DIA/FDA Oligonucleotide-Based Therapeutics Conference

October 28-30 | Bethesda North Marriott Hotel | North Bethesda, MD

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CDER, FDA

Overview

The *DIA/FDA Oligonucleotide-Based Therapeutics Conference* brings together leading experts from industry and regulatory agencies to inform, educate, and share advancements in oligonucleotide-based therapeutic product development. At this conference, you will learn about optimization strategies for drug design, manufacturing, delivery, and clinical testing through three tracks dedicated to covering relevant preclinical, CMC, and clinical topics. Interface with global regulators to discuss developmental advances, safety, and challenges in the field of oligonucleotide-based therapeutics.

Highlights

- Keynote Address Speakers: Arthur Caplan, PhD and C. Frank Bennett, PhD, NYU School of Medicine
- Poster Session and Networking Reception
- Luncheon Round Table Discussions on cutting-edge topics with key thought leaders
- Oligo Safety Working Group (OSWG) Open Meeting
- Visit exhibiting companies during the networking breaks
- Breakfast Plenary Session on Tuesday, 8:15-9:00AM, on Global Regulatory

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

DAY ONE | OCTOBER 28		ROOM
7:00AM-5:00PM	Registration	Salon C Foyer
7:00-8:00AM	Continental Breakfast, Exhibits, and Networking	Salon D
8:00-8:10AM	Mobile App Demonstration	Salon A-C
8:10-8:30AM	**Welcome Remarks and Overview of the 2019 Conference**	Salon A-C
8:30-9:30AM	**Keynote Address**	Salon A-C
9:30-11:00AM	**Session 1:** Rare Diseases	Salon A-C
11:00-11:30AM	Refreshment, Exhibits, and Networking Break	Salon D
11:30AM-1:00PM	**Session 2:** Concurrent Breakout Sessions	
	Track A: Clinical Experience with Immune-Targeting Oligonucleotides and MicroRNAs	Brookside, lower level
	Track B: Targeted Delivery	Salon A-B
	Track C: Recently Approved Oligonucleotide Drugs	Salon C
1:00-2:00PM	Luncheon, Exhibits, and Networking	Salon D
2:00-3:30PM	**Session 3:** Concurrent Breakout Sessions	
	Track A: Oligonucleotide Conjugate Approaches in the Clinic	Brookside, lower level
	Track B: Toxicology Updates on Renal and Platelet Effects of ASOs and 2'-Fluoro Nucleotide Effects of siRNAs	Salon A/B
	Track C: CMC Strategies for Accelerated Approval (Fast Track, Breakthrough, PRIME, etc.) of Oligonucleotide Drugs	Salon C
3:30-4:00PM	Refreshment, Exhibits, and Networking Break	Salon D
4:00-5:30PM	**Session 4:** Concurrent Breakout Sessions	
	Track A/B: Evaluation of QT Prolongation Potential and Assessment of Immunogenicity	Salon A-B
	Track C: Developing Oligonucleotides with Current CMC Guidelines and an Introduction to EPOC	Salon C
5:30-6:30PM	Poster Session and Networking Reception	Salon D

DAY TWO | OCTOBER 29		ROOM
8:00AM-5:00PM	Registration	Salon C Foyer
8:00-9:00AM	Continental Breakfast, Exhibits, and Networking	Salon D
8:15-9:00AM	**Breakfast Plenary Session:** Global Regulatory	Salon A-C
9:00-9:05AM	**Welcome to Day Two**	Salon A-C
9:05-10:05AM	**Keynote Address**	Salon A-C
10:05-10:30AM	Refreshment, Exhibits, and Networking Break	Salon D
10:30AM-12:00PM	**Session 5:** Concurrent Breakout Sessions	
	Track A: Clinical Experience with Lipid Nanoparticle - Based Delivery Of Oligonucleotides	Brookside, lower level
	Track B: Progress in Developing Rna Targeted Drugs for the Treatment of Neurological Diseases	Salon A-B
	Track C: Oligonucleotide Degradation, Stability, and the Question of Terminal Sterilization	Salon C
12:00-1:30PM	Round Table Discussion Luncheon, Exhibits, and Networking	Salon D
1:30-3:00PM	**Session 6:** Concurrent Breakout Sessions	
	Track A/B: Evaluation of Intrinsic Factors/Organ Impairment Studies and of Extrinsic Factors/Drug-Drug Interaction Liability	Salon A-B
	Track C: Control Strategy and Regulatory Considerations for Manufacture of mRNA Drug Substance	Salon C
3:00-3:30PM	Refreshment, Exhibits, and Networking Break	Salon D
3:30-5:30PM	**Session 7:** Hot Topics	Salon A-C
5:30-6:30PM	DIA Oligonucleotide Safety Working Group (OSWG) – Open Meeting	Brookside, lower level

