MARCH 15-16, 2022 | BOSTON, MA

OPT Congress

7th ANNUAL

Oligonucleotide & Precision Therapeutics

IN-PERSON ■ VIRTUAL
FLEXIBLE REGISTRATION

DISCOVERY ■ DEVELOPMENT ■ DELIVERY



CONFERENCE PROGRAMS

Oligonucleotide Discovery and Delivery

Oligonucleotide CMC and Regulatory Strategies

SHORT COURSE

Examining the Safety and Toxicity of Nucleic Acid Therapeutics

KEYNOTE SPEAKERS

Isabel Aznarez, PhD
Co-Founder, Vice President & Head, Biology, Stoke Therapeutics

Richard Geary, PhD
Chief Development Officer and Executive Vice President, Antisense Drug Development, Ionis Pharmaceuticals, Inc.

Arthur M. Krieg
Founder & CSO, Checkmate Pharmaceuticals

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

Michael Segel, PhD
Postdoctoral Fellow, Laboratory of Dr. Feng Zhang, Broad Institute of MIT and Harvard

OPTCongress.com #OPTBoston

Welcome to OPT Congress

Conference Highlights

EXHIBIT HOURS

Tuesday, March 15, 2:50 PM – 6:35 PM
Wednesday, March 16, 10:30 AM – 3:10 PM

NETWORKING RECEPTION & BREAKS
Tuesday, March 15, 5:35 PM – 6:35 PM
Wednesday, March 16, 12:50 PM – 1:25 PM

EVENT-AT-A-GLANCE

TUESDAY, MARCH 15, 2022	WEDNESDAY, MARCH 16, 2022
Short Course	
Oligonucleotide Discovery and Delivery	Oligonucleotide Discovery and Delivery
Oligonucleotide CMC and Regulatory Strategies	Oligonucleotide CMC and Regulatory Strategies

WITH THANKS
TO OUR EXECUTIVE ADVISORY BOARD



Ekkehard Leberer, PhD
Senior Director, R&D Alliance Management, Sanofi



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



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



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



Dmitry Samarsky, PhD
CTO, Sirnaomics



MARCH 15, 2022

SHORT COURSE

Examining the Safety and Toxicity of Nucleic Acid Therapeutics

TUESDAY, MARCH 15 8:00-10:00 AM

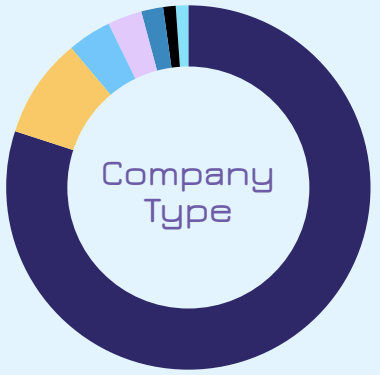
Examining the Safety and Toxicity of Nucleic Acid Therapeutics

Instructors: ***Jeffrey Foy, PhD, Executive Director, Toxicology, Dicerna Pharmaceuticals***
Xiao Shelley Hu, PhD, Senior Director, Head of DMPK and Clinical Pharmacology, Wave Life Sciences
Padma Narayanan, PhD, Head, Preclinical Safety, Wave Life Sciences

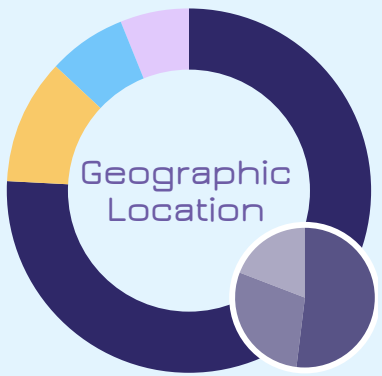
Nucleic acid drugs continue to deliver on their promise to become a third therapeutic modality, in addition to small molecules and biologics. Several antisense oligonucleotide drugs have been on the market for some time, while the first RNAi approval was granted in 2018. In addition, numerous mRNA and CRISPR therapeutic programs have entered clinical stages. Despite the common "nucleic acid" component, the mechanisms of action and non-specific effects differ for each of these drug types. This course discusses some of the preclinical strategies for ADME/safety/tox evaluations and regulatory expectations.

