DIA | FDA U.S. FOOD & DRUG ADMINISTRATION

DIA/FDA Oligonucleotide-Based Therapeutics Conference

April 25-27 | In Person and Live-Stream Virtual

PROGRAM CHAIRS

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Federal Institute for Drugs and Medical Devices, Germany

Overview

DIA/FDA's Oligonucleotide-Based Therapeutics Conference brings together leading experts to inform, educate, and share advancements in oligonucleotide-based therapeutic product development. Developed collaboratively by regulators, industry professionals, and academics, the program covers a wide range of topics from the nonclinical, CMC, and clinical areas. The conference offers a unique experience with multiple perspectives presented, and the opportunity to interface with regulators from around the globe.

Highlights

- **Opening Keynote Address:**

Janet Woodcock, MD
Principal Deputy to the Commissioner, FDA

- **Engaging Poster Reception**
- **Three Educational Tracks: Clinical, Non-Clinical, and CMC** *See next page for descriptions

Who Should Attend

Senior-level professionals and those working in the following areas of oligonucleotide science:

- Drug Discovery
- Preclinical
- Clinical
- CMC
- Quality Assurance
- RNAi
- Vaccines
- Biotechnology
- Delivery Technologies
- Clinical Pharmacology/ Research

Three Tracks

- **Track 1: Clinical -** There are more than a dozen oligonucleotide based products approved for therapeutic use and nearly 100 currently in clinical testing. Track 1 will explore the lessons learned and the ongoing challenges to clinical use of oligos. The Track sessions are divided by tissue, including kidney, brain, eye, liver and other extrahepatic. Another session will cover Clinical Pharmacology and a special concurrent session will cover Individualized ASO Products.
- **Track 2: Non Clinical -** The nonclinical track will focus on development and safety assessments of oligonucleotide-based therapeutics. A variety of modalities, routes of administration, and methodologies will be discussed.
- **Track 3: CMC -** This track provides an interactive forum for innovators and regulators to present and discuss cutting edge topics in oligonucleotide chemistry, manufacturing, and controls (CMC). The track emphasizes topics that are emerging (e.g., use of platform knowledge, ICH Q14, new oligonucleotide modalities) and will require ongoing collaboration with global regulators. Attendees will take away a deeper understanding of key developments, along with insight into current challenges and successful strategies for navigating this complex area.

Schedule At-A-Glance

Track 1: Clinical **Track 2:** Non-Clinical
Track 3: Chemistry, Manufacturing and Controls (CMC)

DAY ONE | MONDAY, APRIL 25

7:00AM-4:45PM	Conference Registration	Grand Ballroom Foyer (Upper Level)
7:00-8:00AM	**Networking Breakfast**	Grand Ballroom E (Upper Level)
8:00-9:00AM	**Welcoming Remarks and Session 1:** Keynote Address - The Coming of Age of Oligonucleotide-Based Therapeutics	Grand Ballroom ABCD (Upper Level)
9:00-10:30AM	**Session 2:** Plenary Session – When Innovation and Need Meet: Development of COVID-19 mRNA Vaccines	Grand Ballroom ABCD
10:30-10:45AM	**Refreshment and Networking Break**	Grand Ballroom E
10:45AM-12:15PM	**Session 3:** CONCURRENT SESSIONS	
	Track 1: Clinical Development of Oligonucleotide Therapeutics for Viral and Kidney Diseases	Brookside (Lower Level)
	Track 2: Advances in Oligonucleotide Delivery	Grand Ballroom ABCD
	Track 3: Platform Approaches and the Application of Prior Knowledge to the Development of Therapeutic Oligonucleotides	White Oak (Lower Level)
12:15-1:15PM	Networking Luncheon	Grand Ballroom E
1:15-2:45PM	**Session 4:** CONCURRENT SESSIONS	
	Track 1: Oligonucleotide Therapies for Brain and Eye Diseases: Learnings From Recent Clinical Trials	Brookeside
	Track 2: Off-Target Effects	Grand Ballroom ABCD
	Track 3: CMC Perspective on Early and Late Stage Oligonucleotide Programs	White Oak

2:45-3:15PM	Refreshment and Networking Break	Grand Ballroom E
3:15-4:45PM	**Session 5:** CONCURRENT SESSIONS	
	Track 1: Liver Targeted Therapeutics, Clinical Experience	Brookside
	Track 2: Advances in CNS Delivery of Oligonucleotides	Grand Ballroom ABCD
	Track 3: ICH Q14 Regulatory Perspective and the Impact on Process Analytical Technology	White Oak
4:45-5:45PM	Poster Reception	Grand Ballroom E

