Co-sponsored by DIA, FDA, Health Canada, and Oligonucleotide Therapeutics Society

Industry and Health Authority Conference on: Oligonucleotide-based Therapeutics

April 19-20, 2007 | DoubleTree Hotel and Executive Meeting Center Bethesda, Bethesda, MD, USA

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Vice President
Regulatory Affairs and
Global Quality Assurance
Coley Pharmaceutical Group, Inc.

KEYNOTE SPEAKER

JOHN J. ROSSI, PhD
Chair and Professor
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Beckman Research Institute of the City of Hope

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RENÉ THÜRMER, PhD
Pharmaceutical Expert, Unit Pharmaceutical Biotechnology, BfArM – Federal Institute for Drugs and Medical Devices, Germany (Regulatory Agency)

GUIDO WUERTH
Clinical Development and Regulatory Affairs Manager
Antisense Pharma GmbH

FEATURED EVENT

This conference will establish dialogue and discussion among Industry and Health Authorities to inform, teach, and share product development and regulatory information in the areas of nonclinical, chemistry, manufacturing and control (CMC) and clinical development of oligonucleotide-based therapeutic drugs, including antisense, RNAi, immunostimulatory and aptamer applications.

ABOUT THE KEYNOTE SPEAKER

John J. Rossi, PhD
Beckman Research Institute of the City of Hope, Duarte, CA.

Dr. Rossi is Professor and Chair of the Division of Molecular Biology, Beckman Research Institute of the City of Hope, and Dean, Graduate School of Biological Sciences, Beckman Research Institute of the City of Hope. Dr. Rossi received his doctoral training in genetics under Dr. Claire Berg at the University of Connecticut in Storrs and postdoctoral training in molecular genetics under Dr. Arthur Landy at Brown University. In the 1980s and 1990s his research focused on the mechanism of action and clinical applications of catalytic RNAs, or ribozymes. His group was the first to demonstrate that hammerhead ribozymes could be used for inhibition of HIV replication. This research program led to two clinical trials in which ribozyme genes have been transduced into hematopoietic stem cells for autologous transplant in HIV infected individuals. He is the recipient of an NIH Merit award for his work on ribozymes and HIV. Work in the laboratory continues to focus upon RNA based therapeutics, with recent emphasis on function and applications of expressed short hairpin RNAs for therapeutic treatment of HIV and cancers. This research has led to a planned clinical trial for RNAi based therapy of HIV infection in a gene therapy setting. He has published over 200 peer reviewed articles and numerous reviews and commentaries on RNAi based therapeutics.

FEATURED SESSIONS

- Mechanisms of Action and Therapeutic Potential
- General Issues in Safety Assessment
- Analytical Characterization for ODN Therapeutics
- Clinical and Regulatory Challenges of Antisense and Antisense-like Technologies in Clinical Oncology
- Specific Issues in the Safety Assessment of Olignonucleotide-based Therapeutics
- Oligonucleotides for Infectious Diseases: Issues and Opportunities
- Challenges in Process Development for Oligonucleotide Synthesis
- General Issues In the ADME Properties of Oligonucleotide Drugs
- Novel Delivery Systems
- Advances and Issues in the Development of Oligonucleotides for The Therapy of Lung Diseases
- CMC Regulatory Considerations
- Oligoncucleotides – Emerging Therapies in Treatment of Retinal Diseases
- Specific Issues in ADME
- Use of ODN TLR9 Agonists as Vaccine Adjuvants: Clinical Experience
- Non Clinical and Clinical Summary and Next Steps

TARGET AUDIENCE

This program will benefit professionals involved in

- Biotechnology
- Biologics
- Vaccines
- Drug discovery
- Chemistry, manufacturing, and quality assurance
- Clinical, regulatory, and business development

CONTACT INFORMATION

Conference: Joanne Wallace Phone +1-215-442-6180 email Joanne.Wallace@diahome.org

