DIA/FDA Oligonucleotide-Based Therapeutic Conference 2015

September 9–11, 2015

Grand Hyatt Washington at Washington Center
Washington, DC

As of September 2, 2015

PROGRAM CO-CHAIRS:

Robert T. Dorsam, PhD
Pharmacology and Toxicology Team Leader
OGD, CDER, FDA

Jim Zisek, BS, MBA
Director
Global CMC Regulatory Affairs
GlaxoSmithKline

PROGRAM COMMITTEE:

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

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

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

Aimee L. Jackson, PhD
Director of Target Development
miRagen Therapeutics

Arthur M. Krieg, MD
President and CEO
Checkmate Pharmaceuticals

Art A. Levin, PhD
Executive VP Research and Development
Avidity NanoMedicines

Jennifer Marlowe, PhD
Group Head
Biochemical, Molecular and Cellular Toxicology
Novartis Institutes for Biomedical Research, Inc.

Saraswathy V. Nochur, PhD, MSc
Senior Vice President
Regulatory Affairs & QA
Alnylam Pharmaceuticals, Inc.

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

Rosanne Seguin, PhD
McGill University
Canada

James D. Thompson, PhD
Head of CMC
Moderna Therapeutics

James Wild, PhD
Pharmacologist
CDER, FDA

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OVERVIEW:

DIA and FDA have once again gathered renowned investigators and key health authorities to discuss the latest developments in oligonucleotide-based therapeutics. The 2015 conference will address a variety of topics on CMC, nonclinical, clinical pharmacology, clinical, and regulatory aspects of antisense, siRNA, and microRNA therapies. The format for this conference has been reconfigured and features:

- General sessions consisting of state-of-the-art presentations, panel discussions, and abstracts, highlighting the most up-to-date in oligonucleotide-based therapeutic research;
- Concurrent sessions with three educational tracks designed to promote discussion between industry and the regulators;
- An enhanced poster presentation session spanning a multitude of topics—available for viewing throughout the conference

FEATURED TOPICS:

- The RNA Revolution and its Translation to Medicine
- Rare Diseases
- Injection Site Reactions
- Impurities

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
- Discuss industry and regulatory agency efforts to partner and address the unmet medical needs of patients

This program has been developed in collaboration with the FDA.

DIA DEVELOP INNOVATE ADVANCE
800 Enterprise Road
Suite 200
Horsham, PA 19044 USA

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- Clinical Research Certificate Program: 10 Elective Units

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DIA 2016

52ND Annual Meeting

PHILADELPHIA, PA

JUNE 26-30, 2016

CALL FOR GENERAL ABSTRACTS NOW OPEN

Submission Deadline: Tuesday, October 6

*Visit **DIAglobal.org/DIA2016** for more information.*

WEDNESDAY, SEPTEMBER 9

7:00AM–5:00PM **REGISTRATION**

7:00–8:00AM **CONTINENTAL BREAKFAST**

8:00–8:30AM **WELCOME REMARKS AND OVERVIEW OF THE 2015 CONFERENCE**

Patricia Gibson
Chief Communications Officer
DIA

Robert T. Dorsam, PhD
Pharmacology and Toxicology
Team Leader
CDER
FDA

Jim Zisek, BS, MBA
Director
Global CMC Regulatory Affairs
GlaxoSmithKline

8:30–9:30AM **KEYNOTE ADDRESS: THE RNA REVOLUTION AND ITS TRANSLATION TO MEDICINE**

Phillip A. Sharp, PhD
Institute Professor
Koch Institute for Integrative Cancer Research
Massachusetts Institute of Technology

RNA based therapeutics and antisense technology promise a new means to treat many gene specific diseases. Therapeutic agents designed around RNA Interference that in somatic cells utilize the microRNA pathway to target mRNAs are advancing through clinical trials. Other RNA designed agents augment or suppress microRNA activity directly. More recently, direct delivery of mRNA is being developed in a variety of clinical settings. New opportunities for RNA based therapies also arise because of recent discoveries concerning long-noncoding RNAs and well as the CRISPR technology. The challenge of delivery of RNA type agents to cellular processes is common of all of these emerging therapies.

