultures and animal models.

2:55 Sponsored Presentation *(Opportunity Available)*

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

PLENARY SESSION

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Gemma Smith, Senior Conference Director, Production, Cambridge Healthtech Institute

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Dmitry Samarsky, PhD, Former CTO, Sirnaomics

4:20 siRNA Chemical Engineering
Anastasia Khvorova, PhD, Professor, RNA Therapeutic Institute, University of Massachusetts Medical School
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Edward Kaye, MD, CEO and Director, Stoke Therapeutics
Targeted Augmentation of Nuclear Gene Output (TANGO) is an RNA splicing approach that enables the upregulation of many proteins. Specifically designed Anti-sense Oligonucleotides (ASOs) splice out retained naturally occurring "poison exons" or NMD exons from pre-mRNA, thus enabling an increase of full length message and full length protein. We are targeting autosomal dominant diseases which are missing 50% of an essential protein to correct the underlying genetic defect.

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6:50 Close of Day

mRNA Design & Delivery

Increased Efficacy, Better Stability, Targeted Delivery, and Improved Safety

WEDNESDAY, MARCH 12

7:30 am Registration and Morning Coffee

NOVEL RNA THERAPIES FOR ONCOLOGY

8:00 Chairperson's Remarks
Jaspreet Khurana, PhD, Senior Director, mRNA Programming, Strand Therapeutics, Inc.

8:05 RNA Activation in Cancer and Rare Genetic Diseases
Nagy Habib, ChM, FRCS, Professor of Surgery, Imperial College London
RNA activation with small activating RNAs can lead to upregulation of transcription in the nucleus resulting in increased mRNA and targeted protein. This can be applied to many genes downregulated in cancer as well as rare genetic diseases like sickle cell disease. Wide bio-distribution is suitable in rare genetic diseases and with diseases related to the dark genome where the reduced long noncoding RNA is tissue-, cell-, and status-specific.

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Ron Weiss, PhD, Professor, Biological Engineering, Massachusetts Institute of Technology
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9:05 Sponsored Presentation *(Opportunity Available)*

9:35 Coffee Break in the Exhibit Hall with Poster Viewing

10:15 Advancing Cancer Immunotherapy with mRNA Synthetic Biology
Jaspreet Khurana, PhD, Senior Director, mRNA Programming, Strand Therapeutics, Inc.
We have developed a platform in which we design RNA-encoded programmable genetic "circuits" that detect molecular cues in a cell to specifically express a payload protein in cells that exhibit a particular molecular signature. We applied this platform to the development of our program which entails systemic delivery of lipid nanoparticle (LNP)-encapsulated mRNA-bearing programmable genetic circuitry that selectively expresses a therapeutic payload within target cells.

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Arthur Krieg, MD, Founder, President and Acting CEO/CSO, Zola Therapeutics
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IN-PERSON ONLY BREAKOUT DISCUSSION: Tackling Challenges with mRNA Delivery
Charles Chen, PhD, Senior Scientist, Advanced Drug Delivery, Pharmaceutical Sciences, AstraZeneca Pharmaceuticals, R&D
Ekkehard Leberer, PhD, Professor of Biochemistry, Technical University of Munich; Senior Consultant, ELBIOCON; Advisor, Neuway Pharma
Dan Peer, PhD, Professor & Director, Laboratory of Precision Nanomedicine; Vice President for Research, Tel Aviv University

IN-PERSON ONLY BREAKOUT DISCUSSION: Overcoming Translational Challenges in RNA Therapeutics Development
Vikram Agarwal, PhD, Head of mRNA Platform Design Data Science, mRNA Center of Excellence, Sanofi
Nagy Habib, ChM, FRCS, Professor of Surgery, Imperial College London
Arthur Krieg, MD, Founder, President and Acting CEO/CSO, Zola Therapeutics

mRNA Design & Delivery

Increased Efficacy, Better Stability, Targeted Delivery, and Improved Safety

OPTIMIZING mRNA THERAPIES

3:25 Chairperson's Remarks

Iris Grossman, PhD, Chief Therapeutics Officer, R&D, Eleven Therapeutics US, Inc.