DAY TWO | TUESDAY, APRIL 26

8:00AM-4:30PM	Registration	Grand Ballroom Foyer
8:00-9:00AM	**Networking Breakfast**	Grand Ballroom E
9:00-10:00AM	**Welcome to Day 2 and Session 6:** Keynote Address Address - Delivery of Oligonucleotide Therapeutics – Going Beyond the Liver	Grand Ballroom ABCD
10:00-10:30AM	**Refreshment and Networking Break**	Grand Ballroom E
10:30AM-12:00PM	**Session 7:** CONCURRENT SESSIONS	
	Track 1: Clinical Pharmacology Considerations in the Development and Approval of Oligonucleotide Therapeutics	Brookside
	Track 2: RNA Activation	Grand Ballroom ABCD
	Track 3: Oligonucleotide Delivery	White Oak
12:00-1:15PM	Networking Luncheon	Grand Ballroom E
1:15-2:45PM	**Session 8:** CONCURRENT SESSIONS	
	Track 1 and 2: Individualized Antisense Oligonucleotide Drug Products	Grand Ballroom ABCD
	Track 3: CMC Perspective on mRNA Therapeutics	White Oak
2:45-3:15PM	**Refreshment and Networking Break**	Grand Ballroom E
3:15-4:45PM	**Session 9:** Hot Topics	Grand Ballroom ABCD
4:45-5:45PM	**DIA Oligonucleotide Safety Working Group (OSWG) – Open Meeting**	Grand Ballroom ABCD

DAY THREE | WEDNESDAY, APRIL 27

7:30AM-12:00PM	Registration	Grand Ballroom Foyer
7:30-8:00AM	**Networking Breakfast**	Grand Ballroom E
8:00-9:30AM	**Session 10:** CONCURRENT SESSIONS	
	Tracks 1 and 2: Alternative Approaches to Other Extrahepatic Delivery	Grand Ballroom ABCD
	Track 3: CMC and Regulatory Experience for Novel Oligonucleotide Therapeutics	White Oak
9:40-10:20AM	**Session 11:** PMDA Highlight - Recent Publication of Japanese Guideline for Non-clinical and CMC Topics Related to Oligonucleotide Medicines	Grand Ballroom ABCD
10:20-10:45AM	**Refreshment and Networking Break**	Grand Ballroom E
10:45-11:45AM	**Session 12:** Co-Track Grand Q&A Panel	Grand Ballroom ABCD
11:45AM-12:00PM	**Closing Remarks**	Grand Ballroom ABCD
12:00PM	**Conference Adjourns**	

Learning Objectives

At the conclusion of this conference, participants should be able to:

- Analyze the latest strategies for clinical use of oligonucleotide therapies and explain the specific challenges of developing RNA-based therapeutics
- Describe the chemistry, manufacturing, and controls challenges associated with the development of oligonucleotides, including formulation and specification issues
- Describe the technology landscape, CMC challenges, and regulatory considerations associated with novel oligonucleotide delivery approaches
- Explain the latest global regulatory updates in oligonucleotide therapeutic developments

DAY ONE | MONDAY, APRIL 25

7:00AM-4:45PM — **Conference Registration** — Grand Ballroom Foyer (Upper Level)

7:00-8:00AM — **Networking Breakfast** — Grand Ballroom E (Upper Level)

8:00-9:00AM — **Welcoming Remarks and Session 1:** Keynote Address - The Coming of Age of Oligonucleotide-Based Therapeutics — Grand Ballroom ABCD (Upper Level)

Session Co-Chairs
Scott Henry, PhD, Vice President, Nonclinical Development, Ionis Pharmaceuticals, Inc.

Ronald Wange, PhD, Associate Director for Pharmacology & Toxicology, Office of New Drugs, CDER, FDA

In her keynote address, Dr. Woodcock will provide her perspective on the current state of RNA-directed therapeutics, the challenges that still confront the field, and a clear-eyed view of the latent potential that these drugs have to treat a broad array of diseases that currently lack effective treatment options.

Keynote Speaker
Janet Woodcock, MD, Principal Deputy to the Commissioner, FDA

9:00-10:30AM — **Session 2:** Plenary Session: When Innovation and Need Meet: Development of COVID-19 mRNA Vaccines — Grand Ballroom ABCD

Session Chair
Scott Henry, PhD, Vice President, Nonclinical Development, Ionis Pharmaceuticals, Inc.

The mRNA vaccine efforts took a giant leap forward with the success of the COVID-19 vaccine programs at Moderna and Pfizer/BioNTech in 2020. This herculean effort was accomplished through not only technological innovation, but the close and collaborative interaction with Regulatory Agencies to make the process as efficient as possible. This session will present some of the experience and lessons-learned from the perspective of the clinical trial management, CMC manufacturing, and review of dossiers.

