DIA/FDA Oligonucleotide-Based Therapeutics Conference

October 25-27 | Bethesda North Marriott Hotel and Conference Center | North Bethesda, MD

Overview

The DIA/FDA Oligonucleotide-Based Therapeutics Conference fosters open discussion with industry and health authorities to inform, educate, and share advancements in oligonucleotide-based therapeutic product development. Designed for regulators and industry from CMC, Nonclinical, Clinical Pharmacology, and Clinical disciplines, the conference will address developmental advances, safety, and challenges in the field of oligonucleotide-based therapeutics.

Highlights

- Keynote Addresses from Arthur M. Krieg, MD, President and CEO, Checkmate Pharmaceuticals, and Philip J. Brooks, PhD, Program Director, Division of Clinical Innovation National Center for Advancing Translational Sciences (NCATS)
- National Institutes of Health representation
- Poster Session
- Special luncheon presentation featuring the Japanese Perspective on Preclinical Safety Assessment of Oligonucleotide Therapeutics
- NEW: Luncheon Round Table Discussions on cutting-edge topics with key thought leaders
- NEW: Oligo Safety Working Group (OSWG) open meeting
- NEW: Visit exhibiting companies during the networking breaks
- Breakfast Session on Thursday, 8:15-9:00AM, on Emergency Single Patient IND for Oligonucleotide Therapy of a Unique Individual Mutation

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
A Message from the Program Committee

Dear Colleagues,

We are pleased to welcome you to the DIA/FDA Oligonucleotide-Based Therapeutics Conference!

This conference is unique in setting the stage for an open, collaborative discussion of important topics and tools for senior-level professionals and those working in oligonucleotide science to navigate the dynamic and quickly changing health care environment. Experts across three central tracks, CMC, Nonclinical, and Clinical, will be presenting in-depth information. We are truly three meetings in one, with plenaries planned to create a cross-functional experience for knowledge-sharing, integrated thought leadership, and proactive networking.

The conference will begin with a cross-track plenary session featuring the emerging landscape of mRNA-based drugs which is immediately followed by track-specific breakout sessions and ending with a poster session and welcome reception.

Day two will open with two Keynote Addresses from Arthur M. Krieg, MD, President and CEO, Checkmate Pharmaceuticals, and Philip J. Brooks, PhD, Program Director, Division of Clinical Innovation National Center for Advancing Translational Sciences (NCATS), who will be discussing the current state of oligonucleotides within FDA and NIH.

We hope you will take advantage of the many opportunities to actively engage in discussions and with each other. Be sure to join us Wednesday evening for the Poster Session and Networking Reception, Thursday during the luncheon to participate in a round table discussion, or join a session inspired by colleagues in Japan to learn more about their perspective on preclinical safety assessment of oligonucleotide therapeutics in comparison with biopharmaceuticals and low molecular new chemical entities. Thursday evening we have an open meeting of the DIA Oligonucleotide Safety Working Group (OSWG). Finally, at the closing session on Friday, leaders from each of the three tracks will come together to highlight key takeaways and moderate an open Q&A with the audience.

Best Regards,

The DIA/FDA Oligonucleotide Program Committee
# Schedule At-A-Glance

## Day One | Wednesday, October 25

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<tr>
<th>Time</th>
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<tbody>
<tr>
<td>7:00AM-5:00PM</td>
<td>Registration</td>
<td>Grand Ballroom Salon C Foyer</td>
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<tr>
<td>7:00-8:00AM</td>
<td>Continental Breakfast, Exhibits, and Networking</td>
<td>Grand Ballroom Salon D</td>
</tr>
<tr>
<td>8:00-8:30AM</td>
<td>Welcome Remarks and Overview of the 2017 Conference</td>
<td>Grand Ballroom Salon A-C</td>
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<tr>
<td>8:30-10:30AM</td>
<td>Session 1: The Emerging Landscape of mRNA-Based Drugs: A New Modality in Vaccines and Therapeutics</td>
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<tr>
<td>10:30-11:00AM</td>
<td>Refreshment, Exhibits, and Networking Break</td>
<td>Grand Ballroom Salon D</td>
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<tr>
<td>11:00AM-12:30PM</td>
<td>Session 2: Concurrent Breakout Sessions</td>
<td>Grand Ballroom Salon C</td>
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<tr>
<td>12:30-1:30PM</td>
<td>Luncheon, Exhibits, and Networking</td>
<td>Grand Ballroom Salon D</td>
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<tr>
<td>1:30-3:00PM</td>
<td>Session 3: Concurrent Breakout Sessions</td>
<td>Grand Ballroom Salon C</td>
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<tr>
<td>3:00-3:30PM</td>
<td>Refreshment, Exhibits, and Networking Break</td>
<td>Grand Ballroom Salon D</td>
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<tr>
<td>3:30-5:00PM</td>
<td>Session 4: Concurrent Breakout Sessions</td>
<td>Grand Ballroom Salon A-C</td>
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<tr>
<td>5:00-6:00PM</td>
<td>Poster Session and Networking Reception</td>
<td>Grand Ballroom Salon D</td>
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## Day Two | Thursday, October 26