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

- Explain the mechanisms of actions for antisense, immunostimulatory ODNs, siRNA and aptamer therapeutic approaches and their potential to treat patients.
- Discuss the issues surrounding the assessment of non-clinical safety for the different classes of ODN-based therapeutics.
- Outline the CMC analytical challenges (technical and regulatory) facing the field of ODN-based therapeutics.
- Recognize the value of ADME in the discovery and development of ODN-based therapeutics.
- Identify issues associated with the generation of PK data for ODN drugs, the relevance of such data in deriving PK/PD relationships and the potential impact and utility of different approaches to drug formulation, dose and schedule.
- Discuss practical and regulatory challenges involved in the development of novel ODN-based therapeutics in complex delivery systems
- Discuss the challenges of synthesizing and scaling up key raw materials as well as the formation and removal of impurities during synthesis and post-synthesis purification of ODN-based products.
- Summarize the scientific and regulatory issues associated with the translation of pre-clinical findings from the bench to the clinic for cancer, pulmonary, infectious diseases, vaccine adjuvant, retinal, metabolic and cardiovascular indications

WEDNESDAY • APRIL 18

6:00-8:00 PM **REGISTRATION**

THURSDAY • APRIL 19

7:15-8:00 AM **REGISTRATION AND CONTINENTAL BREAKFAST**

8:00-8:15 AM WELCOME AND OPENING REMARKS

Nancy D. Smith, PhD
Director, Office of Training & Communications, CDER, FDA
Board of Directors, DIA

David H. Schubert
Vice President, Regulatory Affairs and Global Quality Assurance
Coley Pharmaceutical Group, Inc.

8:15-8:45 AM KEYNOTE ADDRESS

John J. Rossi, PhD
Chair and Professor, Division of Molecular Biology Dean, Graduate School of Biological Sciences, Beckman Research Institute of the City of Hope

8:45-10:00 AM SESSION I

Mechanisms of Action and Therapeutic Potential

CHAIRPERSON

David H. Schubert
Vice President, Regulatory Affairs and Global Quality Assurance
Coley Pharmaceutical Group, Inc.

Oligonucleotide-based therapeutics encompass a wide range of properties, in terms of their mechanism of action and their medical applications. This field has evolved from the traditional strategies of targeting specific mRNA destruction by way of antisense technology to include more recent approaches such as siRNA, oligonucleotide-protein interactions in the form of "aptamers" and immunostimulation through binding to Toll-like receptors (TLR). In this session, leading experts in the field of antisense, immunostimulatory ODNs, siRNA and aptamers will describe the mechanisms of action behind these therapeutic approaches and their potential to treat patients.

Antisense Mechanisms
C. Frank Bennett, PhD
Senior Vice President, Research, Isis Pharmaceuticals, Inc.

Mechanisms and Therapeutic Applications of Oligodeoxynucleotide Toll-like Receptor 9 Agonists
Arthur M. Krieg, MD
Senior Vice President, Research and Development
Chief Scientific Officer, Coley Pharmaceutical Group, Inc.

Progress, Opportunities and Challenges in the Development of Therapeutic siRNAs
Akshay Vaishnaw, MD, PhD
Vice President, Clinical Research, Alnylam Pharmaceuticals, Inc.

Aptamers, A Whole Different Kind of Oligonucleotide Therapeutic
Page Bouchard, DVM
Senior Vice President, Nonclinical Research & Development
Archemix Corporation

10:00-10:30 AM **REFRESHMENT BREAK**

10:30 AM-12:00 PM SESSION 2

General Issues in Safety Assessment, Part 1

Session Chairperson

Arthur A. Levin, PhD
Senior Vice President of Development, Isis Pharmaceuticals, Inc.

This session will provide background information on the safety assessment of oligonucleotide-based therapeutics. Each speaker will address briefly what the issues are with the oligonucleotide class that they are working on and they will point out similarities and differences between the classes. The speakers will discuss briefly both how compounds are being tested as well as the results. The goal of this session is to provide the background understanding needed in order to address specific issues in the following sessions. The talks will be designed to provide all participants at the conference (clinical and manufacturing) an overview of the issues surrounding the assessment of safety of the different classes.