Preparing the Field: Efforts to Expedite COVID-19 Vaccine Development
Peter Marks, MD, PhD, Director, Center for Biologics Evaluation and Research, FDA

Presentation
Jacqueline Miller, MD, Senior Vice President, Therapeutic Area Head, Infectious Diseases, Moderna

Vaccine Development at the Speed of Science
Paul Rohlfing, Executive Director, Global CMC, Regulatory Affairs, Pfizer, Inc.

10:30-10:45AM — **Refreshment and Networking Break** — Grand Ballroom E

10:45AM-12:15PM — **Session 3:** CONCURRENT SESSIONS

Track 1: Clinical Development of Oligonucleotide Therapeutics for Viral and Kidney Diseases — Brookside (Lower Level)

Session Co-Chairs
Laura Sepp-Lorenzino, PhD, Chief Scientific Officer, Intellia Therapeutics, Inc.

Zheng Li, **PhD**, Pharmacologist, FDA

This session will provide updates on siRNAs in clinical development for chronic hepatitis and cancer. Liver-targeted silencers of Hepatitis B Virus are being developed in combination with viral life cycle inhibitors and immune enhancing therapies, with the goal of breaking tolerance and establishing a functional cure

in chronic hepatitis B patients. Phase ½ mono and combination therapy data for two HBV silencers will be presented. The last talk will highlight the clinical experience with an extra-hepatic siRNA candidate being developed for renal cell carcinoma, targeting HIF2.

Clinical Development of VIR-2218, a GalNAc-siRNA Targeting Hepatitis B, in Combination with Immune Enhancing Therapies
Daniel Cloutier, PharmD, Senior Director, Clinical Research, Clinical Lead, HBV Program, Vir Biotechnology, Inc.

Short Interfering RNA JNJ-3989 Combination Therapy
Michael Biermer, Senior Director, Clinical Development, Janssen Pharmaceuticals

ARO-HIF2 for Treatment of Clear Cell Renal Cell Carcinoma Ph1b
James Hamilton, MD, MBA, Senior Vice President, Discovery and Transitional Medicine, Arrowhead Pharmaceuticals

Track 2: Advances in Oligonucleotide Delivery — Grand Ballroom ABCD

Session Co-Chairs
Arthur Levin, PhD, Chief Science Officer, Avidity Biosciences

Phil Gatti, PhD, Pharmacologist, FDA

This session will explore three novel areas of delivery. Oral, lipid conjugated siRNA-dimers and synthetic exosomes. The goal of the session is to consider a small fraction of the diversity of technologies which can be utilized to overcome the challenges of moving highly water-soluble nucleic acid therapeutics through cell membranes to produce pharmacologic activity.

This session should address key questions like- how broadly applicable is this technology across the different modalities of oligonucleotide therapeutics? Does this modality enhance the therapeutic index of a compound? Is this delivery modality amenable to multiple cell and tissue types?

Exosome Mediated Genetic Reprogramming of Tumor Associated Macrophages by exoASO-STAT6
Sriram Sathyanarayanan, PhD, MSc, Chief Scientific Officer, Codiak Biosciences

Branched siRNA for Broad and Durable Target Silencing in the CNS
Stefan McDonough, PhD, Vice President, Neuroscience, Atalanta

Recent Efforts in the Oral Delivery of GalNAc-Conjugated ASOs
Scott Henry, PhD, Vice President, Nonclinical Development, Ionis Pharmaceuticals, Inc.

Track 3: Platform Approaches and the Application of Prior Knowledge to the Development of Therapeutic Oligonucleotides — White Oak (Lower Level)

Session Co-Chairs
Daniel Capaldi, PhD, Vice President, Analytical and Process Development, Ionis Pharmaceuticals, Inc.

Monica Cooper, PhD, Review Chemist, CDER, FDA

Synthetic therapeutic oligonucleotides are commonly manufactured using the same basic unit operations, i.e., solid phase synthesis, cleavage, purification, and isolation. The platform nature of oligonucleotide manufacturing provides opportunities to streamline process development and expedite regulatory submissions through the application of prior knowledge. The session will include presentations from regulatory authority and industry scientists. The presentations will be followed by a panel discussion. Topics for discussion may include how best to define prior knowledge, the areas and extent to which prior knowledge may be applied, limitations and issues associated with the application of prior knowledge, and how such information might be presented in regulatory filings.