3:30 xRNA's PK-PD Profile Unlocks the Therapeutic Potential of mRNA

Iris Grossman, PhD, Chief Therapeutics Officer, R&D, Eleven Therapeutics US, Inc.

Eleven Tx develops a modality called xRNA, which is a synthetic mRNA that utilizes precisely positioned, non-canonical building blocks to resist degradation, increase protein production, and minimize immunogenicity. The outcome is a robust and long-lasting therapeutic effect. A proprietary high-throughput platform facilitates systematic screening of xRNAs and derivation of AI-enabled Structure-Activity-Relationships (SARs). Our hit optimization pipeline of screening, *in vitro* confirmation, and *in vivo* validation demonstrated broad utility.

4:00 Developing mRNA Therapeutics for Cardiovascular Diseases

Ajit Magadum, PhD, Assistant Professor, Department of Cardiovascular Diseases + ACDC, Lewis Katz School of Medicine, Temple University

mRNA therapeutics is rapidly emerging as a groundbreaking strategy for treating cardiovascular diseases (CVD), which affects 650 million people. Despite advances in medicine, the need for curative therapies remains urgent. I will share a decade of work on mRNA therapies that promote cardiac regeneration, and combat fibrosis, cell death, and hypertrophy in CVD models. Additionally, we introduce novel cell-specific mRNA expression platforms, advancing the field of CVD therapeutics.

4:30 Novel mRNA Manufacturing

Craig Martin, PhD, Professor, Chemistry, University of Massachusetts, Amherst

An ounce of prevention is worth a pound of purification. Using a fully immobilized polymerase-DNA scalable platform, we generate RNA that is free of dsRNA, DNA, and enzymes, eliminating the three purifications required in traditional manufacturing. DNA and enzymes remain active for very long production runs, further reducing costs. dsRNA levels, at synthesis, are far lower than can be achieved by downstream purification, enabling sensitive RNA applications.

5:00 Close of Conference

Emerging Oligonucleotide Modalities

Pursuing Circular RNA, tRNA, and Innovative Editing Approaches

TUESDAY, MARCH 11

8:00 am Recommended Short Course*
SC1: Safety & Toxicity of Nucleic Acids
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10:45 Welcome Remarks by Conference Organizer

CIRCULAR RNA THERAPIES

10:55 Chairperson's Remarks
Paloma Giangrande, PhD, CTO, Eleven Therapeutics

11:00 Circular RNA: Transforming a Promising Technology into Cutting-Edge Therapeutics
Edo Kon, PhD, Director of Business Development, RiboX Therapeutics
RiboX Therapeutics is a globally-operated biotech company focusing on discovering and developing fully engineered circular RNA as a therapeutic modality, which offers advantages to address key challenges of mRNA medicines. RiboX has established a plug-and-play circular RNA platform, an ionizable lipid platform, and has unique assets in active targeting LNP under development.

11:30 Circular mRNA and Its Application in Immunotherapy and Genome Engineering
Li Li, PhD, Assistant Professor, RNA Therapeutics Institute, University of Massachusetts Chan Medical School
Circular mRNA (CircRNA) has generated substantial interest as a new mRNA therapeutics platform. Here I will discuss a scalable and column-free method for preparing non-immunogenic circular mRNAs. I will also show its applications in immunotherapy and genome editing.

12:00 pm *In vivo* Cell Engineering Using oRNA
Robert Mabry, PhD, CSO, Orna Therapeutics
In vivo CAR therapy could eliminate the need for patient cell isolation and avoid risks associated with conditioning regimens of CAR T therapies. Orna Therapeutic's panCAR combines a synthetic, circular coding RNA platform (oRNA) and proprietary immunotropic lipid nanoparticle (LNP) to drive immune effector cell (e.g. T cells, NK cells) CAR expression after *in vivo* administration, promising a transient, re-dosable, and scalable immune cell therapy without preconditioning lymphodepletion.