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<tr>
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<tr>
<td>8:00AM-5:00PM</td>
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<tr>
<td>8:00-9:00AM</td>
<td>Continental Breakfast, Exhibits, and Networking</td>
<td>Grand Ballroom Salon D</td>
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<tr>
<td>8:15-9:00AM</td>
<td>Breakfast Plenary Session: Emergency Single Patient IND for Oligonucleotide Therapy of a Unique Individual Mutation</td>
<td>Grand Ballroom Salon A-C</td>
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<tr>
<td>9:00-9:05AM</td>
<td>Welcome to Day Two</td>
<td>Grand Ballroom Salon A-C</td>
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<tr>
<td>9:05-10:05AM</td>
<td>Session 5: Keynote Addresses</td>
<td>Grand Ballroom Salon A-C</td>
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<td>10:05-10:30AM</td>
<td>Refreshments, Exhibits and Networking Break</td>
<td>Grand Ballroom Salon D</td>
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<tr>
<td>10:30AM-12:00PM</td>
<td>Session 6: Concurrent Breakout Sessions</td>
<td>Grand Ballroom Salon C</td>
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<tr>
<td>12:00-1:30PM</td>
<td>Round Table Discussion Luncheon, Exhibits, and Networking</td>
<td>Grand Ballroom Salon D</td>
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<tr>
<td>12:00-1:15PM</td>
<td>Luncheon Presentation: Japanese Perspective on the Preclinical Safety Assessment of Oligonucleotide Therapeutics</td>
<td>Grand Ballroom Salon D</td>
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<tr>
<td>1:30-3:00PM</td>
<td>Session 7: Concurrent Breakout Sessions</td>
<td>Grand Ballroom Salon C</td>
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<tr>
<td>3:00-3:30PM</td>
<td>Refreshment, Exhibits, and Networking Break</td>
<td>Grand Ballroom Salon D</td>
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<tr>
<td>3:30-5:00PM</td>
<td>Session 8: Gene Editing</td>
<td>Grand Ballroom Salon A-C</td>
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<tr>
<td>5:00-5:30PM</td>
<td>DIA Oligonucleotide Safety Working Group (OSWG) – Open Meeting</td>
<td>Brookside, Lower Level</td>
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## Day Three | Friday, October 27

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<tr>
<td>8:00-9:30AM</td>
<td>Session 9: Concurrent Breakout Sessions</td>
<td>Grand Ballroom Salon C</td>
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<tr>
<td>9:30-9:45AM</td>
<td>Refreshment and Networking Break</td>
<td>Grand Ballroom Salon D</td>
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<tr>
<td>9:45-11:15AM</td>
<td>Session 10: Hot Topics in Oligonucleotide Therapeutics</td>
<td>Grand Ballroom Salon A-C</td>
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<tr>
<td>11:15AM-12:00PM</td>
<td>Closing Session: Panel Discussion</td>
<td>Grand Ballroom Salon A-C</td>
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Learning objectives

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

- Identify accomplishments and challenges in the clinical development of oligonucleotide-based therapeutic drugs
- Describe the critical issues in the nonclinical development of oligonucleotides
- Differentiate the chemistry, manufacturing, and controls challenges associated with the development of synthetic oligonucleotides, including formulation and specification issues
- Explain unique aspects and various scientific approaches used during the development of oligonucleotide-based therapeutics
- Recognize the achievements made in the field to date and be able to share the vision with patients about the therapeutic potential that oligonucleotides possess across a wide range of indications

Continuing Education Credit

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If you would like to receive a statement of credit, you must attend the DIA Oligonucleotide-Based Therapeutics Conference, sign in at the registration desk at the end of the conference, 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 1, 2017.

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It is DIA policy that anyone in a position to control the content of a continuing education activity must disclose to the program audience (1) any relevant financial relationships related to the content of their presentation and/or the educational activity, and (2) discussions of unlabeled or unapproved uses of drugs or medical devices. Disclosures will be included in the electronic handout materials.

This educational activity may include references to the use of products for indications not approved by the FDA. Opinions expressed with regard to unapproved uses of products are solely those of the faculty and are not endorsed by the DIA or any of the manufacturers of products mentioned herein. Faculty for this educational activity was asked to disclose any discussion of unlabeled or unapproved uses of drugs or medical devices.