Speakers
Dominik Altevogt, PhD, Associate Director Regulatory Affairs CMC, Novartis, Switzerland

Brian Dooley, Quality Specialist, European Medicines Agency, Netherlands

Panelists
Ashley Boam, MS, Director, Office of Policy for Pharmaceutical Quality, OPQ, CDER, FDA

Lubomir Nechev, PhD, Vice President, Process Sciences, Alnylam Pharmaceuticals

12:15-1:15PM **Networking Luncheon** Grand Ballroom E

1:15-2:45PM **Session 4:** CONCURRENT SESSIONS

Track 1: Oligonucleotide Therapies for Brain and Eye Diseases: Learnings From Recent Clinical Trials — Brookside

Session Co-Chairs
Barry Ticho, MD, PhD, Chief Medical Officer, Stoke Therapeutics

Paul Brown, PhD, ODE Associate Director for Pharmacology and Toxicology, OND, CDER, FDA

Speakers will showcase clinical programs representing brain and eye diseases at various stages of development using intrathecal or intravitreal delivery. Clinical efficacy as well as safety profile of these delivery approaches will be covered. The goal of the session is to update on clinical progress, highlight the advantages of oligo therapeutics for these related organs, and discuss potential issues related to oligo delivery.

Antisense Oligonucleotides for Treatment of Genetic Epilepsy and Optic Atrophy
Barry Ticho, MD, PhD, Chief Medical Officer, Stoke Therapeutics

Antisense Oligonucleotides for Treatment of Neuromuscular Diseases
Toby Ferguson, MD, PhD, Vice President and Head Neuromuscular Development Unit, Biogen

Antisense Oligonucleotides for Inherited Retinal Diseases
Aniz Girach, MD, Chief Medical Officer, ProQR Therapeutics, United Kingdom

Track 2: Off-Target Effects — Grand Ballroom ABCD

Session Co-Chairs
Sebastien Burel, MS, PhD, Associate Director, Ionis Pharmaceuticals, Inc.

James Wild, PhD, Pharmacologist, CDER, FDA

The sequence-specific interaction of single- and double-stranded oligonucleotides with a variable range of off-target sites on pre-mRNA, mRNA and miRNA can result in hybridization-dependent toxicity. Similar off-target concerns, and the risk of introducing nuclease-induced off-target mutations exist for guide RNA in CRISPR-Cas genome-editing nucleases. This session will examine in silico and in vitro methods and strategies for identifying, assessing, and de-risking off-target hybridization for oligonucleotides and CRISPR genome editors. In addition, novel off-target assessment of steric-blocking and splice modulating oligonucleotides will be presented and discussed.

Off-target Effects of CRISPR
Shengdar Tsai, MS, PhD, Assistant Member, St. Jude Faculty, Department of Hematology, St. Jude Children's Research Hospital

De-risking of Off-Target Effects
Joanna Harding, MSc, Director, Toxicology Project Lead, CVRM Safety, AstraZeneca, United Kingdom

Off-target Assessment for Splice Modulators
Erle Holgersen, PhD, Research Scientist, Deep Genomics, Canada

Track 3: CMC Perspective on Early and Late Stage Oligonucleotide Programs — White Oak

Session Chair
Firoz Antia, PhD, Director, ASO Process Development & Manufacturing, Biogen

In recent years, a number of oligonucleotide therapeutics have received market license authorizations in the US, Canada, Europe and other countries. There is also an increasing number of oligonucleotides entering clinical trials worldwide. This session will present recent experience with the review of CMC dossiers of early and late-stage oligonucleotide programs. Presentations from Alnylam and Ionis will be followed by a panel discussion that may include representatives from the FDA and BfArM.

siRNA Lifecyle: Successful Regulatory Strategies
Melissa Marschel, MS, Director, Regulatory Affairs, Alnylam Pharmaceuticals

Regulatory Interactions and Intelligence for Development and Late Phase Programs
Tracey Burr, PhD, MSc, Director, CMC Regulatory Affairs, Ionis Pharmaceuticals

Panelists
Lawrence Perez, PhD, Senior Pharmaceutical Quality Assessor, CDER, FDA, Germany

René Thürmer, PhD, Deputy Head of the Unit Pharmaceutical Biotechnology BfArM, Federal Institute for Drugs and Medical Devices, Germany

2:45-3:15PM **Refreshment and Networking Break** Grand Ballroom E

3:15-4:45PM **Session 5:** CONCURRENT SESSIONS

Track 1: Liver Targeted Therapeutics, Clinical Experience — Brookside

Session Co-Chairs
Louis O'Dea, MD, Chief Medical Officer and President Biorchestra USA, Inc.