9:30–10:00AM **REFRESHMENT BREAK AND NETWORKING**

10:00–11:30AM SESSION 1: CONCURRENT TRACK BREAKOUT SESSIONS

TRACK 1 – CMC

CMC Opportunities and Challenges in Asia

SESSION CHAIR:

Helen Wood, MChem, MSc, CChem, MRSC
Scientific Investigator
GlaxoSmithKline

The goal of this session is to discuss CMC opportunities and challenges in Asia. The first presenter will discuss regulatory considerations for oligonucleotide-based drugs in Japan from the perspective of the PMDA. The focus of the second presentation is regulatory considerations for therapeutics in China. The session concludes with a panel discussion; potential discussion topics include:

- JP compliance
- Analytical method validation and system suitability requirements
- Foreign manufacturers accreditation, memorandum of understanding and in-country testing requirements

Discussion on Regulatory Consideration of Oligonucleotide-Based Drugs in Japan

Kosuke Ito, PhD
Specially Appointed Assistant Professor
Drug Innovation Center
Graduate School of Pharmaceutical Sciences
Osaka University
Japan

CASE STUDY: IND filing to CFDA for Cotsiranib® (STP705), a New Anti-fibrosis siRNA Therapeutic Product

Marc M. Lemaitre, PhD
Chief Operating Officer
Sirnaomics, Inc

Manufacturing Therapeutic Oligonucleotides in China: Particularities and Current Status

Dmitry Samarsky, PhD
Senior Vice President
International Business & Technology
RiboBio
China

Q&A Panel Discussion

JOINING THE SPEAKERS:

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

TRACK 2 – NONCLINICAL

siRNA Conjugates

SESSION CO-CHAIRS:

Michael Placke, PhD
Senior Vice President
Drug Safety & Metabolism
Alnylam Pharmaceuticals, Inc.

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

The focus of this session is primarily GalNac siRNA conjugates and associated PK/PD issues to include plasma, liver, and tissue distribution, metabolites, and persistence. The nonclinical toxicology for seven different GalNac siRNA conjugates will be presented as well as data for an antisense conjugate.

Drug Metabolism and Pharmacokinetic (DMPK) Properties of siRNA-GalNAc Conjugates

Anshul Gupta, MS, DVM
Lead Scientist
Drug Safety & Metabolism
Alnylam Pharmaceuticals

Toxicity, Pathology and Safety Profiles of siRNA GalNAc Conjugates

Natalie Keirstead, DVM, PhD, DABT, DACVP
Director of Pathology
Drug Safety & Metabolism
Alnylam Pharmaceuticals

Targeted Delivery of 2'-MOE ASO to Hepatocytes Using GalNAc Conjugates: Impact on Potency, Therapeutic Index, and Pharmacokinetics

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

Locked Nucleic Acid: Enabling RNA Therapeutics

Mads Aaboe Jensen, MSc, PhD
Principal Scientist
Roche Pharma Research and Early Development
RNA Therapeutics Research
Roche Innovation Center Copenhagen A/S

Q&A Panel Discussion

TRACK 3 – CLINICAL

Neuromuscular

SESSION CHAIR:

Akshay Vaishnaw, MD, PhD, FRCP
Chief Medical Officer
Alnylam Pharmaceuticals, Inc.

The objectives of this session are to highlight recent progress utilizing RNAi and ASO approaches to address high unmet need disorders of the nervous system. The clinical focus will be on two programs in Phase 3, comprising ALN-TTR, a systemically delivered RNAi therapeutic for TTR amyloidosis, a disorder of peripheral nerves, and ISIS-SMNRx, an intrathecally administered ASO for spinal muscular atrophy, a pediatric motor neuron disorder. A third presentation will focus on another neurodegenerative disorder, Huntington's disease, examining recent preclinical progress where again an intrathecally administered ASO is being developed.