Reasonable accommodations will be made available to persons with disabilities who attend an educational activity. Contact the DIA office in writing at least 15 days prior to event to indicate your needs.
### DAY ONE | WEDNESDAY, OCTOBER 25

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speakers/Co-Chairs</th>
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<tbody>
<tr>
<td>7:00AM-5:00PM</td>
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<tr>
<td>8:00-8:30AM</td>
<td>Welcome Remarks and Overview of the 2017 Conference</td>
<td>Sudip Parikh, PhD, James Thompson, PhD, James Wild, PhD</td>
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<td>Senior Vice President, DIA, Head, CMC Project Management, Moderna Therapeutics,</td>
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<td></td>
<td>Pharmacologist, CDER, FDA</td>
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<tr>
<td>8:30-10:30AM</td>
<td>Session 1: The Emerging Landscape of mRNA-Based Drugs: A New Modality in Vaccines and Therapeutics</td>
<td>Tal Zaks, MD, PhD, Ramachandra G Naik, MD, Sarah Beach Voytek, PhD, Keith Peden, PhD</td>
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<td></td>
<td></td>
<td>Chief Medical Officer, Moderna Therapeutics, Principal Scientist, Novartis Institutes For Biomedical Research, Inc., Chief, Laboratory of DNA Viruses, CBER, FDA</td>
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<td>mRNA therapeutics are unique, relative to most oligonucleotide-based modalities like antisense, siRNAs, and aptamers in that mRNAs enable expression of the encoded protein rather than act as antagonists to inhibit target protein translation or activity. Early clinical data indicate that mRNA-based drugs may be effective vaccines and their potential as therapeutics is now emerging. This session will describe the general approach to mRNA manufacture, present emerging preclinical and clinical data on mRNA vaccines and therapeutics, and provide a regulatory perspective on the product-related (CMC) aspects of mRNA drug development.</td>
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<td>Translating mRNA Vaccines and Therapeutics: First Clinical Steps, Clinical Development of mRNA Vaccines and Immunotherapies: Experiences and Lessons Learned, Regulatory Perspective on the Product-Related (CMC) Aspects of mRNA Vaccines</td>
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<td>Tal Zaks, MD, PhD, Ramachandra G Naik, MD, Ulrike Gnad-Vogt, MD, Keith Peden, PhD,</td>
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<td>Chief Medical Officer, Moderna Therapeutics, Primary Reviewer/Regulatory Project,</td>
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<td>Manager, OVRR, CureVac AG, Germany, Chief, Laboratory of DNA Viruses, CBER, FDA</td>
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<td>Considerations for the Nonclinical Development of Systemically-Administered Therapeutic mRNA, Panel Discussion</td>
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<td>Sarah Beach Voytek, PhD, Ulrike Gnad-Vogt, MD, Ulrike Gnad-Vogt, MD</td>
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<td>Principal Scientist, Novartis Institutes For Biomedical Research, Inc.</td>
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<tr>
<td>10:30-11:00AM</td>
<td>Refreshment, Exhibits, and Networking Break</td>
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## DAY ONE | WEDNESDAY, OCTOBER 25