12:30 Transition to Lunch

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:10 Session Break

DEVELOPING tRNA BASED THERAPIES

1:50 Chairperson's Remarks
Austin Draycott, PhD, CEO, Cloverleaf Bio

1:55 Engineered Inhibitory tRNAs as Novel Therapeutics for Oncology
Austin Draycott, PhD, CEO, Cloverleaf Bio
At Cloverleaf Bio, we are developing a new class of engineered tRNA therapeutics. Our tRNAs target an underappreciated vulnerability of cancer: addiction to high levels of tRNA modifying enzymes. Cloverleaf's approach to drugging tRNA modifying enzymes uses engineered "trojan horse" tRNAs. The programmability, potency, and specificity of our tRNAs will potentially improve cancer treatment across a range of indications.

2:25 FEATURED PRESENTATION: Design and Delivery of tRNA Therapeutics to Treat Stop Codon Disease
William Kiesman, PhD, Chief Technology Officer, Alltrna
This talk will explore designing, manufacturing, and delivering transfer RNA (tRNA) as a new therapeutic modality. We will examine how this innovative technology can be applied across diseases caused by a premature termination codon (PTC), collectively referred to as Stop Codon Disease, and discuss initial proof-of-concept experiments to unlock the potential in tRNA biology to create a universal precision medicine to treat diseases with shared genetic mutations.

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WEDNESDAY, MARCH 12

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IN-PERSON ONLY BREAKOUT DISCUSSION: Designing and Optimizing New RNA Modalities as Therapeutics
William Kiesman, PhD, Chief Technology Officer, Alltrna
Edo Kon, PhD, Director of Business Development, RiboX Therapeutics
Li Li, PhD, Assistant Professor, RNA Therapeutics Institute, University of Massachusetts Chan Medical School

Emerging Oligonucleotide Modalities

Pursuing Circular RNA, tRNA, and Innovative Editing Approaches

DEVELOPING EDITING THERAPIES

3:25 Chairperson's Remarks

Jonathan Watts, PhD, Professor, RNA Therapeutics Institute, University of Massachusetts Chan Medical School

3:30 Therapeutic Applications for Hepatic and Extrahepatic RNA Editing via Endogenous ADAR Enzymes

Ian Harding, PhD, Senior Scientist I, Wave Life Sciences

AIMers are oligonucleotides that engage endogenous ADAR enzymes to induce highly efficient and specific A-to-I RNA base editing. Our recently optimized AIMer design increases the potency, target space, and tissue-targeting capabilities of RNA editing. Optimized AIMers support efficient RNA editing in both hepatic and extrahepatic tissues, including the central nervous system, kidney, and lung. We will show that AIMers support RNA editing of disease-relevant targets in multiple tissues.

4:00 Developing Novel RNA-Editing Therapies to Address Unmet Needs for Rare and Highly Prevalent Diseases

Venkat Krishnamurthy, PhD, Senior Vice President & Head of Platform, Korro Bio

This talk will focus on creating transformative genetic medicines for diseases of the liver, CNS, and beyond. At Korro, we use the "OPERA" (Oligonucleotide Promoted Editing of RNA) platform as a differentiated approach to identifying highly potent RNA editing therapeutics. This talk will also discuss Korro's lead program, KRRO-110, which is potentially a best-in-class therapeutic for the treatment of Alpha-1 Antitrypsin Deficiency (AATD).

4:30 Approaches to Optimize Safety and Potency of LNP-Based CRISPR-Based Medicines Delivered *In Vivo*

Steven Wolk, PhD, Vice President, Analytical Chemistry, Editas Medicine

The goal for the next generation of CRISPR-based medicines is the development of potent and safe therapeutics that can be delivered *in vivo* specifically to the target cells of interest. The mRNA/LNP format is currently showing the most promise to achieve this challenging goal, and various factors can be optimized to enhance performance, including vehicle (lipid composition and targeting elements), cargo (mRNA and gRNA), and analytical method development.