Antisense Oligonucleotides Drugs For the Treatment of Neurodegenerative Diseases

Laurence Mignon, PhD
Director, Clinical Development
Isis Pharmaceuticals, Inc.

Antisense Oligonucleotide Therapies for the Treatment of Huntington's Disease

Holly Kordasiewicz, PhD
Director
Neuroscience Drug Discovery
Isis Pharmaceuticals, Inc.

Update on ALN-TTR Programs for the Treatment of Transthyretin Amyloidosis

Jared Gollob, MD
Vice President
Clinical Research
Alnylam Pharmaceuticals, Inc

Q&A Panel Discussion

11:30AM–1:00PM **LUNCH AND NETWORKING**

1:00–2:30PM **SESSION 2: CONCURRENT TRACK BREAKOUT SESSIONS**

TRACK 1 – CMC

Emerging Trends

SESSION CHAIR:

Steve Sofen, PhD
CMC Team Director
Biogen Idec

This session will focus on the emerging field of mRNA therapeutics and feature two presentations followed by a panel discussion. The presenters will discuss CMC challenges associated with the manufacture of long coding RNAs. Potential topics for discussion include:

- Purity requirements for long RNA
- RNA stability

cGMP Manufacturing of mRNA Products: Considerations and Challenges

Gary Lee, PhD
Research Scientist
Sangamo BioSciences, Inc.

Manufacturing of Long, Coding RNAs

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

Q&A Panel Discussion

JOINING THE SPEAKERS:

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

James D. Thompson, PhD
Head of CMC
Moderna Therapeutics

TRACK 2 – NONCLINICAL

miRNA

SESSION CO-CHAIRS:

Aimee L. Jackson, PhD
Director of Target Development
miRagen Therapeutics

Renqin Duan, PhD
Toxicologist
CDER
FDA

During this session the focus will be on major challenges associated with development of microRNA-based therapeutics, demonstration of PK/PD relationships, and validation of translational biomarkers to optimize clinical dosing. Nonclinical and clinical data addressing these challenges will be presented.

Development of microRNA-based Therapeutics

Aimee L. Jackson, PhD
Director of Target Development
miRagen Therapeutics

Controversies with miRNA Development

John S. Grundy, PhD
Vice President
DMPK & Toxicology
Regulus Therapeutics

Delivery Challenges Facing Small and Large Nucleic Acid-based Therapeutics

Christopher Cheng, MPhil, PhD
Development Scientist II
Nucleric Acid Drug Formulations
Alexion Pharmaceuticals

Q&A Panel Discussion

TRACK 3 – CLINICAL

Cardio/Metabolic

SESSION CHAIR:

Sotirios Tsimikas, MD
Cardiovascular Franchise Leader
Vice President of Clinical Development
Isis Pharmaceuticals, Inc.

This session will review early to late stage clinical development for two oligonucleotide technologies, aptamers and antisense therapeutics, being developed in the cardiovascular and metabolic therapeutic areas. The targets and applications range from Factor IXa antagonism in the coagulation pathway using an aptamer technology to antisense and antisense GalNAc conjugates to knockdown several independent lipid cardiovascular risk factors.

Phase 3 Evaluation of Revolixys Kit: Study Summary and Lessons Learned

Chris Rusconi, PhD
Chief Scientific Officer
Senior Vice President
Discovery/Preclinical Development
Regado BioSciences, Inc.

Antisense Therapies for Unmet Clinical Needs in Lipid Disorders: ApoC-III, Lp(a) and ANGPTL3

Sotirios Tsimikas, MD
Cardiovascular Franchise Leader
Vice President of Clinical Development
Isis Pharmaceuticals, Inc.

Interim Results of a Phase 1 Study of ALN-PCSsc, an RNAi Therapeutic for the Treatment of Elevated LDL Cholesterol

Pushkal Garg, MD
Senior Vice President
Clinical Development
Alnylam Pharmaceuticals, Inc.