DAY THREE | OCTOBER 30		
7:00AM-12:30PM	Registration	Salon C Foyer
7:00-8:00AM	Continental Breakfast and Networking	Salon D
8:00-10:00AM	**Session 8:** Concurrent Breakout Sessions	
	Track A/B: Hybridization-Dependent Off-Target Events	Salon A-B
8:30-10:00AM	**Track C:** General CMC Q&A Session	Salon C
10:00-10:15AM	Refreshments and Networking Break	Salon D
10:15-11:45AM	**Session 9:** ON Therapeutic Survey Sponsored by EFPIA	Salon A-C
11:45AM-12:30PM	**Closing Session:** Panel Discussion	Salon A-C

Learning Objectives

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

- Analyze the latest delivery strategies for clinical use of oligonucleotide therapies
- Discuss the non-clinical toxicology profile of oligonucleotide therapies and the latest improvements in predicting effects in humans
- Describe the chemistry, manufacturing, and controls challenges associated with the development of oligonucleotides, including formulation and specification issues
- Explain the latest global regulatory updates in oligonucleotide therapeutic developments
- Evaluate the best mechanism of interactions with patients and partner organizations to address critical needs in the rare disease community

Continuing Education Credit

DIA has been accredited as an Authorized Provider by the International Association for Continuing Education and Training (IACET).

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If you would like to receive a statement of credit, you must attend the entire primer, short course and/or all three days of the forum, sign in each day at the DIA registration desk upon arrival and complete the online credit request process through My Transcript. Participants will be able to download a statement of credit upon successful submission of the credit request. My Transcript will be available for credit requests beginning **November 13, 2019**.

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DAY ONE | OCTOBER 28

7:00AM-5:00PM — **Registration** — Salon C Foyer

7:00-8:00AM — **Continental Breakfast, Exhibits, and Networking** — Salon D

8:00-8:10AM — **Mobile App Demonstration** — Salon A-C

8:10-8:30AM — **Welcome Remarks and Overview of the 2019 Conference** — Salon A-C

Sudip Parikh, PhD, Senior Vice President and Managing Director, Americas, DIA

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

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

8:30-9:30AM — **Keynote Address** — Salon A-C

Keynote Speaker
Arthur Caplan, PhD, Drs. William F. and Virginia Connolly Mitty Professor of Bioethics Director, Division of Medical Ethics, NYU School of Medicine

9:30-11:00AM — **Session 1:** Rare Diseases — Salon A-C

Session Co-Chairs
Phil Gatti, PhD, Pharmacologist, FDA

Edward Kaye, MD, Chief Executive Officer, Stoke Therapeutics

Personalized medicine is a major goal in development of new drugs and in medical care in general. Unfortunately, this is very difficult considering the myriad of genetic variations and pathological mutations in people. Oligonucleotide treatments, however, allow for the targeted development of treatment in not only rare and ultrarare diseases, but recently for one person. In today's Rare Diseases session, the speakers will demonstrate examples of this type of development program with its successes and challenges.

Batten Disease Patient Story Update
Timothy Yu, MD, PhD, Division of Genetics and Genomics, Boston Children's Hospital, Assistant Professor, Harvard Medical School, Associate Member, Broad Institute

Ultra-Rare Disease Development Scenario
Matt Buck, JD, Vice President, Regulatory Affairs, Ionis Pharmaceuticals, Inc.

Ultra-Rare Disease Development Scenario
Lucas Kempf, MD, Medical Officer, FDA

11:00-11:30AM — **Refreshment, Exhibits, and Networking Break** — Salon D

11:30AM-1:00PM — **Session 2:** Concurrent Breakout Sessions

Track A: Clinical Experience with Immune-Targeting Oligonucleotides and MicroRNAs — Brookside, lower level

Session Chair
Arthur Krieg, MD, CEO and CSO, Checkmate Pharmaceuticals

Therapeutic oligonucleotides offer a remarkable breadth of mechanisms and applications aside from inducing the cleavage of a target mRNA. This session explores a few of these including activating anti-tumor immunity with CpG DNA through TLR9 or with RNA and regulating the function of microRNAs.