### Session 2 Concurrent Breakout Sessions

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<th>TRACK A</th>
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<tbody>
<tr>
<td><strong>Control Strategy for Double-Stranded Oligonucleotides</strong></td>
<td><strong>Assessing the Implications of Oligonucleotide Uptake into Cells</strong></td>
<td><strong>Cardiovascular/Metabolic Diseases</strong></td>
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<tr>
<td><strong>Session Chair</strong></td>
<td><strong>Session Co-Chairs</strong></td>
<td><strong>Session Co-Chairs</strong></td>
</tr>
<tr>
<td>Samantha Gao-Sheridan, PhD</td>
<td>Xuan Chi, MD, PhD</td>
<td>Peter Wijngaard, PhD</td>
</tr>
<tr>
<td>Senior Director, Regulatory Affairs CMC</td>
<td>Pharmacology/Toxicology Reviewer, Division of Cardiovascular and Renal Products, Office of New Drugs</td>
<td>Senior Vice President, ACC GIG Health Science Leader, The Medicines Company</td>
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<tr>
<td>Alnylam Pharmaceuticals</td>
<td>CDER, FDA</td>
<td>Science Leader, The Medicines Company</td>
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<tr>
<td><strong>Focus on the control strategy elements to be considered for the development and registration of double-stranded oligonucleotide therapies.</strong></td>
<td><strong>Examine the cellular uptake and lysosomal processing of single-stranded oligonucleotides by the most frequently affected tissues and cells following systemic administration (kidney and macrophages) and intrathecal administration (neurons).</strong></td>
<td><strong>Review progress made in the clinical development of RNA therapeutics in the cardiovascular and metabolic therapeutic areas. The targets and applications range from Factor XI antagonism in the coagulation pathway using antisense oligonucleotides to the inhibition of PCSK9 synthesis via RNA interference and GalNAc conjugation to reduce cardiovascular risk factors.</strong></td>
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<tr>
<td><strong>European Regulatory Perspective on Double-Stranded Oligonucleotides</strong></td>
<td><strong>Renal and Macrophage Uptake of Systemically Administered Oligonucleotides</strong></td>
<td><strong>Antisense Reduction of FXI for Thromboprophylaxis: A Novel Therapeutic Approach</strong></td>
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<tr>
<td>René Thürmer, PhD</td>
<td>Kendall Frazier, DVM, PhD</td>
<td>Sanjay Bhanot, MD, PhD</td>
</tr>
<tr>
<td>Deputy Head of the Unit Pharmaceutical Biotechnology</td>
<td>Director, Cellular and Molecular Pathology</td>
<td>Vice President, Metabolic Diseases, Research and Development</td>
</tr>
<tr>
<td>BfArM - Federal Institute for Drugs and Medical Devices, Germany</td>
<td>GlaxoSmithKline</td>
<td>Ionis Pharmaceuticals, Inc.</td>
</tr>
<tr>
<td><strong>Characterization and Control of siRNA Impurities</strong></td>
<td><strong>Neuronal Uptake of Intrathecally Administered Oligonucleotides</strong></td>
<td><strong>Volanesorsen: Targeting ApoC-III for Treatment of Patients with Familial Chylomicronemia Syndrome (FCS)</strong></td>
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<tr>
<td>Matthias Kretschmer, PhD</td>
<td>Jeffery A. Engelhardt, DVM, PhD, DACVP, FIATP</td>
<td>Louis St.L. O’Dea, MB, BCh, BAO, CSPQ, FRCPC</td>
</tr>
<tr>
<td>Senior Director, Analytical Development</td>
<td>Vice President, Pathology and Nonclinical Drug Safety</td>
<td>Executive Vice President, Chief Medical Officer and Head, Regulatory Affairs AKCEA Therapeutics</td>
</tr>
<tr>
<td>Alnylam Pharmaceuticals</td>
<td>Ionis Pharmaceuticals, Inc.</td>
<td>AKCEA Therapeutics</td>
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<tr>
<td><strong>Panel Discussion</strong></td>
<td><strong>A Report from the ESTP Expert Panel on Adversity of Lysosomal Accumulation</strong></td>
<td><strong>PCSK9 Synthesis Inhibition: siRNA Therapeutic for Large Indications</strong></td>
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<td><strong>Joining the speakers:</strong></td>
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<td><strong>Peter Wijngaard, PhD</strong></td>
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<tr>
<td>Ramesh Raghavachari, PhD</td>
<td>James Willard, PhD</td>
<td>Senior Vice President, ACC GIG Health Science Leader, The Medicines Company</td>
</tr>
<tr>
<td>Chief, Branch I, DPMAT, OLDP, OPQ CDER, FDA</td>
<td>Pharmacologist, DCaRP CDER, FDA</td>
<td><strong>Panel Discussion</strong></td>
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<td>Vidhya Gopalakrishnan, PhD</td>
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<td>Louis St.L. O’Dea, MB, BCh, BAO, CSPQ, FRCPC</td>
</tr>
<tr>
<td>Senior Vice President, Pharmaceutical Development</td>
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<td>Executive Vice President, Chief Medical Officer and Head, Regulatory Affairs AKCEA Therapeutics</td>
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<td><strong>Panel Discussion</strong></td>
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### 12:30-1:30PM Luncheon, Exhibits, and Networking
### DAY ONE | WEDNESDAY, OCTOBER 25

**1:30-3:00PM Session 3 Concurrent Breakout Sessions**

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<tr>
<td>Starting Materials: Beyond Simple DNA and RNA Derived Phosphoramidites</td>
<td>Understanding the Effects of 2’-MOE ASO Treatment on PLT Count in Non-Human Primates and Humans</td>
<td>New Approaches in the Development of Immune Stimulatory Oligonucleotides in Oncology</td>
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**Session Chair**
Fran Wincott, PhD  
President  
Wincott & Associates, LLC

There has been a dramatic increase in the complexity of drug candidates being promoted into preclinical and clinical development. These oligonucleotides often have significant chemical modifications requiring specialty starting materials. Furthermore, recent communications from regulatory authorities regarding the selection and justification of starting materials have been issued. This session will address the general starting material principles outlined in Q11 and the accompanying Q&A document. In addition, strategies for defining and sourcing non-standard oligonucleotide-specific starting materials will be presented. The presentations will be followed by a 30 minute panel discussion.