Q&A Panel Discussion

2:30–3:00PM **REFRESHMENT BREAK AND NETWORKING**

3:00–4:30PM **SESSION 3: CONCURRENT TRACK BREAKOUT SESSIONS**

TRACK 1 – CMC

Analytical Method Validation

SESSION CHAIR:

Kate Arnot, MSc
CMC Director
Global Regulator Affairs, Patient Safety & QA
AstraZeneca
United Kingdom

This session will highlight analytical method validation. The first presenter will discuss analytical method validation from the FDA perspective, with reference to recently published FDA guidance. The second presenter will discuss some of the challenges associated with developing and validating analytical methods for oligonucleotide-based therapeutics. The presentations will be followed by a 30-minute panel discussion. Discussion topics may include:

- Platform approaches to analytical method validation
- Validation of identity, assay and impurity tests with regard to specificity System suitability requirements
- Challenges associated with using orthogonal purity methods

New FDA Guideline on Analytical Method Validation

Lucinda Buhse, PhD
Office Director (Acting), Office of Testing and Research, OPQ, CDER
FDA

Validation of Analytical Methods for Oligonucleotide Therapeutics

Claus Rentel, PhD
Executive Director
Analytical Development and Quality Control
Isis Pharmaceuticals, Inc.

Q&A Panel Discussion

JOINING THE PANEL:

Susan Srivatsa, PhD
President
Elixin Pharma

Matthias Kretschmer, PhD
Director
Analytical Sciences
Alnylam Pharmaceticals

TRACK 2 – NONCLINICAL

mRNA Therapeutics

SESSION CO-CHAIRS:

Jennifer Marlowe, PhD
Group Head
Biochemical, Molecular and Cellular Toxicology
Novartis Institutes for Biomedical Research, Inc.

Sree Rayavarapu, DVM, PhD
Toxicologist
CDER
FDA

A new therapeutic modality, mRNA therapeutics, is the topic for this session. Representatives from three different companies will present nonclinical data associated with their new mRNA therapeutic candidates including a self-replicating mRNA vaccine.

Translation of Messenger RNA Therapeutics from Pre-clinical Research into Clinical Studies

Pad Chivukula, PhD
Chief Scientific Officer and Chief Operating Officer
Arcturus Therapeutics

Lipid Nanoparticle-based mRNA Therapeutics

Ying Tam, PhD
Director of Preclinical Studies
Acuitas Therapeutics

Self-amplifying mRNA Vaccines

Andrew Geall, PhD
Vice President
Chemistry and Formulations
Avidity NanoMedicines

Q&A Panel Discussion

TRACK 3 – CLINICAL

Antiviral

SESSION CHAIR:

Art Levin, PhD
Executive Vice President
Research and Development
Avidity NanoMedicines

The first application of an oligonucleotide agent in 1978 was to inhibit viral replication (Zamecnik, and Stephens, 1978 PNAS) and the first approved oligonucleotide drug. Fomivirsen was an antiviral. Presently, there are multiple oligonucleotide therapeutics in clinical trials including siRNA, miRNA, and antisense modalities. In this session several new approaches to antiviral activities will be presented. A novel Nucleic Acid Polymer system for the treatment of HBV will be discussed. An siRNA approach that uses a lipid nanoparticle to deliver multiple siRNAs and a conjugated anti-miR will also be presented. Each brings to the meeting a unique prospective for the development of oligonucleotide therapeutics.

Clinical Experience with Nucleic Acid Polymers in the Treatment of Chronic HBV and HBV / HDV Co-infection

Andrew Vaillant, PhD
Chief Scientific Officer and Vice President, Operations
REPLICor Inc.
Canada

TKM-HBV, a Lipid Nanoparticle RNA Interference Treatment for Chronic Hepatitis B

Amy Lee
Research Director
Tekmira Pharmaceutical Corporation
Canada

miR-122 – Potential as a Therapeutic Target for Treating Chronic Hepatitis c Infection