> "This conference was both educational and inspirational. My group will pursue at least one new research collaboration based on novel information presented."
>
> **Senior Research Advisor, Eli Lilly**

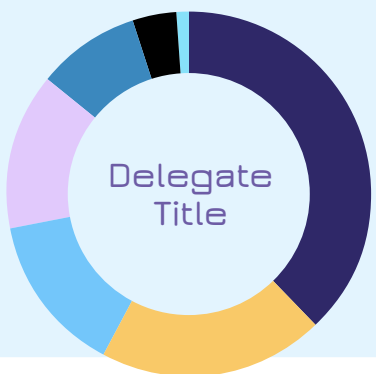
2021 Attendee Demographics



Biotech & Pharma	80%
Academic	9%
Healthcare	4%
Services	3%
Other	2%
CRO	1%
Financial	1%



USA	76%
East Coast	52%
West Coast	29%
Midwest	19%
Europe	11%
Asia	7%
Rest of World	6%



Scientist/Technologist	38%
Director	20%
Executive	14%
Sales & Marketing	14%
Manager	9%
Professor	4%
Assistant	1%

Oligonucleotide Discovery and Delivery

Optimizing Design, Delivery and Performance

TUESDAY, MARCH 15

7:00 am Short Course Registration

8:00 Recommended Pre-Conference Short Course*

SC1: Examining the Safety and Toxicity of Nucleic Acid Therapeutics
**All Access Premium Pricing or separate registration required. See short course page for details.*

9:15 Main Conference Registration and Morning Coffee

10:15 Organizer's Welcome Remarks
Tanuja Koppal, PhD, Senior Conference Director, Cambridge Healthtech Institute

ADVANCES IN TARGETED DELIVERY

10:25 Chairperson's Opening Remarks
Dmitry Samarsky, PhD, CTO, Sirnaomics

10:30 mxRNA: Miniaturized RNAi Triggers Composed of Single Oligonucleotides
Dmitry Samarsky, PhD, CTO, Sirnaomics
Sirnaomics has developed proprietary GalNAc-RNAi therapeutic platform GalAhead, with mxRNA comprising one of its key technological components. mxRNAs (or miniaturized RNAi triggers) are composed of single 31-33 nt long oligonucleotides, demonstrating excellent activity in primary hepatocytes and in mice. In addition to these experiments, we will present results of our 13-week study in non-human primates conducted with the candidate molecule for our frontrunner GalAhead therapeutic program.

11:00 Development of a GalNAc-asiRNA Platform for Treatment of Liver Disorders
Behfar Ardehali, PhD, Senior Scientist, OliX Pharmaceuticals
To address the unmet needs in treatment of liver disorders caused by overabundance of hepatocyte factors, OliX Pharmaceuticals has developed a N-acetyl galactosamine (GalNAc) conjugation platform for high-efficiency, ASGPR-mediated delivery of asiRNA compounds to hepatocytes. We have also established dynamic discovery and preclinical stage programs to target multiple hepatic disorders, among them, nonalcoholic steatohepatitis (NASH) and HBV. Here we present the latest advancements in our liver programs.

11:30 Exploring Chemical Space for Improving Properties of RNA Therapeutics
Thazha Prakash, PhD, Executive Research Fellow, Ionis Pharmaceuticals, Inc.
Advancements in the chemical design of oligonucleotide drugs have improved potency, safety and duration leading to better clinical outcomes. Efforts to expand the boundaries of existing chemical space to further enhance the properties of RNA therapeutics will be presented.

12:00 pm Session Break

12:10 Luncheon Presentation to be Announced
ChemGenes CORPORATION
Speaker to be Announced

12:40 Session Break

1:15 Chairperson's Opening Remarks
Leo Ziqing Qian, PhD, Co-Founder & Vice President, Discovery Research, Entrada Therapeutics

1:20 Delivery of RNA Therapeutics: The Great Endosomal Escape
Steven Dowdy, PhD, Professor, Department of Cellular & Molecular Medicine, University of California San Diego School of Medicine
RNA therapeutics have great potential to selectively treat human disease, especially cancer, COVID and neurological disorders. However, due to their size and 20-40 negatively charged phosphates, RNAs have limited (<1%) to no ability to overcome a billion years of evolutionary defenses that prevent RNAs from escaping across the endosomal lipid bilayer membrane into the cytoplasm. Consequently, endosomal escape remains The Technological Problem to solve for wide-spread development of RNA therapeutics.

1:50 Development of Endosomal Escape Vehicles to Enhance the Intracellular Delivery of Oligonucleotides
Leo Ziqing Qian, PhD, Co-Founder & Vice President, Discovery Research, Entrada Therapeutics
We have developed a novel oligonucleotide delivery platform by conjugation with Entrada's proprietary Endosomal Escape Vehicle (EEV), a class of cyclic peptides designed to facilitate intracellular delivery and endosomal escape. The preclinical results have confirmed the significant therapeutic potential of the strategy for DMD and demonstrated that the EEV platform can serve as a general and highly efficient delivery technology for the extrahepatic delivery of therapeutic oligonucleotides.