**Identification of Starting Materials for Oligonucleotides by Applying ICH Q11**
Timothy J. N. Watson, PhD  
Senior Director, CMC Advisory Office  
Pfizer Inc

**Integrating LNA Phosphoramidites into the Regular Supply Chain**
Christoph Rosenbohm, PhD, MBA  
Vice President, Head of Discovery Operations  
Roche Innovation Center  
Copenhagen, Denmark

**GalNAc Solid Support as Starting Material for Oligonucleotide Manufacturing**
Lubomir Nechev, PhD  
Vice President, Process Sciences  
Alnylam Pharmaceuticals

**Panel Discussion**

Joining the speakers:

Olen Stephens, PhD  
Chemist  
CDER, FDA

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

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

Ronald L. Wange, PhD  
Pharmacology and Toxicology Reviewer, Division of Metabolism and Endocrinology Products  
FDA

**Examine the overall experience with this class of oligonucleotides on PLT count in both monkeys and humans using a database comprised of multiple compounds. Comparisons will be made between monkeys and humans, include special patient populations that have recently reported severe thrombocytopenia. Background information on PLT biology and the current status investigation into the mechanism of potential PLT changes will be presented.**

**PLT Biology 101: Platelets and the Immune Continuum**
Joseph E. Italiano, PhD  
Director Cellular and Molecular Pathology  
Division of Hematology  
Brigham and Women’s Hospital

**Characterizing the Nature and the Mechanism of PLT Changes Observed in Monkeys Treated with 2’ MOE ASO**
Scott Henry, PhD, DABT  
Vice President Nonclinical Drug Development  
Ionis Pharmaceuticals Inc.

**Human PLT Database for 2’-MOE ASO and Recent Experience in FCS and TTR Phase 3 Trials**
Richard Geary, PhD  
Executive Vice President, Drug Development  
Ionis Pharmaceuticals Inc.

**Panel Discussion**

3:00-3:30PM Refreshment, Exhibits, and Networking Break
DAY ONE | WEDNESDAY, OCTOBER 25

3:30-5:00PM  
Session 4  
Concurrent Breakout Sessions

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| **Session Chair**  
Andrew Teasdale, PhD  
Chair A2 Impurities Advisory Group  
AstraZeneca, United Kingdom  

Members of the Oligonucleotide Safety Working Group (OSWG) met regularly over the past 12 months to discuss oligonucleotide impurities. This joint session for the CMC and nonclinical tracks will feature two presentations that attempt to summarize the output of these discussions. Chemistry and safety aspects of oligonucleotide impurities will be presented. The presentations will be followed by a 30 minute panel discussion. Questions for discussion may include:

- What types of oligonucleotide impurities are commonly observed?
- What are appropriate characterization expectations for oligonucleotide impurities?
- What are appropriate reporting, identification, and qualification thresholds for oligonucleotide therapeutics?
- How should oligonucleotide impurities be qualified?
- Can platform data be used to help characterize and qualify oligonucleotide impurities?

**Chemistry Considerations for Oligonucleotide Impurities**
Daniel Capaldi, PhD  
Vice President, Analytical and Process Development  
Ionis Pharmaceuticals, Inc.

**Safety Considerations for Oligonucleotide Impurities**
Scott Henry, PhD, DABT  
Vice President, Nonclinical Development  
Ionis Pharmaceuticals, Inc.

**Panel Discussion**
Joining the speakers
James Wild, PhD  
Pharmacologist  
CDER, FDA
Cathaline Den Besten  
Senior Director, Head Toxicology, ADME, PK  
ProQR Therapeutics, The Netherlands

| Session Co-Chairs  
Saraswathy V. Nochur, PhD, MSc  
Senior Vice President, Regulatory Affairs and QA  
Alnylam Pharmaceuticals, Inc.  
Lois M. Freed, PhD  
Supervisory Pharmacologist  
CDER, FDA  

Several oligonucleotide-based therapeutic candidates have been evaluated in the clinic for the treatment of neuromuscular diseases, including two for rare diseases. This session will explore the development of three different molecules, one about to enter the clinic, another getting ready for NDA, and a third that has been approved by FDA and EMA. While each of the disease states for these agents are distinct, there are similarities in the clinical development strategies and the challenges faced. Clinical data will be shared.

**Development and Approval of Nusinersen for Spinal Muscular Atrophy: Challenges and Successful Strategies**
Wildon R. Farwell, MD, MPH  
Senior Director, Clinical Development  
Biogen

**Hereditary ATTR Amyloidosis: Long-Term Clinical Experience with Patisiran, an Investigational RNAi Therapeutic, in an Open Label Study**
John L. Berk, MD  
Associate Professor of Medicine, Boston University School of Medicine; Assistant Director, Boston University School of Medicine Amyloidosis Center  
Boston University

**Development of Ionis-MAPTRx, the First Tau-Lowering Antisense Oligonucleotide, in Patients with Mild AD**
Laurence Mignon, PhD  
Director, Clinical Development  
Ionis Pharmaceuticals, Inc.