Overcoming Resistance to Checkpoint Inhibition with Intratumoral or Systemic Injection of a CpG-A TLR9 Agonist
Arthur Krieg, MD, CEO and CSO, Checkmate Pharmaceuticals

Antitumoral T-Cell Immunity Triggered by Systemic RNA Lipoplex Vaccination in Cancer Patients
Mathias Vormehr, PhD, Head of Cancer Vaccines, BioNTech RNA Pharmaceuticals GmbH, Germany

Clinical Development of microRNA Inhibitors
Diana Escolar, MD, FAAN, Senior Vice President Medical Science, miRagen Therapeutics, Inc.

Track B: Targeted Delivery — Salon A-B

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

Donald Jensen, DVM, MS, Pharmacologist, FDA

Single and double stranded oligonucleotide therapeutics share the challenge of limited uptake into many cell types of therapeutic interest. This restricted cellular uptake is one of the major hurdles to solve before oligonucleotides can be utilized to their full potential. One way to increase productive uptake is to hitchhike on receptors that internalize ligands, best exemplified by GalNAc-conjugated oligonucleotides to increase uptake into hepatocytes via the asioalyglycoprotein receptor. This session will cover new DMPK understanding of GalNAc conjugated siRNA and antisense oligonucleotides like parameters driving potency, bioavailability, and intracellular trafficking as well as aspects of receptor saturation studied in preclinical models and the clinic. The session will also cover novel strategies of targeted delivery of miR-29 mimics to the lung as well as delivery to muscle using antibody-conjugates targeting the transferrin receptor.

Oligonucleotide Therapeutics: Now on Target
Arthur Levin, PhD, Executive Vice President, Research and Development, Avidity Biosciences

Preclinical and Clinical PK of GalNAc SSOs at Doses Below and Above ASGPR Saturation
Ben-Fillippo Krippendorff, PhD, DABT, DMPK/PD Project Leader, Pharmaceutical Sciences, Roche Pharma Research and Early Development, Roche Innovation Center, Switzerland

Preclinical and Clinical PK of GalNAc SSOs at Doses Below and Above ASGPR Saturation
Charlotte Bon, DVM, PhD, Translational Modeling and Simulation Scientist, F. Hoffman-La Roche AG, Switzerland

ADME Properties of GalNAc siRNAs
Jing-Tao Wu, PhD, Vice President, Early Development, Alnylam Pharmaceuticals Inc.

Targeted Delivery (Lung) of MicroRNA-Modulating Drugs
Rusty Montgomery, PhD, Director, Research, miRagen Therapeutics Inc.

Track C: Recently Approved Oligonucleotide Drugs — Salon C

Session Chair
G. Susan Srivatsa, PhD, President, ElixinPharma

This session will address the CMC challenges associated with the review and approval of inotersen and patisiran. Presentations will be followed by a panel discussion.

Strategies for Addressing Regulatory Agency Questions During Marketing Application Review for Oligonucleotides Drugs
Jennifer Franklin, PhD, Director, CMC Regulatory Affairs, Ionis Pharmaceuticals, Inc.

ONPATTRO® (Patisiran) A First-in-Class RNA Interference (RNAi) Therapeutic
Helene Brough, Director, Regulatory Affairs, CMC, Alnylam Pharmaceuticals, Inc.

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

Lawrence Perez, Review Chemist, FDA

Ian Dobson, Team Leader, Evaluator, Health Canada

1:00-2:00PM — **Luncheon, Exhibits, and Networking** — Salon D

2:00-3:30PM — **Session 3:** Concurrent Breakout Sessions

Track A: Oligonucleotide Conjugate Approaches in the Clinic — Brookside, lower level

Session Co-Chairs
Saraswathy Nochur, PhD, MSc, Chief Regulatory Officer, Alnylam Pharmaceuticals, Inc.

Jessica Hawes, PhD, Deputy Director, FDA

Conjugation of oligonucleotides with various ligands provides opportunities for targeted delivery of these molecules to specific tissues. Conjugate approaches with siRNAs and antisense oligonucleotides will be discussed and clinical data will be showcased.

Clinical Experience with Lumasiran, an Investigational RNAi Therapeutic for the Treatment of Adult and Pediatric Patients with Primatry Hyperoxaluria 1
Tracy McGregor, MD, MSCI, Director, Clinical Development, Alnylam Pharmaceuticals, Inc.