Paul Grint, MD
Chief Medical Officer
Regulus Therapeutics

Q&A Panel Discussion

4:30–5:30PM **POSTER SESSION AND NETWORKING RECEPTION**

THURSDAY, SEPTEMBER 10

7:00AM–5:00PM **REGISTRATION**

7:00–8:00AM **CONTINENTAL BREAKFAST**

8:00–8:30AM WELCOME TO DAY 2 AND TRACK REPORT OUTS

Welcome Remarks

Robert T. Dorsam, PhD
Pharmacology and Toxicology Team Leader
CDER
FDA

CMC Track Report Out

Kate Arnot, MSc
CMC Director, Global Regulator Affairs, Patient Safety & QA
AstraZeneca
United Kingdom

Nonclinical Track Report Out

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

Clinical Track Report Out

Speaker Invited

8:30–10:10AM SESSION 4: RARE DISEASES

SESSION CHAIR:

Susan Sobolov, PhD
Executive Director
mRNA portfolio leader
Alexion Pharmaceuticals

As a genetic technology, oligonucleotides can be specifically designed to modulate gene expression through multiple mechanisms and have a beneficial impact genetically defined rare diseases. The first speaker will provide an overview of RNA approaches to rare diseases and the expanding opportunity. The second speaker will discuss the FDA's perspective on oligonucleotide-based therapeutics in rare disease. The next two speakers will focus on two clinical candidates in development for rare diseases. The first will present on ISIS- DMPK 2.5Rx an antisense oligonucleotide in Phase I/II for the treatment of myotonic dystrophy, and the last will discuss the Phase I results of ALN-AT3, an RNAi therapeutic for the treatment of hemophilia.

An Overview of Oligonucleotide in Rare Diseases

Susan Sobolov, PhD
Executive Director
mRNA portfolio leader
Alexion Pharmaceuticals

FDA's Perspective on Oligonucleotide-based Therapeutics in Rare Diseases

Richard Moscicki, MD
Deputy Center Director for Science Operations
OCD, CDER
FDA

DM1 in Myotonic Dystrophy

Laurence Mignon, PhD
Director, Clinical Development
Isis Pharmaceuticals, Inc.

A Subcutaneously Administered Investigational RNAi Therapeutic (ALN-AT3) Targeting Antithrombin for Treatment of Hemophilia: Phase 1 Study Results

Benny Sorensen, MD, PhD
Senior Director
Clinical Development
Alnylam Pharmaceuticals

Q&A Panel Discussion

10:10–10:30AM **REFRESHMENT BREAK AND NETWORKING**

10:30AM–12:00PM SESSION 5: CONCURRENT TRACK BREAKOUT SESSIONS

TRACK 1 – CMC

Conjugates

SESSION CHAIR:

Mohan K. Sapru, PhD
CMC Lead
Office of Pharmaceutical Quality
CDER
FDA

This session will feature two presentations on the manufacture and analysis of oligonucleotide conjugates, followed by a panel discussion. The first presentation will focus on pegylated Spiegelmers, while the second speaker will discuss GalNAc-conjugated double-stranded RNAi molecules. Discussion topics may include:

- Definitions of starting materials
- Characterization expectations
- Pro-drug considerations

Characterization and Control Strategy for Pegylated Aptamers

Stefan Vonhoff, PhD
Vice President Chemistry Manufactuting and Controls
NOXXON Pharma AG
Germany

GalNac siRNA

Matthias Kretschmer, PhD
Director
Analytical Sciences
Alnylam Pharmaceuticals, Inc.

Q&A Panel Discussion

JOINING THE SPEAKERS:

Fran Wincott, PhD
President
Wincott & Associates LLC

TRACK 2 – NONCLINICAL & CLINICAL COMBINATION

Injection Site Reactions

SESSION CO-CHAIRS:

Koos Burggraaf, MD, PhD
Research Director CVS & Metabolism
Centre For Human Drug Research
Netherlands

L. Peyton Myers, PhD
Senior Pharmacology & Toxicology Reviewer
Division of Antiviral Products
FDA

Injection Site Reactions After Subcutaneous Oligonucleotide Therapy in Humans

Koos Burggraaf, MD, PhD
Research Director CVS & Metabolism
Centre For Human Drug Research
Netherlands

Characterization and Mechanistic Investigation of Non-CpG MOE ASO-Mediated Injection Site Inflammation Across Species

Sebastien Burel, PhD
Associate Director
Isis Pharmaceuticals, Inc.