**Panel Discussion**

5:00-6:00PM  
Poster Session and Networking Reception

SAVE THE DATE!  
DIA 2018  
Boston, MA | June 24-28  
DIAGlobal.org/DIA2018
DAY TWO | THURSDAY, OCTOBER 26

8:00AM-5:00PM Registration

8:00-9:00AM Continental Breakfast, Exhibits, and Networking

8:15-9:00AM Breakfast Plenary Session
Emergency Single Patient IND for Oligonucleotide Therapy of a Unique Individual Mutation: A Case Study in Batten’s Disease

Session Chair
Arthur M. Krieg, MD
President and CEO
Checkmate Pharmaceuticals

Tim W. Yu, MD, PhD
Division of Genetics and Genomics, Boston Children’s Hospital; Assistant Professor, Harvard Medical School; Associate Member, Broad Institute

9:00-9:05AM Welcome to Day Two
James Thompson, PhD
Head, CMC Project Management
Moderna Therapeutics

9:05-10:05AM Session 5
Keynote Addresses

Session Co-Chairs
James Wild, PhD
Pharmacologist
CDER, FDA

James Thompson, PhD
Head, CMC Project Management
Moderna Therapeutics

Keynote Speakers
Arthur M. Krieg, MD
President and CEO
Checkmate Pharmaceuticals

Philip J. Brooks, PhD
Program Director, Division of Clinical Innovation
National Center for Advancing Translational Sciences (NCATS), National Institutes of Health

10:05-10:30AM Refreshment, Exhibits, and Networking Break

10:30AM-12:00PM Session 6
Concurrent Breakout Sessions

TRACK A
Thinking Ahead: Oligonucleotide Drug-Device Combination Products

Session Chair
Mohan Sapru, MS, PhD
CMC Lead, Office of Pharmaceutical Quality
CDER, FDA

The session is aimed to broadly discuss oligonucleotide drug-device combination products, an emerging trend in oligonucleotide-based therapeutics, from industry and regulatory perspectives. Specifically, the presentations and panel discussion will focus on:

• Industry perspective concerning salient considerations and challenges of developing drug-device combination products for oligonucleotide therapeutics
• Design control, drug-device verification, and validation processes
• Promises and challenges in using drug/device combination approach for targeted oligonucleotide drug delivery
• Strategies for ensuring product quality, including uniformity of dose delivery, under conditions of use
• Regulatory perspective concerning human factors studies and related clinical study considerations in combination product design and development

Development Considerations for Oligonucleotide Combination Products
Bret Coldren, PhD
Director, Pharmaceutical Development
Ionis Pharmaceuticals

Human Factors Studies - Related Considerations in Combination Product Design and Development
Guynh Nhu Nguyen, MS
Associate Director for Human Factors, Division of Medication Error Prevention and Analysis (DMEPA)
CDER, FDA

Panel Discussion
Joining the speakers:
Ryan McGowan
Associate Director, Combination Products
AstraZeneca

TRACK B/C
What, Where, and How: Biomarkers Inform Disease Targets, Biodistribution, and Function of Oligonucleotide Therapeutics

Session Co-Chairs
Aimee L. Jackson, PhD
Senior Director of Research
miRagen Therapeutics, Inc.

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

This session will present preclinical and clinical data on the identification and validation of biomarkers for oligonucleotide therapeutics. Discussions will include methods to identify pharmacodynamic biomarkers, use of biomarkers to define PK/PD and dose-response relationships, the application of biomarkers to establish mechanistic proof-of-concept and guide dose optimization, and how biomarkers can inform disease status and patient enrichment.

Translating PD Biomarkers from Preclinical Studies to Clinical Trials: MRG-106, an Oligonucleotide Inhibitor of miR-155, Cooperatively Regulates Multiple Survival Pathways to Reduce Cellular Proliferation, and Survival in Cutaneous T-Cell Lymphoma
Aimee L. Jackson, PhD
Senior Director of Research
miRagen Therapeutics, Inc.

Translating PD Biomarkers from Preclinical Studies to Clinical Trials: MRG-201, an Oligonucleotide Mimic of miR-29, Inhibits Collagen Expression, and Reduces Fibroplasia in Cutaneous Wounds
Corrie L Gallant-Behm, PhD, MQARS
Research Scientist III
Miragen Therapeutics, Inc.