Xuan Chi, MD, PhD, Supervisory Pharmacologist, CDER, FDA

The speakers will present data on 3 clinical programs using liver-directed RNA therapeutic modalities. The programs will cover late phase development of a GalNAc-amended SiRNA (Inclisiran), a mid-phase GalNAc-amended ASO (Pelacarsen) and on early phase development of an LNP-formulated Crispr molecule. In addition to providing an update on the progress of each program, the session will allow the audience to compare and contrast the various programs, approaches, and challenges, and how each sponsor has found solutions that can be applied more broadly across the field of oligo therapeutics. Finally, the session is planned to allow time for fruitful exchanges between attendees and speakers.

Inclisiran (Leqvio), a GalNAc-siRNA Anti-PCSK9 Late-phase Clinical Development and Experience From Early Post-Marketing Data
Tom Thuren, MD, PhD, Executive Director, Novartis

Pelacarsen, a GalNAc-ASO against Apo(a) in CVD: Phase 2 Results and Phase 3 Plan
Sotirios Tsimikas, MD, Senior Vice President, Global Cardiovascular Development, Ionis Pharmaceuticals

In Vivo CRISPR/Cas9 Editing of the TTR Gene with NTLA-2001 in Patients with Transthyretin Amyloidosis: Phase 1 Results
David Lebwohl, MD, Chief Medical Officer, Intellia Therapeutics

Track 2: Advances in CNS Delivery of Oligonucleotides — Grand Ballroom ABCD

Session Co-Chairs
Jeffrey Foy, PhD, Vice President, Toxicology, PepGen Inc.

Lois Freed, PhD, Director of the Division of Pharmacology/Toxicology-Neuroscience (DPT-N), CDER, FDA

This session will focus on current research efforts in the area of neurological diseases. Improved oligonucleotide delivery and pharmacokinetics/interspecies scaling for neurological assessment based on age and exposure levels will be the focus of the session

Expanding the Reach of RNAi Therapeutics
Lan Dang, PhD, Senior Scientist, Alnylam Pharmaceuticals

Comparison of PK Exposure Between Juvenile and Adult Animals After Intrathecal Administration
Daniel Norris, PhD, RPh, Executive Director, Pharmacokinetics and Clinical Pharmacology, Ionis Pharmaceuticals

Overcoming the Blood–Brain Barrier for RNA Therapeutics
Branden Ryu, PhD, Cheif Executive Officer, BIORCHESTRA Co., Ltd., Korea

Track 3: ICH Q14 Regulatory Perspective and the Impact on Process Analytical Technology — White Oak

Session Chair
Claus Rentel, PhD, Vice President, Analytical Development and Quality Control, Ionis Pharmaceuticals, Inc.

A new quality guideline, ICHQ14, on analytical procedure development is being developed. The intent of this guideline is to harmonize scientific approaches of analytical procedure development in both traditional and enhanced approaches. Thus, resulting in improved regulatory communication between industry and regulators by facilitating efficient and science-based change management. The session will include presentations from a member of the working group as well as industry experience implementing PAT for an oligonucleotide therapeutic. The presentations will be followed by a panel discussion.

Speakers
Daniel Hill, MBA, Associate Director Digital Development and Analytics, Biogen

Nina Cauchon, PhD, RAC, Director Regulatory Affairs CMC, Amgen

Panelists
Bryan Castle, Senior Research Advisor, Synthetic Molecule Design & Development, Eli Lilly and Company

Bogdan Kurtyka, PhD, Senior Process Quality Assessor, OPQ, CDER, FDA

René Thürmer, PhD, Deputy Head of the Unit Pharmaceutical Biotechnology BfArM, Federal Institute for Drugs and Medical Devices, Germany

4:45-5:45PM **Poster Reception** — Grand Ballroom E

DAY TWO | TUESDAY, APRIL 26

8:00AM-4:30PM **Registration** — Grand Ballroom Foyer

8:00-9:00AM **Networking Breakfast** — Grand Ballroom E

9:00-10:00AM **Welcome to Day 2 and Session 6:** Keynote Address - Delivery of Oligonucleotide Therapeutics – Going Beyond the Liver — Grand Ballroom ABCD

Andrew Adams, PhD, Vice President, Genetic Medicine, Eli Lilly and Company

Discussion of the challenges and opportunities of next generation delivery approaches for RNA and DNA based medicines. Approaches spanning direct conjugation of ligands, antibody/peptide conjugates, blood brain barrier shuttles and nanoparticles will be covered, as well as potential therapeutic applications.