Evolution of a Platform: Clinical Experience Improving Pro-inflammatory Characteristics of Second Generation 2'-MOE Antisense Oligonucleotides

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

Q&A Panel Discussion

12:00–1:30PM LUNCH AND NETWORKING

1:30–3:00PM **SESSION 6: CONCURRENT TRACK BREAKOUT SESSIONS**

TRACK 1 – CMC AND NONCLINICAL COMBINATION

Impurities

SESSION CHAIR:

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

This joint session for the CMC and nonclinical tracks will focus on impurities in oligonucleotide and RNA-based therapeutics. The first presenter will discuss recently published guidelines on genotoxic impurities (ICH M7) and elemental impurities (ICH Q3D). The second presentation will be given by CMC and nonclinical representatives and aims to discuss oligonucleotide impurities. The presentations will be followed by a 30-minute panel discussion. Questions for discussion may include:

- Does ICH M7 apply to oligonucleotides?
- What are appropriate identification and qualification thresholds for oligonucleotide impurities?
- Impurities vs related substances: Is there a difference?

M7 and Q3D

Andrew Teasdale, PhD
Chair AZ Impurities Advisory Group
AstraZeneca
United Kingdom

Qualification of Oligonucleotide Impurities

Brigitte Burm, PhD
Manager Analytical Development
BioMarin Nederland BV
Netherlands

Cathaline den Besten, PhD, PMP
Director of Toxicology
BioMarin Nederland BV
Netherlands

Q&A Panel Discussion

JOINING THE SPEAKERS:

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

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

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

TRACK 2 – CLINICAL

Oncology and Pulmonary

SESSION CHAIR:

Art Krieg, MD
President and CEO
Checkmate Pharmaceuticals

This session will present systemic oligonucleotide-based approaches to the treatment of cancer and inhaled delivery of oligonucleotides for asthma immunotherapy. The mechanisms to be discussed will include antisense and immune modulation, including both activation and inhibition of Toll-like receptor 9.

Synthetic Oligonucleotide-based Antagonist of Endosomal TLRs: Preclinical and Clinical Proof-of-Concept

Sudhir Agrawal, PhD
President of Research
Idera Pharmaceuticals

Dynavax/AZ Experience: Inhaled Oligos for Asthma

Sam Jackson, MD, MBA
Executive Director
Clinical Development & Drug Safety
Dynavax Technologies

Preclinical and Clinical Studies with STAT3 ASOs

Paul Lyne, PhD
Executive Director
Senior Project Leader Oncology
AstraZeneca

Q&A Panel Discussion

3:00–3:30PM **REFRESHMENT BREAK AND NETWORKING**

3:30–5:00PM SESSION 7: INTERACTIVE DISCUSSION OF CLINICAL, NONCLINICAL, AND CMC ISSUES AND LEARNINGS

SESSION CHAIR:

Kim M. Tyndall
Director
CMC Regulatory Affairs
GlaxoSmithKline

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

PANELISTS:

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

Michael Hodges, MD
Independent Consultant
Arcturus Therapeutics

Art Levin, PhD
Executive Vice President Research and Development
Avidity NanoMedicines

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

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

Paul F. Agris, PhD
Professor of Biological Sciences and Chemistry, Director
The RNA Institute – University of Albany-SUNY