The Emerging Safety and Activity of TRiM™ Platform Based siRNA Drugs
James Hamilton, MD, MBA, Vice President, Clinical Development, Arrowhead Pharmaceuticals

IONIS FXI-LRX, a FXI GalNac Conjugated Antisense Drug, Produces Potent, and Sustained Reduction in FXI Activity in Normal Volunteers
Richard Stephen Geary, PhD, Senior Vice President, Development, Ionis Pharmaceuticals, Inc.

Track B: Toxicology Updates on Renal and Platelet Effects of ASOs and 2'-Fluoro Nucleotide Effects of siRNAs — Salon A-B

Session Co-Chairs
Ronald Wange, PhD, Associate Director for Pharm/Tox ODE3, CDER, Office of New Drugs Immediate Office, FDA

Jeff Engelhardt, DVM, PhD, DACVP, FRCPath, Fellow IATP, Fellow ATS, Vice President, Pathology and Nonclinical Drug Safety, Ionis Pharmaceuticals, Inc.

This session will examine the renal accumulation of ASOs in animals, mechanisms of ASO-related glomerular injury, and the broader experience of clinical renal toxicity with the class. The current hypothesis on the pathogenesis of ASO-related thrombocytopenia in nonhuman primates and potential strain dependence will be discussed along with potential clinical ramifications. The safety studies of 2'-deoxy-2'-fluoro nucleotides in GalNAc-siRNA conjugates will also be discussed in view of toxicity concerns from previous drugs containing 2'-F-modified nucleobases, such as fialuridine.

Examination of Glomerular Toxicity Risk Across ASO Platforms and Trials
Kendall Frazier, DVM, PhD, Director, Cellular and Molecular Pathology, GlaxoSmithKline

Current Understanding of Mechanism for ASO-Related Thrombocytopenia
Padma Kumar Narayanan, DVM, PhD, MS, Executive Director, Toxicology, Ionis Pharmaceuticals, Inc.

Safety Evaluation of 2'-Deoxy-2'-Fluoro Nucleotides in GalNAc-siRNA Conjugates
Ivan Zlatev, PhD, Principal Scientist, Research, Alnylam Pharmaceuticals, Inc.

Track C: CMC Strategies for Accelerated Approval (Fast Track, Breakthrough, PRIME, etc.) of Oligonucleotide Drugs — Salon C

Session Chair
Fran Wincott, PhD, President, Wincott & Associates LLC

There is a growing trend in the pharmaceutical industry towards accelerated development of therapeutics to address unmet medical needs. The shorter timelines coupled with increasing complexity of the development candidates presents extraordinary challenges for managing the chemistry, manufacturing, and controls activities. This session will provide a background on the existing regulatory expedited pathways. Approaches for successful clinical development, regulatory approval, and commercialization of therapeutic oligonucleotides within the framework of accelerated development will be discussed.

CMC Strategies for Accelerated Approval (Development) of Oligonucleotide Drugs
Olen M. Stephens, PhD, Chemist Reviewer, CMC Reviewer, Office of New Drugs, FDA

Nicole Del Canto, Director, Global Regulatory CMC, Biogen Inc.

Veronika Jekerle, PhD, RPh, Quality Specialist, European Medicines Agency, Netherlands

Panelist
Benjamin Stevens, PhD, MPH, Associate Director, Regulatory Affairs CMC, Alnylam Pharmaceuticals, Inc.

3:30-4:00PM **Refreshment, Exhibits, and Networking Break** — Salon D

4:00-5:30PM **Session 4:** Concurrent Breakout Sessions

Track A/B: Evaluation of QT Prolongation Potential and Assessment of Immunogenicity — Salon A-B

Session Co-Chairs
Hobart Rogers, PharmD, PhD, Pharmacologist, FDA

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

Oligonucleotide therapeutics have unique characteristics that often require differential pre-clinical and clinical assessment compared to small molecules. This session will address two of these topics: Topic One will focus on the nonclinical and clinical aspects of the assessment of QT prolongation potential; Topic Two will focus on the evaluation of the nonclinical and clinical aspects regarding immunogenicity. Both topics will have perspective presentations from both industry and regulatory speakers. Following the presentations, a joint panel will convene to further discuss these topics with implications for guiding future regulatory oversight.