10:00-10:30AM **Refreshment and Networking Break** — Grand Ballroom E

10:30-12:00PM **Session 7:** CONCURRENT SESSIONS

Track 1: Clinical Pharmacology Considerations in the Development and Approval of Oligonucleotide Therapeutics — Brookside

Session Chair
Hobart Rogers, PharmD, PhD, Clinical Pharmacologist, Division of Translational and Precision Medicine, Office of Clinical Pharmacology, CDER, FDA

This session will provide timely updates on various important topics pertaining to the clinical pharmacology of oligonucleotides. Specifically, this session will address how FDA regulators evaluate common clinical pharmacology issues relating to assessment of oligonucleotides. In addition, this session

will discuss the 2020 FDA approval of OXLUMO (Lumasiran) as the first therapy approved in the US for the treatment of primary hyperoxaluria type 1, a serious, ultra-rare, inherited disease that is usually diagnosed in childhood. This session will review how the key challenges faced during the development were overcome including: establishing a novel surrogate endpoint, pediatric dose selection (encompassing allometric scaling and predictive modeling), and clinical trial design.

An Assessment of Immunogenicity and Cardiac Electrophysiology of Oligonucleotide Therapeutics: An FDA Perspective
Hobart Rogers, PharmD, PhD, Clinical Pharmacologist, Division of Translational and Precision Medicine, Office of Clinical Pharmacology, CDER, FDA

Oligonucleotide Therapeutics: Assessment of Organ Impairment and Drug-Drug Interactions
Anuradha Ramamoorthy, PharmD, PhD, Policy Lead, OCP, OTS, CDER, FDA

Clinical Development of Lumasiran, the First-Approved Pediatric RNAi Therapeutic
Gabriel Robbie, PhD, Senior Vice President, Clinical Pharmacology and Pharmacometrics, Alnylam Pharmaceuticals, Inc.

Track 2: RNA Activation — Grand Ballroom ABCD

Session Co-Chairs
Patrik Andersson, PhD, Principal Scientist, Discovery Safety Specialist AstraZeneca R&D, Sweden

Imran Khan, PhD, Pharmacologist, OMPT, OND, ODEI, DPP, CDER, FDA

A rapidly evolving area for nucleotide based medicines is upregulation of protein for treatment of a wide range of disease types. This session will cover mechanisms, delivery and some unconventional nonclinical studies for three different platforms. You will learn about two different approaches that induce expression of target mRNA for treatment of cancer and Dravet syndrome as well as therapeutic application of mRNA expressing VEGF for treatment of heart failure.

MTL-CEBPA Transcriptional Level Changes in Machinery
Nagy Habib, Head of Research and Development, MiNA Therapeutics Limited, United Kingdom

AZD8601, VEGF mRNA for Cardiac Regeneration
Anna Collén, PhD, Global Project Leader, Early Cardiovascular, Renal and Metabolism, AstraZeneca, Sweden

Targeted Augmentation of Nuclear Gene Output (TANGO) Technology for Upregulating Target Protein Expression
Meena, PhD, Vice President of Bioanalytical, DMPK & Biomarker Development, Stoke Therapeutics

Track 3: Oligonucleotide Delivery — White Oak

Session Chairs
Ramin Darvari, PhD, MS, Associate Research Fellow, Pfizer Inc.

Rohit Tiwari, PhD, Senior Research Scientist, Global Regulatory Affairs-CMC, Eli Lilly & Company

Efficient delivery of oligonucleotide therapeutics to their intended target organs remains a hot topic for enhanced selectivity beyond the liver. Oligonucleotides conjugated to targeting moieties or encapsulated within nanoparticle modalities have enabled commercialization of drug products by improving the pharmacokinetic and pharmacodynamic properties of oligonucleotide therapeutics. This session will feature some of the advancements in this area along with developmental and chemistry, manufacturing and controls related to regulatory aspects.

CMC Considerations for Protein-Oligonucleotide Conjugates
Adam Dinerman, PhD, Executive Director, Head of Chemistry, Manufacturing and Controls (CMC), Aro Biotherapeutics

Regulatory Reliance in the Age of Complex Modalities
Ramin Darvari, PhD, MS, Associate Research Fellow, Pfizer, Inc.

Panelists
Brian Dooley, Quality Specialist, European Medicines Agency, Netherlands

Rachel Johns, PhD, Senior Director, Analytics and Formulations, Avidity Biosciences, Inc.