Use of Biomarkers in the Development of RNAi Therapeutics
William Querbes, PhD
Director, Research
Alnylam

Panel Discussion
DAY TWO | THURSDAY, OCTOBER 26

12:00-1:30PM Round Table Discussion Luncheon, Exhibits, and Networking

12:00-1:15PM Luncheon Presentation
Japanese Perspective on the Preclinical Safety Assessment of Oligonucleotide Therapeutics

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

Representatives from Japanese regulatory and industrial joint working teams, including EWG members for ICH S6(R1), have discussed over the past two years the preclinical safety assessment of oligonucleotide therapeutics in comparison with biopharmaceuticals and low molecular new chemical entities. Unique perspectives will be shared with time for Q&A.

Japanese Initiative to Develop a White Paper for Oligonucleotide Therapeutics
Yoko Hirabayashi, MD, PhD
Division Head, Cellular Molecular Toxicology Center, Biological Safety and Research
National Institute of Health Sciences (NIHS), Japan

Study Design and Species Selection to Detect On-Target and Off-Target Effects
Kazushige Maki, DVM, PhD
Senior Scientist, Toxicology
PMDA, Japan

Lessons Learned from Biopharmaceuticals
Takahiro Nakazawa, PhD
CSO
AnGes, Inc., Japan

1:30-3:00PM Session 7 Concurrent Breakout Sessions

TRACK A Recently Approved and Late-Stage Oligonucleotide Drugs

Session Chair
G. Susan Srivatsa, PhD
President
ElixinPharma

This session will cover recent experience with approved and late-stage oligonucleotide drugs. The first presentation will address the CMC challenges associated with the review and approval of Nusinersen, and the second will cover regulatory experience with late-stage development of an siRNA drug. There will be a panel discussion that may include representatives from the FDA and BfArM.

SPINRAZA (nusinersen) Approval: CMC Strategies and Lessons Learned
Firoz Antia, PhD
Director, Technical Development
Biogen

CMC Strategies for Late-Stage Development of siRNA Oligonucleotides
Vidhya Gopalakrishnan, PhD
Senior Vice President, Pharmaceutical Development
Quark Pharmaceuticals, Inc.

Panel Discussion
Joining the speakers:
Olen Stephens, PhD
Chemist
CDER, FDA

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

TRACK B/C Predicting Clinical Safety from Nonclinical Data: Case Studies

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

Barbara Wilcox, PhD
Pharmacologist, OMPT, OND, ODEI, DNP
CDER, FDA

The most fundamental goal of toxicity studies is to predict the safety of drugs in clinical trials. This session will focus on some case-studies of how nonclinical data are being used to avoid adverse effects in clinical trials and how nonclinical data can be used to understand safety signals from clinical trials. In addition, the session features a discussion of the Agency’s database of oligonucleotide therapeutics how the data are collected and being used.

Using Nonclinical Data to Interpret Clinical Safety Signals
John Vest, MD
Senior Director, Clinical Development
Alnylam Pharmaceuticals, Inc.

A Sensitive In Vitro Screening Approach to Assess the Hybridization-Dependent Toxic Potential of High Affinity Single Stranded Gapmer Oligonucleotides
Andreas Dieckmann, PhD
Senior Principal Scientist
F. Hoffmann-La Roche, Switzerland

Regulatory Application of a Nonclinical Database for Oligonucleotide Therapeutics at FDA
Xuan Chi, MD, PhD
Pharmacology/Toxicology Reviewer, Division of Cardiovascular and Renal Products, OND
CDER, FDA

Panel Discussion

3:00-3:30PM Refreshment, Exhibits, and Networking Break
CRISPR is a powerful new technology whose genome editing versatility is being harnessed to usher in a new class of potential genetic therapies. While offering the promise of “one and done” treatments, human genome-based therapies also pose unique challenges for drug development. This session will examine two examples of early stage CRISPR-based medicines being developed to treat rare genetic diseases of the liver using systemic lipid nanoparticles and of the eye using subretinal delivery of AAV5. Preclinical evaluation of proof of concept, delivery, and specificity will be presented. As the CRISPR field evolves, so do the regulatory considerations regarding patient safety and risk-benefit. FDA’s perspective and insights on preclinical data needed to support the transition of CRISPR-based medicines into the clinic will be discussed.

Robust In Vivo Gene Editing with Systemic Lipid Nanoparticle Delivery of CRISPR/Cas9 RNA Components
Amy Rhoden Smith, PhD
Principal Scientist
Intellia

Preclinical Development of AAV5 Encoding CRISPR/SaCas9 for the Treatment of Infantile Blindness Caused by Leber Congenital Amaurosis Type 10
Gerald F. Cox, MD, PhD
Chief Medical Officer
Editas Medicine, Inc.

Preclinical Considerations for Gene Therapy Products Involving Gene Editing Technology: An FDA Perspective
Ying Huang, PhD
Pharmacologist, Office of Tissues and Advanced Therapies
CBER, FDA

DIA Oligonucleotide Safety Working Group (OSWG) – Open Meeting
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 newest hot topics.