Evaluation of QT Prolongation Potential
Are Oligonucleotide Therapeutics too "Large" to Interact with Cardiac Ion Channels:

Insights from the FDA Database
Wendy Yan Wu, PhD, Pharmacologist, Division of Applied Regulatory Science, CDER, FDA

Oligonucleotide Nonclinical Safety Testing, a CRO Perspective
James Kramer, PhD, Principal Scientist, Charles River Laboratories

Clinical QT Assessment for Oligonucleotide-Based Therapeutics: Regulatory Experience and Current Thinking
Nan Zheng, PhD, Scientific Lead, Office of Clinical Pharmacology, CDER, FDA

QT Evaluation for Antisense Oligonucleotides, Ionis Experience
Yanfeng Wang, PhD, Executive Director, Ionis Pharmaceuticals, Inc.

Panel Discussion: Q&A

Assessment of Immunogenicity
FDA Presentation: Assessment of Immunogenicity Studies

Zhenzhen Liu, PhD, Biologist, FDA

Immunogenicity Assessments for Antisense Oligonucleotides
Rosie Yu, PhD, Executive Director, Ionis Pharmaceuticals, Inc.

Industry Presentation
Daniel Mytych, PhD, Scientific Director, Clinical Immunology, Department of Translational Medicine, Amgen, Inc.

Panel Discussion: Q&A

Track C: Developing Oligonucleotides with Current CMC Guidelines and an Introduction to EPOC — Salon C

Session Chair
Nigel Richardson, PhD, Head Analytical Technology and Automation, CMC Analytical, Product Development and Supply, GlaxoSmithKline

There is currently no regulatory guidance specifically for the development of oligonucleotide therapeutic agents, and as a result existing small molecule guidance is interpreted by sponsors. This, and the lack of consensus in approach within the pharmaceutical industry can lead to duplication of effort resulting in inefficiencies for both industry and regulatory agencies. The session will provide an overview of key CMC development topics which would benefit from harmonization and sharing of prior knowledge and will contain detailed examples of industry collaboration on focused topics. The collaborative work discussed in the session has been initiated by the European Pharma Oligonucleotide Consortium (EPOC), an example of how industry is collaborating to pool experience, share data, and publish in oligonucleotide development topics to drive consensus and engagement with the regulator environment.

Stating Materials
William Kiesman, PhD, Senior Director, Biogen, Inc.

ID Testing
Nadim Akhtar, PhD, Principle Scientist, AstraZeneca, United Kingdom

Panelists
Rohit Tiwari, PhD, Chemist, FDA

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

Hiroshi Takeda, PhD, Technical Officer, Pharmaceuticals and Medical Devices Agency

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5:30-6:30PM **Poster Session and Networking Reception** — Salon D

DAY TWO | OCTOBER 29

8:00AM-5:00PM — **Registration** — Salon C Foyer

8:00-9:00AM — **Continental Breakfast, Exhibits, and Networking** — Salon D

8:15-9:00AM — **Breakfast Plenary Session:** Global Regulatory — Salon A-C

Session Co-Chairs
Paul Brown, PhD, ODE Associate Director for Pharmacology and Toxicology, OND, CDER, FDA

Laurence Whiteley DVM, PhD, ACVP, Senior Director, Global Pathology Team Leader, Pfizer

Representatives from the Pharmaceutical and Medical Devices Agency (PMDA) of Japan will present their proposal for a regulatory guidance for oligonucleotide therapeutics. Discussion will focus on the overall approach and whether aspects can be more widely applied. The information presented may also support discussion in other sessions of the meeting.

Draft Guideline for Non-Clinical Safety Evaluation of Oligonucleotide Therapeutics in Japan
Yoko Hirabayashi, MD, Director, Center for Biological Safety and Research, National Institute of Health Sciences, Japan

9:00-9:05AM — **Welcome to Day Two** — Salon A-C

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

9:05-10:05AM — **Keynote Address** — Salon A-C

C. Frank Bennett, PhD, Senior Vice President, Research, Ionis Pharmaceuticals Inc.

10:05-10:30AM — **Refreshment, Exhibits, and Networking Break** — Salon D

10:30AM-12:00PM — **Session 5:** Concurrent Breakout Sessions

Track A: Clinical Experience With Lipid Nanoparticle-Based Delivery Of Oligonucleotides — Brookside, lower level

Session Co-Chairs
Christine Swenson, Head, Global Regulatory Affairs, Moderna Therapeutics

Anuradha Ramamoorthy, PhD, Policy Lead, FDA

Delivery of oligonucleotides using lipid nanoparticles (LNP) has been an emerging area of interest over the past decade. Clinical progress with LNP-mediated delivery of siRNAs, mRNAs, and saRNAs will be discussed.