2:20 Sponsored Presentation *(Opportunity Available)*

2:50 Refreshment Break in the Exhibit Hall with Poster Viewing

FEATURED SESSION: EMERGING OLIGO THERAPIES

3:30 Chairperson's Opening Remarks
Paloma H. Giangrande, PhD, Vice President, Platform and Discovery Sciences Biology, Wave Life Sciences



3:35 FEATURED PRESENTATION: Small Activating RNA from Concept to Phase 2 Clinical Trials
Nagy Habib, ChM, FRCS, Head of R&D and CMO, MiNA Therapeutics Ltd.
Small activating RNAs (saRNA) are double stranded 21-nucleotide RNA that target promoters or enhance genes leading to mRNA upregulation. MTL-CEBPA is an investigative drug that resulted from the conjugation of saRNA CEBPA with NOV 340 lipsomes that targets tumour associated macrophages. MTL-CEBPA has been administered safely in over 100 patients with advanced cancer and improved clinical outcome in a sub-set of patients when co-administered with TKI or check point inhibitor.



4:05 FEATURED PRESENTATION: Advancing and Applying Base Editing Technologies

Luke Koblan, PhD, Former Graduate Student, Laboratory of David Liu, Department of Chemistry and Chemical Biology, Harvard University and Broad Institute of MIT and Harvard

Base editors hold significant promise to precisely correct the underlying genetic cause of many diseases. Correcting pathogenic mutations in disease-relevant contexts has remained challenging due to low editing efficiencies and limited editor delivery modalities. Systematic improvements to base editor performance and delivery enabled efficient adenine base editor-mediated correction of the predominant mutation underlying Hutchinson-Gilford Progeria Syndrome in a mouse model of this disease, ultimately rescuing major hallmarks of disease pathology.



4:35 FEATURED PRESENTATION: Chemically Modified Guides and Donors for Precision Genome Editing

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

We describe progress toward complete chemical modification of CRISPR guides and their *in vivo* genome editing. We have identified patterns of backbone and sugar modifications that allow robust gene editing activity in mRNA and RNP formats, *in vitro* and *in vivo*. We describe a broadly accessible modification strategy for DNA donors used as templates for homology-directed repair, which improves the efficiency of HDR up to 8-fold over normal DNA donors.



5:05 FEATURED PRESENTATION: Chemically Optimized Stereopure Oligonucleotides Direct ADAR-Mediated RNA Editing

Paloma H. Giangrande, PhD, Vice President, Platform and Discovery Sciences Biology, Wave Life Sciences

The talk will cover proof-of-concept preclinical *in vivo* data demonstrating effective and durable editing of human SERPINA1 Z allele mRNA in the liver, resulting in a therapeutically meaningful increase in circulating, functional wild-type AAT protein. These initial *in vivo* studies utilize Wave's proprietary transgenic mouse model, which has both the human SERPINA1 Z-allele as well as human ADAR that is expressed comparably to human cells.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:35 Close of Day

WEDNESDAY, MARCH 16

7:30 am Registration Open

BREAKFAST INTERACTIVE DISCUSSIONS

8:00 Breakfast Interactive Discussions

Interactive 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. For in-person events, the facilitator will lead from the front of the room while attendees remain seated to promote social distancing. For virtual attendees, the format will be in a Zoom room. 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 Interactive Discussion page on the conference website for a complete listing of topics and descriptions.

CO-PRESENTATION: INTERACTIVE DISCUSSION: Innovations In Oligo Design & Delivery

Thazha Prakash, PhD, Executive Research Fellow, Ionis Pharmaceuticals, Inc.
Arthur M. Krieg, Founder & CSO, Checkmate Pharmaceuticals

- Advancements in chemical design for oligonucleotide drugs
- Advancements in targeted delivery for oligonucleotide drugs

8:45 Session Break

OLIGO DRUGS FOR DIVERSE DISEASE INDICATIONS

8:55 Chairperson's Opening Remarks

Bianca Matthee, COO, Hybridize Therapeutics

9:00 A Novel, RNA-Based Anti-Viral Approach to Limit BK Virus Propagation in Immunocompromised Patients

Bianca Matthee, COO, Hybridize Therapeutics

BK virus (BKV) is a universal latent renal virus that reactivates in kidney transplantation patients and can lead to graft loss. No treatment exists for combatting BK virus. As such, treatment options for BKV are vital. At Hybridize, we have developed an innovative RNA-based direct-acting antiviral strategy that prevents BKV-mediated disease.