Donald Parsons, PhD, Vice President, Early Technical Development and LNP Process Development, Moderna

12:00-1:15PM **Networking Luncheon** Grand Ballroom E

1:15-2:45PM **Session 8:** CONCURRENT SESSIONS

Tracks 1 and 2: Individualized Antisense Oligonucleotide Drug Products — Grand Ballroom ABCD

Session Co-Chairs
Timothy Yu, MD, PhD, Assistant Professor, Harvard Medical School, Division of Genetics and Genomics, Boston Children's Hospital

Ronald Wange, PhD, Associate Director for Pharmacology & Toxicology, Office of New Drugsof New Drugs, CDER, FDA

The availability of annotated, complete human genome databases, and the ability to conduct whole-genome sequencing rapidly and cheaply, have given individual clinicians tools that can allow them to pinpoint the exact genetic cause of a given patient's disease. This makes it possible for clinicians to rapidly identify experimental oligonucleotide-based drug candidates that are tailored to an individual patient's specific disease-causing genetic variant. To support this important advance in treatment availability for those with very rare genetic diseases, the US FDA has recently published a series of draft guidances to aid sponsor investigators in developing these "n of 1" treatments. This session will include presentations on the recommendations contained in the draft guidances as well as examples of the great potential and challenges associated with developing these products.

Regulatory Considerations in Developing Individualized ASOs: Challenges and Approaches
Peter Stein, MD, Director, Office of New Drugs, CDER, FDA

Presentation
Timothy Yu, MD, PhD, Assistant Professor, Harvard Medical School Division of Genetics and Genomics, Boston Children's Hospital

N of 1 Development: The Global Perspective
Annemieke Aartsma-Rus, PhD, MSc, Professor, Translational Genetics Leiden University Medical Center (LUMC), Netherlands

Panelist
Sarah Glass, PhD, Chief Development Officer, N-Lorem Foundation

Track 3: CMC Perspective on mRNA Therapeutics — White Oak

Session Chair
Nedim Emil Altaras, PhD, Senior Vice President, Technical Development, Moderna

The remarkable and rapid advances of SARS-CoV2 mRNA-based vaccines have established the first generation of the many CMC principles for the mRNA-based products. While the industrial manufacturing processes and associated analytical control strategies have been in development for a decade or more, these were scaled-up and readied for commercialization rapidly to meet the needs of pandemic response. The platform nature of mRNA technologies enables common CMC principles, but as application of this flexible technology expands from vaccines to therapeutics, CMC principles will need to diverge or adapt. The sessions will cover these CMC perspectives along with lessons learned and the outlook from both regulatory and industrial viewpoint. The presentations will be followed by a panel discussion with a focus on overcoming the CMC challenges of future mRNA therapeutics.

CMC Development of an mRNA-Based Vaccine to Fight COVID-19 – Lessons Learned
Andreas Kuhn, PhD, Senior Vice President RNA Biochemistry and Manufacturing, Biontech SE, Germany

Regulatory Perspectives for the Evaluation of the Quality, Safety and Efficacy of Prophylactic mRNA Vaccines
Keith Peden, Laboratory Chief, Laboratory of DNA Viruses, DVP, CBER

Panelists
Heide Muckenfuß, Biochemist, Section 2/1 Viral Vaccines, Paul-Ehrlich-Institut, Germany

Donald Parsons, PhD, Vice President, Early Technical Development and LNP Process Development, Moderna

Olen Stephens, PhD, Chemist Reviewer, CMC Reviewer, OND, CDER, FDA

2:45-3:15PM **Refreshment and Networking Break** Grand Ballroom E

3:15-4:45PM **Session 9:** Hot Topics Grand Ballroom ABCD

Session Co-Chairs
Arthur Levin, PhD, Chief Science Officer, Avidity Biosciences

Emily Place, PhD, MPH, Pharmacologist, Office of New Drugs, CDER, FDA

Attendees at this session will hear about novel technologies that are bridging the gap between early research and clinical development. Each is an area that holds the promise of creating a new platform for oligonucleotide therapeutics.
Featured in this session are:

- A novel delivery platform using a conjugate approach
- Circular RNAs as potential therapeutics
- A novel and personalized aptamer technology in oncology

AUMMUNE Therapy Driven by Effect
Irit Carmi-Levy, PhD, Chief Scientific Officer and Vice President R&D, Aummune, Israel

A Novel Antibody Platform for Nucleic Acid Delivery with Broad Therapeutic Potential
Chris Duke, Chief Operating Officer, Gennao Bio

The Therapeutic Potential of oRNA
Robert Mabry, PhD, Chief Scientific Officer, Orna Therapeutics, Inc

4:45-5:45PM **DIA Oligonucleotide Safety Working Group (OSWG) – Open Meeting** Grand Ballroom ABCD

DAY THREE | WEDNESDAY, APRIL 27

7:30AM-12:00PM **Registration** Grand Ballroom Foyer

7:30-8:00AM **Networking Breakfast** Grand Ballroom E

8:00-9:30AM **Session 10:** CONCURRENT SESSIONS

Track 1 and 2: Alternative Approaches to Other Extrahepatic Delivery Grand Ballroom ABCD

Session Co-Chairs
Andrew Slugg, MBA, MS, Senior Vice President, Global Head of Regulatory Affairs, Alnylam Pharmaceuticals