Development and Approval of ONPATTRO, the First RNAi Therapeutic
Pushkal Garg, MD, Chief Medical Officer, Alnylam Pharmaceuticals, Inc.

Emerging Clinical Data for Intratumor and Systemic Administration of mRNA Therapies
Christine Swenson, Head, Global Regulatory Affairs, Moderna Therapeutics

MTL-CEBPA, The First Small Activating RNA Therapy in Clinical Development
Nagy Habib, Head of Research and Development, MiNA Therapeutics Limited, United Kingdom

Track B: Progress in Developing Rna Targeted Drugs for the Treatment of Neurological Diseases — Salon A-B

Session Co-Chairs
Lois Freed, PhD, Supervisory Pharmacologist, CDER, FDA

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

The approval of Spinraza for the treatment of spinal muscular atrophy has demonstrated that locally administered RNA targeting drugs have the potential to treat a broad array of neurological disease. The challenge is to fully understand how these compounds are interacting with the CNS compartment and how studies in animals can inform the design of patient clinical trials. This session will review progress toward developing antisense and siRNA drugs for the treatment of CNS diseases. The focus will be on nonclinical safety testing, systemic, tissue exposure evaluation, and regulatory considerations.

Big Vacuoles; Small Problem De-Risking Hippocampal Neuron Macrovesicular Vacuolation
Martin Lamb, BVetMed, MRCVS, DACVP, Principal Investigator, Comparative Pathology, Biogen

Recent Developments for Delivery and PD Activity of siRNAs in the CNS
Jeff Allen, PhD, Associate Director, Toxicology, Alnylam Pharmaceuticals, Inc.

FDA Presentation
David Carbone, PhD, Toxicologist, FDA

Track C: Oligonucleotide Degradation, Stability, and the Question of Terminal Sterilization — Salon C

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

This session will focus on the impact of terminal sterilization to oligonucleotide product quality. Formulation development, cycle optimization, and container closure considerations to minimize oligonucleotide degradation during sterilizing heat treatment processes will also be presented. Key learnings will be presented studying oligonucleotide product terminal sterilization as preferred route for sterilization.

Key Considerations in Terminal Sterilization Development of Oligonucleotides
Daniel DeCollibus, MS, Scientist I, Biogen

Sterilizing Oligonucleotide-Containing Formulations
Bianca Matthee, MSc, PharmD, MPharm, Vice President CMC, ProQR Therapeutics, Netherlands

Panelist:
Jonathan Burgos, PhD, Lieutenant Commander, US Public Health Service Commissioned Corps CDER, FDA

12:00-1:30PM — **Round Table Discussion Luncheon, Exhibits, and Networking** — Salon D

1:30–3:00 PM — **Session 6:** Concurrent Breakout Sessions

Track A/B: Evaluation of Intrinsic/Extrinsic Factors — Salon A-B

Session Co-Chairs
Hobart Rogers, PharmD, PhD, Clinical Pharmacologist, FDA

Gabriel Robbie, Vice President, Clinical Pharmacology and Pharmacometrics, Alnylam Pharmaceuticals, Inc.

Oligonucleotide therapeutics have unique characteristics that often require differential pre-clinical and clinical assessment compared to small molecules. This session will address two of these topics: Topic One will focus on the evaluation of both renal and hepatic impairment; Topic Two will focus on the assessment of drug-drug interactions liability with oligonucleotides. Both topics will have perspective presentations from industry and regulatory speakers. Following the presentations, a joint panel will convene to further discuss these topics with implications for guiding future regulatory oversight.

Evaluation of Intrinsic Factors/Organ Impairment Studies

FDA Evaluation of Renal/Hepatic Impairment
Martina Sahre, PhD, Policy Lead, OCP, FDA

Evaluation of Renal/Hepatic Impairment on the Pharmacokinetics of Antisense Oligonucleotides
Yanfeng Wang, PhD, Executive Director, Ionis Pharmaceuticals, Inc.

Evaluation of Oligonucleotide Therapeutics in Patients with Renal and Hepatic Impairment
Bahru Habtemariam, PharmD, Senior Director of Clinical Pharmacology, Alnylam Pharmaceuticals, Inc.