9:30 Self-Delivering FANA ASO Targeting Human FOXP3 For Cancer Immunotherapy

Wayne W. Hancock, MD, PhD, Professor of Pathology & Lab Medicine, University of Pennsylvania and Children's Hospital of Philadelphia

The efficacy of immunotherapy is limited by T-regulatory (Treg) and myeloid-derived suppressive cells. We developed antisense oligonucleotides (ASO) that knockdown human FOXP3 and decrease human Treg suppressive function, including in humanized mice. We also developed ASO that knocked-down murine Foxp3 mRNA, decreased Treg suppressive function and inhibited tumor growth in syngeneic lung tumor models. Hence, we have developed ASO that target Tregs, promote antitumor immunity and thereby warrant clinical development.

Oligonucleotide Discovery and Delivery

Optimizing Design, Delivery and Performance

10:00 Talk Title to be Announced
Speaker to be Announced

10:15 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 MicroRNA Therapeutics: Targeting Fibrotic Diseases
Ekkehard Leberer, PhD, Senior Life Sciences Consultant, ELBIOCON; Scientific Managing Director, COMPACT Consortium
MicroRNAs are short non-coding RNAs that regulate biochemical pathways by RNA interference (RNAi). Dysregulation of microRNAs is associated with many diseases including fibrosis. The presentation shows the development of anti-fibrotic therapeutic strategies using anti-miRs as therapeutic molecules.

11:40 A GalNAc-MCJ siRNA as a Novel Mitochondrial Regulator for Treating NASH
Cynthia M. Arbeeny, PhD, CSO, Mitotherapeutix LLC
Mitotherapeutix has identified MCJ/DNAJC15, a novel negative regulator of mitochondrial metabolism, as a key target to treat NASH and other metabolic diseases. We have performed SAR and selected a lead GalNAc-MCJ siRNA as a clinical candidate for NASH. Treatment targets hepatocytes and effectively knocks down MCJ reducing disease severity in NASH models. Activity has been confirmed in non-human primates. Preclinical toxicology and PK/PD studies are planned to support an IND-filing.

12:10 pm Session Break

12:20 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:50 Dessert Break in the Exhibit Hall with Poster Viewing

KEYNOTE SESSION: OLIGO THERAPIES – OPPORTUNITIES & CHALLENGES

1:25 Chairperson's Opening Remarks
Isabel Aznarez, PhD, VP, Discovery Research, Stoke Therapeutics



1:30 KEYNOTE PRESENTATION: A Novel RNA-Based Approach to Treat Genetic Diseases
Isabel Aznarez, PhD, VP, Discovery Research, Stoke Therapeutics
Targeted augmentation of nuclear gene output (TANGO) is a novel technology that exploits antisense oligonucleotide (ASO)-mediated modulation of pre-mRNA splicing to increase full length, fully functional protein expression. In haplo insufficiencies; e.g., Dravet syndrome and autosomal dominant optic atrophy, TANGO ASOs increase protein expression by leveraging the wild type allele. TANGO can target a wide range of gene types, functions and sizes to address genetic diseases amenable to protein upregulation.



2:00 KEYNOTE PRESENTATION: RNA Targeting Progress in Severe and Rare Disease
Richard Geary, PhD, Chief Development Officer and Executive Vice President, Antisense Drug Development, Ionis Pharmaceuticals, Inc.
More than ten RNA targeted products have been approved and launched in the rare and severe disease space. Both increase and decrease in protein target production have been utilized with RNA engaging oligonucleotides. Pipeline progress will be summarized along with the challenges and opportunities that have become apparent as the research continues.

2:30 Refreshment Break in the Exhibit Hall & Last Chance for Poster Viewing



3:10 KEYNOTE PRESENTATION: Intratumoral Delivery of a CpG-A TLR9 Agonist Using a Virus-Like Particle Can Overcome Resistance to PD-1 Blockade in Patients with Advanced Melanoma
Arthur M. Krieg, Founder & CSO, Checkmate Pharmaceuticals
Innate immune activation is an appealing approach to overcoming resistance to PD-1 blockade in patients with advanced cancer, and yet positive results in murine tumor models have usually not translated into human clinical data. CpG-A TLR9 agonists have unique immune effects that are enhanced by delivery using an immunogenic virus-like particle, leading to enhanced systemic anti-tumor effects in preclinical models and in humans.