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DAY THREE | FRIDAY, OCTOBER 27

7:00AM-12:00PM
Registration

7:00-8:00AM
Continental Breakfast and Networking

8:00-9:30AM
Session 9
Concurrent Breakout Sessions

### TRACK A
Interactive Discussion of CMC Challenges and Moving Forward

**Session Chair**
Kim Tyndall  
Director of CMC Regulatory Affairs  
GlaxoSmithKline

During this session you will have the opportunity to interact with panelists to discuss current and future concerns in the development of oligonucleotide programs. This open discussion will focus on a set of questions and topics that have been predetermined prior to the conference and will include examples from case-studies as well as complications faced by regulators.

**Panelists**
- Ramesh Raghavachari, PhD  
  Chief, Branch I, DPMAT, OLDP, OPQ  
  CDER, FDA
- Ashley Boam, PhD  
  General Health Scientist  
  CDER, FDA
- René Thürmer, PhD  
  Deputy Head of the Unit Pharmaceutical Biotechnology  
  BfArM - Federal Institute for Drugs and Medical Devices, Germany

**Session Co-Chairs**
- Patrik Andersson, PhD, ERT  
  Principal Scientist, Discovery Safety Specialist  
  AstraZeneca R&D, Sweden
- Sree Rayavarapu, PhD  
  Toxicologist  
  FDA

This joint preclinical/clinical session will present novel translational insights of GalNAc-conjugated ASOs as well as novel targeting strategies for increasing productive uptake into cell types that normally are challenging to reach with oligonucleotide therapeutics. These include muscle and immune cells as well as pancreatic islets. The presentations will be followed by a 30 minute panel discussion.

Discussion topics include:
- Main utilities and obstacles of targeted delivery of oligos
- Specific regulatory considerations to targeting approaches

**Translational Development of a GalNAC-Conjugated LNA-Based Single Stranded Oligonucleotide**
Wouter Driessen, PhD, MS  
DMPK Project Leader  
F. Hoffmann-La Roche AG, Switzerland

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

**Targeting Antisense Oligonucleotides to Pancreatic Islets**
Patrik Andersson, PhD, ERT  
Principal Scientist, Discovery Safety Specialist  
AstraZeneca R&D, Sweden

**Panel Discussion**

9:30-9:45AM
Refreshments and Networking Break

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### DAY THREE | FRIDAY, OCTOBER 27

#### 9:45-11:15AM

**Session 10**  
Hot Topics in Oligonucleotide Therapeutics

**Session Co-Chairs**

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

Shwu-Luan Lee, PhD  
Pharmacologist, OHOP, DHOT  
CDER, FDA

As we learn more about RNA biology, its importance in the regulation of gene expression, and its role in disease processes, it is becoming clear there are many more ways to use oligonucleotides as therapeutic agents. With the identification of novel exploitable mechanism of RNA modulation, the range of diseases that can be targeted increases. This session will explore multiple novel ways to modulate RNA biology that may ultimately be used as a way to address disease processes and become the foundation for new therapeutic agents.

**Antisense-Mediated Control of RNA Splicing to Treat Monogenic Diseases**

Huw M. Nash, PhD  
Chief Executive Officer  
Stoke Therapeutics, Inc.

**A to I Editing and Neuronal Plasticity**

Joshua Rosenthal, PhD  
Senior Scientist  
The Marine Biological Laboratory, University of Chicago

**A Site-Directed RNA Editing Strategy to Correct Genetic Mutations**

Maria Montiel-Gonzalez, PhD  
Post Doctoral Fellow  
The Marine Biological Laboratory, University of Chicago

**Stereodefined LNA Phosphorothioates: A New Perspective in RNA Therapeutics**

Troels Koch, PhD, MSc  
Vice President, Head of Research, RNA Therapeutics  
Roche Innovation Center Copenhagen, Denmark

#### 11:15AM-12:00PM

**Closing Session**  
Panel Discussion

**Session Co-Chairs**

James Thompson, PhD  
Head, CMC Project Management  
Moderna Therapeutics

James Wild, PhD  
Pharmacologist  
CDER, FDA

This panel discussion is meant to highlight the challenges and issues with the development of oligonucleotide-based products in general, and as brought forth at this conference. The intention is to transform this discussion into action-oriented objectives to address the regulatory and industry issues and challenges affecting us all.

**Panelists**

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

Jeffery A. Engelhardt, DVM, PhD, DACVP, FIATP  
Vice President, Pathology and Nonclinical Drug Safety  
Ionis Pharmaceuticals, Inc.

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

Arthur M. Krieg, MD  
President and CEO  
Checkmate Pharmaceuticals

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

Kim Tyndall  
Director of CMC Regulatory Affairs  
GlaxoSmithKline

#### 12:00PM

**Conference Adjourned**