Preclinical Safety Assessment of Aptamer Therapeutics
Page Bouchard, DVM
Senior Vice President, Nonclinical Research & Development
Archemix Corporation

From Bench to Bedside with Immunostimulatory Oligonucleotide Therapeutics: Issues in Drug Development
Arthur M. Krieg, MD
Senior Vice President, Research and Development
Chief Scientific Officer
Coley Pharmaceutical Group, Inc.

Locked Nucleic Acid: Properties and Therapeutic Potential
Troels Koch, PhD
Vice President, Drug Discovery & Manufacture, Santaris

12:00-1:30 PM **LUNCHEON**

SESSION 3 BREAKOUTS

1:30-3:00 PM SESSION 3A, NONCLINICAL TRACK

General Issues in Safety Assessment, Part 2

Session Chairperson

Arthur A. Levin, PhD
Senior Vice President of Development, Isis Pharmaceuticals, Inc.

This session will provide background information on the safety assessment of oligonucleotide-based therapeutics. Each speaker will address briefly what the issues are with the oligonucleotide class that they are working on and they will point out similarities and differences between the classes. The speakers will discuss briefly both how compounds are being tested as well as the results. The goal of this session is to provide the background understanding needed in order to address specific issues in the following sessions. The talks will be designed to provide all participants at the conference (clinical and manufacturing) an overview of the issues surrounding the assessment of safety of the different classes.

The Toxicity of Oligonucleotide Therapeutics: A Mechanistic Approach
Scott Henry, PhD, DABT
Vice President, Toxicology, Isis Pharmaceuticals, Inc.

FDA Perspective
Lilliam Rosario, PhD
Team Leader, Study Endpoints and Label Development, Office of New Drugs, FDA

Panel Discussion

1:30-3:00 PM SESSION 3B, CMC TRACK

Analytical Characterization for ODN Therapeutics

Session Chairperson

Professor, Dr. Apr. Dieter Deforce
Laboratory of Pharmaceutical Biotechnology
Faculty of Pharmaceutical Sciences, University Gent, Belgium

This session will focus on the analytical challenges faced in the emerging field of oligonucleotide therapeutics. Experts from industry and academia will provide their view on analytical technology used and regulatory aspects concerning the analytical aspects for this class of therapeutics. Following the presentations a panel discussion will allow the participants to interact with the presenters.

Analytical Challenges for ODN Therapeutics and What Regulators Would Expect
Professor, Dr. Apr. Dieter Deforce
Laboratory of Pharmaceutical Biotechnology
Faculty of Pharmaceutical Sciences, University Gent, Belgium

Analytical Challenges in Characterizing PEGylated Oligonucleotide Drug Products
Jim Jianming Mo, PhD
Research Fellow, Analytical Research and Development
Pfizer, inc Inc.

Controlling Oligonucleotide Quality through Identification of Critical Impurities in Phosphoramidites
Claus Rentel, PhD
Associate Director, Analytical Development and Quality Control, Isis Pharmaceuticals, Inc.

1:30-3:00 PM SESSION 3C, CLINICAL TRACK

Advances and Issues in the Development of Oligonucleotides for the Therapy of Lung Diseases

Session Chairperson

Paolo M Renzi, MD
Chief Scientific Officer and Founder, Topigen Pharmaceuticals Inc.

This session will address the current status of development of oligonucleotide programs for the therapy of lung diseases. Representative examples of oligonucleotide applications will be discussed with their advantages and their potential issues. In addition, feedback from regulatory agencies with regards to their view on issues will be given formally and during a panel discussion.

Phosphorothioate-based Backbone Chemistry: Efficacy and Issues with Topical Delivery to the Lungs
Paolo Renzi, MD
Chief Scientific Officer and Founder, Topigen Pharmaceuticals Inc.

New Chemistries: Toxicology Issues in Mice and Plans to Address Them in Humans
Susan A Gregory, PhD
Vice President, Clinical Development, Isis Pharmaceuticals, Inc.