3:40 KEYNOTE PRESENTATION: Engineering Antibody Oligonucleotide Conjugates (AOCs): Taking Receptor-Mediated Uptake One Step Further
Arthur Levin, PhD, CSO, Avidity Biosciences
The promise of oligonucleotide therapeutics is to use Watson-Crick-Franklin base-pairing rules to design drugs directly and rationally based on genomic information. Until recently, that has remained elusive because of cell barriers to oligonucleotide uptake. Receptor-mediated uptake through bioconjugation oligonucleotides has changed that. Avidity's AOC technology uses monoclonal antibodies to cell surface proteins that are internalized to facilitate the functional delivery of oligo into a broad range of cell/tissue types.



4:10 KEYNOTE PRESENTATION: Harnessing Endogenous Retroviral-Like Proteins for RNA Delivery
Michael Segel, PhD, Postdoctoral Fellow, Laboratory of Dr. Feng Zhang, Broad Institute of MIT and Harvard
Retroelement derived proteins are scattered throughout the human genome. One such protein, the retroviral-like Gag protein PEG10, can be harnessed to facilitate efficient intercellular delivery of cargo RNAs in mammalian cells.

4:40 Close of Conference

Oligonucleotide CMC and Regulatory Strategies

Accelerating Product Development and Commercial Success

TUESDAY, MARCH 15

7:00 am Short Course Registration

8:00 Recommended Pre-Conference Short Course*

SC1: Examining the Safety and Toxicity of Nucleic Acid Therapeutics
**All Access Premium Pricing or separate registration required. See short course page for details.*

9:15 Main Conference Registration and Morning Coffee

10:15 Organizer's Welcome Remarks

OLIGONUCLEOTIDE DESIGN & SYNTHESIS

10:25 Chairperson's Opening Remarks
Mike Webb, PhD, Independent Consultant, MikeWebbPharma Ltd.; Former Vice President, API Chemistry & Analysis, GSK



10:30 FEATURED PRESENTATION: Living in the World of RNA Therapeutics
Mano Manoharan, PhD, Distinguished Scientist & Senior Vice President, Innovation Chemistry, Alnylam Pharmaceuticals
This talk will cover chemical modifications and structure-activity relationships; delivery mechanisms and clinical advances and going beyond liver using oligonucleotide therapeutics.



11:00 FEATURED PRESENTATION: Rethinking Oligonucleotides in a P(V) World
Phil Baran, PhD, Chair & Professor, Department of Chemistry, Scripps Research Institute
This talk will discuss the development of new tools to synthesize and potentially manufacture small (cyclic dinucleotides, CDNs) and large oligonucleotides using the naturally occurring oxidation state of phosphorus: P(V). A suite of commercially available reagents, developed in collaboration with BMS, will be described and showcase how they can be used to generate exotic CDNs, chimeric oligonucleotides, and other P-based nucleoside analogs such as di- and tri-phosphates.

11:30 BOOST- Biocatalytic Oligonucleotide Synthesis Technology ALMAC
Dr. Jill Caswell, Biology Technical Leader, Almac Sciences, Almac Group
Biocatalysis has transformed chemical synthesis of small molecule APIs. Enzymes are now seeing applications beyond small molecule and are being exploited in the application of oligonucleotide synthesis. This presentation will showcase how enzymes can be used in both single and double stranded oligonucleotide synthesis. It will highlight Almac's '3-2-3-2' hybrid biocatalytic approach for oligonucleotide synthesis that alleviates the pressures on existing solid phase capacities and utilizes more convergent synthesis.

11:45 Sponsored Presentation *(Opportunity Available)*

12:00 pm Session Break

12:10 Luncheon Presentation to be Announced ChemGenes Corporation
Speaker to be Announced

12:40 Session Break

OLIGO IDENTITY & STABILITY TESTING

1:15 Chairperson's Opening Remarks
Mike Webb, PhD, Independent Consultant, MikeWebbPharma Ltd.; Former Vice President, API Chemistry & Analysis, GSK

1:20 Computational Prediction of RNA Higher Order Structures
Christina Bergonzo, PhD, Research Chemist, National Institutes of Standards and Technology
Computational modeling can be used to screen covalent modifications to RNA structure quickly and at low cost, relating to the intended function of the drug product through thermodynamic measurements. Previous work has shown that dsRNA modeled *in silico* quantitatively agrees with solution state experimental data. Combining high quality all-atom models with the predicted behavior of oligonucleotide modifications, we propose a set of primary sequence-based rules which direct oligonucleotide product stability.