NOVEL PHOSPHORAMIDITES

5:00 Novel Phosphoramidites Enabling a Cationization of The Selective Segments of Oligonucleotides

David Tabatadze, PhD, President, ZATA Pharmaceuticals, Inc.

ZATA's amidites enable incorporation of ON backbone modifying (cationization) groups by direct automated synthesis. Such groups can be incorporated at any number and location enabled by size of ONs. Incorporated groups do not compromise any key properties, such as hybridization, solubility, stability, and others.

5:30 Close of Conference

Poster Information

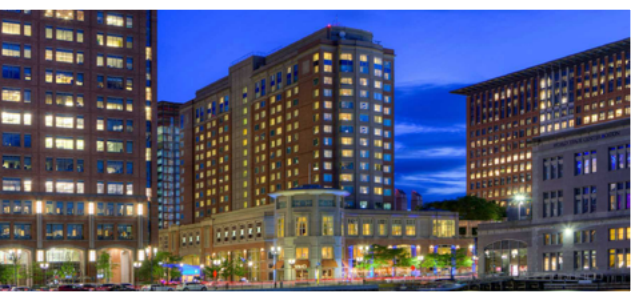
Present a Poster and Save $50!

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster session. To secure an onsite poster board and/or ensure your poster is included in the conference materials, your submission must be received, and your registration paid in full by **January 31, 2025.**

Reasons you should present your research poster at this conference:

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

Hotel and Travel



Conference Venue and Hotel:
Seaport Hotel Boston
One Seaport Lane
Boston, MA 02110

Discounted Room Rate: $257 s/d
Discounted Room Rate Cut-off Date: February 11, 2025

For Reservations and Additional Information: Visit optcongress.com/hotel-travel

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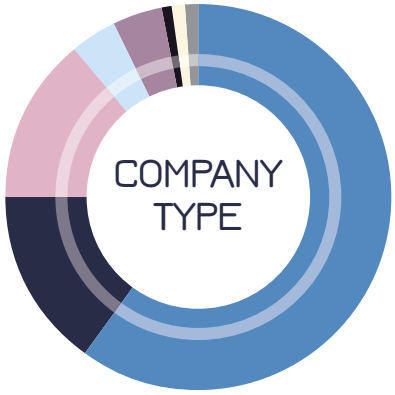
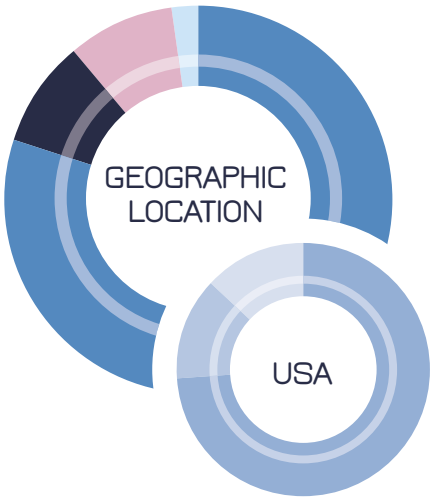
Kristin Skahan
Senior Business Development Manager
781.972.5431
kskahan@healthtech.com

2024 Attendee Demographics



Biotech	60%
Academic	15%
Pharma	14%
Healthcare	4%
Services	4%
Financial	1%
Government	1%
Societies	1%



USA	80%	**US Breakdown**	
Asia	9%	East Coast	74%
Europe	9%	Midwest	13%
Rest of World	2%	West Coast	13%

Scientist/Technologist	60%
Director	15%
Executive	14%
Sales & Marketing	4%
Professor	4%
Manager	1%
Assistant	1%

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