Panel Discussion: Q&A

Evaluation of Extrinsic Factors/Drug-Drug Interaction Liability

Evaluation of Extrinsic Factors/Drug-Drug Interaction Liability In Vitro
Oluseyi Adeniyi, PharmD, PhD, Reviewer, CDER, FDA

In Vitro/In Vivo
Faraz Kazmi, PhD, Senior Scientist, Drug Metabolism and Pharmacokinetics, Janssen Research and Development

Evaluating Clinical Drug Interactions for Oligonucleotide Therapeutics
Venkateswaran Chithambarampillai, MS, PhD, Senior Staff Fellow, Office of Clinical Pharmacology, CDER, FDA

Panel Discussion: Q&A

Track C: Control Strategy and Regulatory Considerations for Manufacture of mRNA Drug Substance — Salon C

Session Co-Chairs
Silke Klick, PhD, Regulatory Director CMC, AstraZeneca, Sweden

Brian Stultz, MS, Staff Scientist, Division of Cellular and Gene Therapies, FDA

This session will provide an overview of the manufacturing strategy for mRNA Drug Substance and how mRNAs differ from synthetic oligonucleotides. The presentations will address key critical quality attributes, describe control strategies, and provide a regulatory overview. The session will include a panel discussion on regulatory considerations for mRNA Drug Substance.

Manufacture and Control of mRNA Drug Substance
James Thompson, PhD, CMC Therapeutic Area Lead, Moderna Therapeutics

Brian Stultz, MS, Staff Scientist, Division of Cellular and Gene Therapies, CBER, FDA

Panelists
Silke Klick, PhD, Regulatory Director CMC, AstraZeneca, Sweden

Andreas Kuhn, PhD, Vice President RNA Biochemistry, BioNTech RNA Pharmaceuticals GmbH, Germany

James Thompson, PhD, CMC Therapeutic Area Lead, Moderna Therapeutics

Brian Stultz, MS, Staff Scientist, Division of Cellular and Gene Therapies, FDA

Christine Swenson, Head, Global Regulatory Affairs, Moderna Therapeutics

John Talian, PhD, Senior Vice President, CureVac Inc.

3:00-3:30PM **Refreshment, Exhibits, and Networking Break** Salon D

3:30-5:30PM **Session 7:** Hot Topics Salon A-C

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

The hot topics session is designed to provide the attendees with a glimpse at future oligonucleotide therapeutics. This session is a chance to see how the field is developing and what kind of novel approaches or applications are being studied in academia and industry. With this early look at these approaches, it is hoped that the audience can envision the promise of new technologies and have a preview of the kind of challenges these technologies will face or pose to the current regulatory environment.

Robert Ward, Chairman and CEO, Eloxx Pharmaceuticals

Experience with FDA's Complex Innovative Design (CID) Pilot
Jennifer Panagoulias, RAC, Vice President, Regulatory Affairs, Wave Life Sciences

Development of Fatty Acid siRNA Conjugates for Ophthalmic Disease
Arthur Suckow, PhD, CEO, CSO, Co-Founder, DTxPharma

Potent siRNA Silencing in the Brain
Chantal Ferguson, University of Massachusetts Medical School

How AI is Accelerating Drug Discovery: From Novel Target to Drug Candidate in 18 Months
Brendan Frey, PhD, FRSC, Co-Founder and CEO, Deep Genomics, Professor, Engineering and Medicine, University of Toronto, Co-Founder, Vector Institute for Artificial Intelligence, Canada

5:30-6:30PM **DIA Oligonucleotide Safety Working Group (OSWG) – Open Meeting** Brookside, lower level

Attend to learn more or meet fellow members, hear about what's happening in the working group, and join in the latest discussions on the latest hot topics.

DAY THREE | OCTOBER 30, 2019

7:00AM-12:30PM **Registration** Salon C Foyer

7:00-8:00AM **Continental Breakfast and Networking** Salon D

8:00-10:00 AM **Session 8:** Concurrent Breakout Sessions

Track A/B: Hybridization-Dependent Off-Target Events Salon A-B

Session Co-Chairs
Arthur Levin, PhD, Executive Vice President, Research and Development, Avidity Biosciences

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

In 2012, the Oligonucleotide Safety Working Group published guidelines that outline approaches for assessing hybridization-dependent off-target events. Significant progress has been made in the intervening years in our understanding of this phenomena and new technologies have been more widely accepted that allow us to assess off-target events more thoroughly. Also, in the intervening years, there have been increasing reports of hybridization dependent toxicities being identified in non-clinical studies. It is now time to re-interrogate

how to best study off-target events and define new guidelines. The attendees at this session should come away with a greater understanding of the nature and mechanisms of off-target effects and how bioinformatics approaches can minimize them and how to assess them.