1:50 Strategies for Identity Testing of Therapeutic Oligonucleotide Drug Substances and Drug Products
Daniel Capaldi, PhD, Vice President, Analytical and Process Development, Ionis Pharmaceuticals
A risk-based approach for routine identity testing of therapeutic oligonucleotide drug substances and drug products will be presented. Risk analysis of solid phase oligonucleotide synthesis indicates that intact mass measurement is a powerful technique for confirming synthesis of the intended oligonucleotide. Further risk assessment suggests the addition of a second, sequence-sensitive identity test, which relies on comparison of some property of the sample to a reference standard of proven identity.

2:20 Considerations for Terminal Sterilization of Oligonucleotide Drug Products
Nadim Akhtar, PhD, Senior Principal Scientist, New Modalities, AstraZeneca R&D
The terminal sterilization process has always been the preferred choice of the regulators. The recent EMA guidance demands a substantial effort to enable terminal sterilization and a robust data package to justify an aseptic sterile filtration process. This guidance also applies to oligonucleotides which due to their structural complexity and lack of regulations pose many challenges. This presentation will discuss specific considerations and challenges associated with terminal sterilization of oligonucleotides.

2:50 Refreshment Break in the Exhibit Hall with Poster Viewing

FEATURED SESSION: EMERGING OLIGO THERAPIES

3:30 Chairperson's Opening Remarks
Paloma H. Giangrande, PhD, Vice President, Platform and Discovery Sciences Biology, Wave Life Sciences



3:35 FEATURED PRESENTATION: Small Activating RNA from Concept to Phase 2 Clinical Trials
Nagy Habib, ChM, FRCS, Head of R&D and CMO, MiNA Therapeutics Ltd.
Small activating RNAs (saRNA) are double stranded 21-nucleotide RNA that target promoters or enhance genes leading to mRNA upregulation. MTL-CEBPA is an investigative drug that resulted from the conjugation of saRNA CEBPA with NOV 340 lipsomes that targets tumour associated macrophages. MTL-CEBPA has been administered safely in over 100 patients with advanced cancer and improved clinical outcome in a sub-set of patients when co-administered with TKI or check point inhibitor.



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

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Paloma H. Giangrande, PhD, Vice President, Platform and Discovery Sciences Biology, Wave Life Sciences

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6:35 Close of Day

WEDNESDAY, MARCH 16

7:30 am Registration Open

BREAKFAST INTERACTIVE DISCUSSIONS

8:00 Breakfast Interactive Discussions

Interactive 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. For in-person events, the facilitator will lead from the front of the room while attendees remain seated to promote social distancing. For virtual attendees, the format will be in a Zoom room. 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 Interactive Discussion page on the conference website for a complete listing of topics and descriptions.

CO-PRESENTATION: INTERACTIVE DISCUSSION: CMC & Regulatory Considerations for Oligo Drug Development

Marc Lemaitre, PhD, Oligonucleotide Therapeutics CMC/Strategy Consultant, ML_Consult LLC

Jennifer Franklin, PhD, Executive Director, CMC Regulatory Affairs, Ionis Pharmaceuticals, Inc.

Mike Webb, PhD, Independent Consultant, MikeWebbPharma Ltd.; Former Vice President, API Chemistry & Analysis, GSK

- Oligonucleotide drug substance specifications
- Starting material for oligonucleotides
- Identity testing of oligonucleotides and impurity limits

8:45 Session Break

CMC & REGULATORY INSIGHTS

8:55 Chairperson's Opening Remarks

Marc Lemaitre, PhD, Oligonucleotide Therapeutics CMC/Strategy Consultant, ML_Consult LLC

9:00 CMC/Regulatory for Oligonucleotide Therapeutic Submission

Marc Lemaitre, PhD, Oligonucleotide Therapeutics CMC/Strategy Consultant, ML_Consult LLC

CMC (chemistry, manufacturing and control) for oligonucleotides synthesized by solid phase synthesis and purified by chromatography is an unusual regulatory situation compared to small molecules and synthetic peptides due to the relative short experience and the various types of oligonucleotides. Some of the usual ICH guidelines for drug substances and drug products do not fully apply. This talk will provide some suggestions on what can be done based on experience.