Elena Braithwaite, PhD, Toxicologist, CDER, FDA

Targeted delivery of oligonucleotide-based therapeutics allows for the possibility of unlocking previously inaccessible targets, enhancing target engagement leading to increased therapeutic outcomes with reduced doses and the potential for fewer off-target effects. This session will discuss a number of

Speakers
Arthur Levin, PhD, Chief Science Officer, Avidity Biosciences

Robert MacLeod, PhD, Chief Scientific Officer, Senior Vice President Research and Development, Flamingo Therapeutics, Belgium

Daniel Siegwart, PhD, Associate Professor, Department of Biochemistry, SCCC, University of Texas Southwestern Medical Center

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Track 3: CMC and Regulatory Experience for Novel Oligonucleotide Therapeutics — White Oak

Session Co-Chairs
Rima Patel-Goel, MS, Senior Director Regulatory CMC, AADi Biosciences, Inc.

Benjamin Stevens, PhD, MPH, Director CMC Policy and Advocacy, GlaxoSmithKline

Several oligonucleotide classes (e.g., siRNAs, ASOs) have recently matured to validated therapeutic approaches with demonstrated utility across several indications. While industry and regulatory authorities have worked together to establish pathways for commercialization of these leading oligonucleotide classes, novel modalities present unique challenges to CMC development and broad regulatory acceptability. This session will include industry presentations representing two distinct novel oligonucleotide therapeutic modalities and their perspectives on CMC development challenges and experience with regulatory acceptability. The presentations will be followed by a panel discussion with representatives from both industry and regulatory authorities.

Speakers
Kristy Wood, PhD, Vice President Nucleic Acid Therapeutics Development & Manufacturing Intellia Therapeutics

Rachel Johns, PhD, Senior Director, Analytics and Formulations, Avidity Biosciences, Inc

Panelists
Adam Dinerman, PhD, Executive Director, Head of Chemistry, Manufacturing and Controls (CMC), Aro Biotherapeutics

Martin Nemec, PhD, Senior Biologist/Evaluation, Health Canada

Olen Stephens, PhD, Chemist Reviewer, CMC Reviewer, CDER/OPQ/ONDP, FDA

9:40-10:20AM

Session 11: PMDA Highlight - Recent Publication of Japanese Guideline for Non-clinical and CMC Topics Related to Oligonucleotide Medicines — Grand Ballroom ABCD

Session Chair
Scott Henry, PhD, Vice President, Nonclinical Development, Ionis Pharmaceuticals, Inc.

This session will briefly review the Japanese Guideline regarding preclinical assessment of oligonucleotide medicines. This session will also introduce the outline of the points to consider document, and review issue related to CMC in Japan. Common questions will be addressed pertinent to this class of therapeutics.

Points to Consider Document on CMC of Oligonucleotide Therapeutics in Japan
Kosuke Ito, PhD, Principal Reviewer, Pharmaceuticals and Medical Devices Agency (PMDA), Japan

Japanese Perspective on Non-clinical Safety Assessment for Oligonucleotide Therapeutics
Kazushige Maki, DVM, PhD, Senior Scientist, Toxicology, Pharmaceuticals and Medical Devices Agency (PMDA), Japan

Kiyoshi Kinoshita, PhD, Associate Principal Scientist, Regulatory Affairs, Area Japan Development, Japan Pharmaceutical Manufacturers Association (JPMA), MSD K.K., Japan

10:20-10:45AM	**Refreshment and Networking Break**	Grand Ballroom ABCD
10:45-11:45AM	**Session 12:** Co-Track Grand Q&A Panel	Grand Ballroom ABCD

Session Chair
Ramesh Raghavachari, PhD, Chief, Branch I, DPMA1, OLDP, OPQ, CDER, FDA

Panelists
Nedim Emil Altaras, PhD, Senior Vice President, Technical Development, ModernaPaul Brown, PhD, ODE Associate Director for Pharmacology and Toxicology, OND, CDER, FDA

Daniel Capaldi, PhD, Vice President, Analytical and Process Development, Ionis Pharmaceuticals, Inc.

Jeffrey Foy, PhD, Vice President, Toxicology, PepGen Inc.

Lois Freed, PhD, Director of the Division of Pharm/Tox-Neuroscience (DPT-N), CDER, FDA

Laura Sepp-Lorenzino, PhD, Chief Scientific Officer Intellia Therapeutics, Inc.

Barry Ticho, MD, PhD, Chief Medical Officer, Stoke Therapeutics

11:45AM-12:00PM	Closing Remarks	Grand Ballroom ABCD
12:00PM	Conference Adjourns	

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