FRIDAY, SEPTEMBER 11

7:00AM–5:00PM REGISTRATION

7:00–8:00AM CONTINENTAL BREAKFAST

8:00–8:30AM WELCOME TO DAY 3 AND TRACK REPORT OUTS

Jim Zisek, BS, MBA
Director
Global CMC Regulatory Affairs
GlaxoSmithKline

CMC Track Report Out

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

Nonclinical Track Report Out

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

Clinical Track Report Out

Art Krieg, MD
President and CEO
Checkmate Pharmaceuticals

8:30–9:30AM SESSION 8: HOT TOPICS

SESSION CHAIRS:

Art Levin, PhD
Executive Vice President Research and Development
Avidity NanoMedicines

Emily J. Place, PhD, MPH
Pharmacologist
OND, OHOP, DHOT
CDER
FDA

There are numerous ways the oligonucleotides have been used for the treatment of disease. The most prominent ones have worked via RNAase H, splice switching, siRNA, apatmer, and immuinomodulaor mechanisms. There are many more potential ways to apply oligonucleotides as therapeutic agents. This session will explore two additional mechanisms, U1 Adaptor Oligonucleotides, and the CRISPR cas. The evolution of novel technologies will undoubtedly influence the field moving forward.

Development of U1 Adaptor Gene Silencing Oligonucleotide Therapeutics

Samuel Gunderson
Associate Professor
Rutgers University

CRISPR Therapeutics

Alexandra Glucksmann, PhD
Chief Operating Officer
Editas Medicine

Q&A Panel Discussion

9:30–9:45AM REFRESHMENT BREAK AND NETWORKING

9:45–10:45AM SESSION 9: CONCURRENT TRACK BREAKOUT SESSIONS

TRACK 1 – CMC

Reference Materials and Measurements for Nucleic Acid-based Therapeutics

SESSION CHAIR:

Jim Zisek, BS, MBA
Director
Global CMC Regulatory Affairs
GlaxoSmithKline

This session will feature presenters from the National Institute of Standards and Technology (NIST) and The RNA Institute. Session topics will include a discussion of how measurement science and standards support development of biosimilars and new therapeutics. Examples of research areas and projects, including protein particle measurements, development of a mAb reference material and NMR fingerprint-like characterization of protein therapeutics will be presented. The session will conclude with a panel discussion to determine how NIST and The RNA Institute might contribute in developing methods, tools and analytics for oligonucleotide and RNA-based therapeutics.

Measurements and Standards for Biotherapeutic Drugs: Proteins are the Present. Are Nucleic Acids the Future?

Andrea L. Szakal, PhD
Research Chemist
National Institute of Standards and Technology

Power and Promise of Oligonucleotide Therapeutics: Need for Standards, Measurements and Tools in CMC

Paul F. Agris, PhD
Director
Professor of Biological Sciences and Chemistry
The RNA Institute – University of Albany-SUNY

Q&A Panel Discussion

JOINING THE SPEAKERS:

Claus Rentel, PhD
Executive Director
Analytical Development and Quality Control
Isis Pharmaceuticals, Inc.

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

Peter Vallone, PhD
Leader, Applied Genetics Group
National Institute of Standards and Technology

TRACK 2 – NONCLINICAL & CLINICAL COMBINATION

Thrombocytopenia – OSWG

SESSION CO-CHAIRS:

Scott Henry, PhD
Vice President, Nonclinical Development
Isis Pharmaceuticals, Inc.

Robert T. Dorsam, PhD
Pharmacology and Toxicology Team Leader
CDER
FDA

Progress in Understanding the Mechanism of ASO-Mediated Platelet Decrease in Non-human Primates

Padma Kumar Narayanan, PhD
Executive Director, Toxicology
Isis Pharmaceuticals, Inc.

OSWG Update

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

10:45AM–12:00PM **CLOSING SESSION: CONFERENCE HIGHLIGHTS AND PANEL DISCUSSION**

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:

Saraswathy V. Nochur, PhD, MSc
Senior Vice President
Regulatory Affairs & QA
Alnylam Pharmaceuticals, Inc.

James D. Thompson, PhD
Head of CMC
Moderna Therapeutics

Art Levin, PhD
Executive Vice President Research and Development
Avidity NanoMedicines

Scott Henry, PhD, DABT
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