9:30 Challenges in Establishing Commercial Analytical Control Strategy for the Lifecycle of a Therapeutic Oligonucleotide

Mike Webb, PhD, Independent Consultant, MikeWebbPharma Ltd.; Former Vice President, API Chemistry & Analysis, GSK

The talk will discuss how the analytical control strategy for an oligonucleotide drug substance and product needs to address the challenges of oligonucleotides, satisfying regulatory requirements and supporting QC for a fast-moving supply chain. We will discuss the regulatory strategies required to deal with issues of control of starting materials and drug substance identity, diastereomeric control (of phosphorothioates), assays, impurity profiling, and reducing testing with no value to the patient.

10:00 Turning Tides Together: Oligonucleotide Manufacturing at Bachem BACHEM

Joseph Fraone, Business Development Manager, Oligonucleotides, Business Development, Bachem Americas, Inc.

Bachem known as the leading CMO for pharmaceutical grade peptides is expanding its technology platform

to offer chemical manufacturing services for nucleic acid based APIs. We would like to take the opportunity to present Bachem's capabilities as the first CMO servicing the global TIDES market.

10:15 **Sponsored Presentation** *(Opportunity Available)*

10:30 **Coffee Break in the Exhibit Hall with Poster Viewing**

11:10 **Regulatory Interactions and Intelligence for Development and Late Phase Programs**
Jennifer Franklin, PhD, Executive Director, CMC Regulatory Affairs, Ionis Pharmaceuticals, Inc.
Current regulatory intelligence for early development and late-phase filings will be discussed, including common health authority requests and recent regulatory guidance, and approaches for their phase appropriate implementation. Use of agency interactions for guiding development activities will also be discussed and examples provided.

11:40 **CMC Challenges and Regulatory Strategies for the Development and Approval of RNAi Therapeutics**
Sergei Poletaev, Associate Director, Regulatory Affairs CMC, Alnylam Pharmaceuticals
The development and approval of several RNAi therapeutics denote a significant milestone in the field of oligonucleotide-based drug development. This talk explores the CMC challenges and regulatory strategies for the development and approval of RNAi therapeutics including the delivery challenges of siRNAs and the applicability of available guidance on regulatory control strategies for oligonucleotides.

12:10 pm **Session Break**

12:20 **Luncheon Presentation** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:50 **Dessert Break in the Exhibit Hall with Poster Viewing**

KEYNOTE SESSION: OLIGO THERAPIES – OPPORTUNITIES & CHALLENGES

1:25 **Chairperson's Opening Remarks**
Isabel Aznarez, PhD, VP, Discovery Research, Stoke Therapeutics



1:30 KEYNOTE PRESENTATION: **A Novel RNA-Based Approach to Treat Genetic Diseases**
Isabel Aznarez, PhD, VP, Discovery Research, Stoke Therapeutics
Targeted augmentation of nuclear gene output (TANGO) is a novel technology that exploits antisense oligonucleotide (ASO)-mediated modulation of pre-mRNA splicing to increase full length, fully functional protein expression. In haplo insufficiencies; e.g., Dravet syndrome and autosomal dominant optic atrophy, TANGO ASOs increase protein expression by leveraging the wild type allele. TANGO can target a wide range of gene types, functions and sizes to address genetic diseases amenable to protein upregulation.



2:00 KEYNOTE PRESENTATION: **RNA Targeting Progress in Severe and Rare Disease**
Richard Geary, PhD, Chief Development Officer and Executive Vice President, Antisense Drug Development, Ionis Pharmaceuticals, Inc.
More than ten RNA targeted products have been approved and launched in the rare and severe disease space. Both increase and decrease in protein target production have been utilized with RNA engaging oligonucleotides. Pipeline progress will be summarized along with the challenges and opportunities that have become apparent as the research continues.

2:30 **Refreshment Break in the Exhibit Hall & Last Chance for Poster Viewing**



3:10 KEYNOTE PRESENTATION: **Intratumoral Delivery of a CpG-A TLR9 Agonist Using a Virus-Like Particle Can Overcome Resistance to PD-1 Blockade in Patients with Advanced Melanoma**
Arthur M. Krieg, Founder & CSO, Checkmate Pharmaceuticals
Innate immune activation is an appealing approach to overcoming resistance to PD-1 blockade in patients with advanced cancer, and yet positive results in murine tumor models have usually not translated into human clinical data. CpG-A TLR9 agonists have unique immune effects that are enhanced by delivery using an immunogenic virus-like particle, leading to enhanced systemic anti-tumor effects in preclinical models and in humans.