Update from OSWG-Oligo Hybridization-Dependent Off-Target Events and Surveillance Across Platforms/Mechanism of Action
Arthur Levin, PhD, Executive Vice President, Research and Development, Avidity Biosciences

Large-Scale Selectivity Assessment of Gapmer Antisense Oligonucleotides
Sagar Damle, PhD, Molecular Biology, Associate Director, Functional Genomics Ionis Pharmaceuticals, Inc.

Preclinical and Clinical PK of GalNAc SSOs at Doses Below and Above ASGPR Saturation Approaches to siRNA "Off-Target" Assessment
Mark Schlegel, PhD, Principal Scientist, RNAi Discovery, Alnylam Pharmaceuticals

A Discussion on the Off-Target Assessment Recommendation in the Chronic Hepatitis B, Viral Infection Drug Development Draft Guidance
Eric Donaldson, PhD, Virology Reviewer, CDER, OND, OAP, Division of Antiviral Products, FDA

Track C: General CMC Q&A Session — Salon C

Session Chair
Kim Tyndall, CMC Regulatory Consultant, CMC Tyndall Consultant LLC

8:30-10:00AM

During this session, you will have the opportunity to interact with regulators and experts to discuss current and future concerns in the development of oligonucleotide programs. This open discussion will focus on pre-submitted questions and open the floor to questions from the audience. It is your time to explore the oligonucleotide regulatory arena. There will be regulators from FDA, EMA, PMDA, bFarm, and academia.

Panelists
Veronika Jekerle, PhD, RPh, Quality Specialist, European Medicines Agency

Hiroshi Takeda, PhD, Technical Officer, Pharmaceuticals and Medical Devices Agency

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

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

Ian Dobson, Team Leader, Evaluator, Health Canada

10:00:10:15AM — **Refreshments and Networking Break** — Salon D

10:15-11:45AM — **Session 9:** ON Therapeutic Survey Sponsored by EFPIA — Salon A-C

Session Co-Chairs
Paul Brown, PhD, ODE Associate Director for Pharmacology and Toxicology, OND, CDER, FDA

Laurence Whiteley, DVM, PhD, ACVP, Senior Director, Global Pathology Team Leader, Pfizer

Representatives from the European Federation of Pharmaceutical Industries and Associations (EFPIA) will present findings of a recent survey they conducted about oligonucleotide therapeutic development. Industry insights will be presented on considerations related to the toxicological evaluation of oligonucleotides. The industry perspective regarding the need for and possible content of a regulatory guidance on oligonucleotide therapeutics will be presented. A group of regulatory and industry representatives and the audience will discuss the need for possible content of a regulatory guidance on oligonucleotide therapeutics.

This discussion will draw on the EFPIA survey and other information presented earlier in the meeting such as the PMDA presentation.

What Is Everyone Else Doing? Learnings and Surprises From the EFPIA Oligo WG Survey
Yaan Tessier, DVM, MPH, Senior Toxicology Project Leader, Roache, Denmark

Guiderails for Oligo Development: Industry Perspectives on an Oligo-Specific Guidance From the EFPIA Oligo WG Survey
Lauren Mihalcik, PhD, DABT, Senior Scientist, Toxicologist, Comparative Biology and Safety Sciences, Amgen

Two Species or Not Two Species (And Other Toxicology Considerations): Insights From the EFPIA Oligo WG Survey
William Achanzar, PhD, DABT, Director, Toxicology, Therapeutic Area Head, Cardiovascular Diseases, Drug Safety Evaluation, Research and Development, Bristol-Myers Squibb

Panelist
Yoko Hirabayashi, MD, Director, Center for Biological Safety and Research, National Institute of Health Sciences, Japan

11:45AM-12:30PM **Closing Session:** Panel Discussion — Salon A-C

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

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

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

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

G. Susan Srivatsa, PhD, President, ElixinPharma

Hobart Rogers, PharmD, PhD, Pharmacologist, FDA

Saraswathy Nochur, PhD, MSc, Chief Regulatory Officer, Alnylam Pharmaceuticals Inc.