3:40 KEYNOTE PRESENTATION: **Engineering Antibody Oligonucleotide Conjugates (AOCs): Taking Receptor-Mediated Uptake One Step Further**
Arthur Levin, PhD, CSO, Avidity Biosciences
The promise of oligonucleotide therapeutics is to use Watson-Crick-Franklin base-pairing rules to design drugs directly and rationally based on genomic information. Until recently, that has remained elusive because of cell barriers to oligonucleotide uptake. Receptor-mediated uptake through bioconjugation oligonucleotides has changed that. Avidity's AOC technology uses monoclonal antibodies to cell surface proteins that are internalized to facilitate the functional delivery of oligo into a broad range of cell/tissue types.



4:10 KEYNOTE PRESENTATION: **Harnessing Endogenous Retroviral-Like Proteins for RNA Delivery**
Michael Segel, PhD, Postdoctoral Fellow, Laboratory of Dr. Feng Zhang, Broad Institute of MIT and Harvard
Retroelement derived proteins are scattered throughout the human genome. One such protein, the retroviral-like Gag protein PEG10, can be harnessed to facilitate efficient intercellular delivery of cargo RNAs in mammalian cells.

4:40 **Close of Conference**

Sponsorship, Exhibit, and Lead Generation Opportunities

CHI offers comprehensive sponsorship packages which include presentation opportunities, exhibit space, branding and networking with specific prospects. Sponsorship allows you to achieve your objectives before, during, and long after the event. Any sponsorship can be customized to meet your company's needs and budget. Signing on early will allow you to maximize exposure to qualified decision-makers.

2022 Sponsor & Exhibitor Sample Package Options:

Podium Presentations — Limited to 6!! Available within Main Agenda! Showcase your solutions to a guaranteed, targeted audience through a 15- or 30-minute presentation during a specific program, breakfast, lunch, or a pre-conference workshop. Package includes exhibit space, onsite branding, and access to cooperative marketing efforts by CHI. Presentations will sell out quickly! Sign on early to secure your talk.

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 the invitations, to venue suggestions, CHI will deliver your prospects and help you make the most of this invaluable opportunity.

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

Additional branding and promotional opportunities including:

- Conference Tote Bags
- Literature Distribution (Tote Bag Insert or Chair Drop)
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Past Sponsors Include:

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For more information regarding sponsorship and exhibit opportunities, please contact:

Aimee Croke
Business Development Manager
781-292-0777
acroke@cambridgeinnovationinstitute.com

Hotel & Travel

Conference Venue and Hotel:
Revere Hotel Boston Common
200 Stuart Street| Boston, MA 02116

Discounted Room Rate: $205.00
Discounted Room Rate Cut-off Date: February 14, 2022

For additional information please go to
the **TRAVEL PAGE** of OPTCongress.com.





CHI's Mandatory COVID-19 Vaccination Policy

Your Safety is Our Top Priority

To ensure maximum safety, CHI has instituted a mandatory COVID-19 vaccination policy for all in-person participants of our events. Attendees will be asked to furnish proof of vaccination. Additional details on the vaccine policy will be provided upon registration.

Attendees that cannot participate because of this policy, or due to travel restrictions, are encouraged to participate using our virtual event platform. CHI virtual events provide you with an in-person experience at your convenience, anywhere, anytime. See our website for details.

Our Code of Conduct

All in-person attendees must agree to CHI's Code of Conduct



FLEXIBLE REGISTRATION

Seamlessly switch between In-person and/or Virtual

Select an in-person or virtual option, and you have the flexibility to switch your preferred event experience at any time leading up to the conference. Our flexible registration is designed to take the uncertainties out of these uncertain times.

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REGISTRATION PACKAGES	Commercial	Academic, Government, Hospital-affiliated
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1 SHORT COURSE	$599	$349
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Advance Rate until February 11	$1999	$949
Standard Registration and On-Site	$2199	$1049
STANDARD IN-PERSON AND VIRTUAL PACKAGE *(Includes access to two days of conference programming. Does not include access to short course.)*		
Advance Rate until February 11	$1699	$699
Standard Registration and On-Site	$1899	$799

For additional registration options, visit our website: OPTCONGRESS.COM

POSTER DISCOUNT: $50 OFF*

POSTER SUBMISSION: Poster materials are due by **February 11, 2022.** Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract and other materials. If you do not receive your link within 5 business days, please contact jring@healthtech.com.

**this discount does not apply to product or service providers*

CHI reserves the right to publish your poster materials in various marketing materials and products.

LEARN MORE.

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