Health Canada's Experience with Oligonucleotides, What Are the Important Issues
Gordon James Gallivan, MSc, PhD
Clinical Trials Division, Center for Evaluation of Radiopharmaceuticals and Biotherapeutics, Biologics and Genetic Therapies Directorate, Health Canada

Methods for Assessing the Potential Toxicity of Oligonucleotides in the Lungs
Sally Wenzel, MD
Professior of Medicine, Director Asthma & Allergic Diseases, Universtiy of Pittsburgh

3:00-3:30 PM **REFRESHMENT BREAK**

SESSION 4 BREAKOUTS

3:30-5:00 PM SESSION 4A, NONCLINICAL TRACK

Specific Issues in the Safety Assessment of Oligonucleotide-based Therapeutics
Session Chairperson
S. Leigh Verbois
Pharmacologist, FDA

This session will highlight specific issues in the safety assessment of oligonucleotide based therapeutics. It is recognized that the non-clinical development of oligonucleotide-based therapeutics may include distinct considerations. Thus, to ensure the successful non-clinical development of these products, there is a need to understand and address specific toxicities that have been commonly associated with oligonucleotide-based therapeutics. This session will discuss the impact of immunogenicity, design of non-clinical studies, and current methods to enhance our understanding of toxicities associated with oligonucleotides.

Assessing Toxicities of Oligonucleotides: Use of Surrogate Molecules and Animal Models
Arthur A. Levin, PhD
Senior Vice President of Drug Development, Isis Pharmaceuticals, Inc.

Acute Toxicity Concerns for Oligonucleotides
Robert Tressler, PhD
Executive Director, Preclinical Development, Geron Corporation

Immunotoxicity and Immunogenicity Issues of Nucleotide-based Therapeutics
Cindy L. Berman, PhD
Senior Director, Nonclinical Safety
Coley Pharmaceutical Group, Inc.

What Microarrays Teach Us About RNAi Specificity
Peter Linsley
Executive Director, Cancer Biology, Rosetta Inpharmatics

3:30-5:00 PM SESSION 4B, CMC TRACK

Novel Delivery Systems
Session Chairperson
Lilian A. Radesca, PhD
Director, Manufacturing, Alnylam Pharmaceuticals, Inc.

The potential for oligonucleotide therapeutics has grown rapidly in the last few years. Early programs focused on local drug administration leading to two product approvals (Vitravene® and Macugen®) in the US and Europe. However, to facilitate clinical ease of use, systemic as well as other more efficient direct delivery of these novel therapeutics to targeted sites are being developed, and have proved to be significantly more challenging. This session will provide a review of the creative approaches being studied to facilitate effective drug delivery to the desired cellular targets. In addition, special consideration will be given to the practical and regulatory challenges involved in the development of these novel therapeutics in complex delivery systems.

Process Development for Lipoplex Formulations
Maaike Vinkenburg - van Slooten, PhD
Project Leader, OctoPlus N.V.

Case Study: TPI ASM8, A Dual Oligonucleotide Drug Product for Asthma
Luc Paquet, PhD
Vice-President, Discovery, Topigen Pharmaceuticals

Intratumoral Convection Enhanced Delivery of the TGF-beta 2 Antisense Oligonucleotide AP 12009 in Recurrent High-Grade Glioma Patients: The Way to Conclusive Phase 2 Results
Hubert Heinrichs, MD
Chief Medical Officer, Antisense Pharma GmbH

Considerations for the Development of Lipid Encapsulated siRNA
Ian MacLachlan, PhD
Chief Scientific Officer, Protiva Biotherapeutics

3:30-5:00 PM SESSION 4C, CLINICAL TRACK

Oligonucleotides for Infectious Diseases: Issues and Opportunities
Session Chairperson
Daniela Verthelyi, MD, PhD
Senior Staff Fellow, Division of Thereapeutics Proteins
CBER, FDA

This session will cover scientific and regulatory issues associated with the translation of pre-clinical findings from the bench to the clinic for infectious diseases indications and will review examples of representative products in ongoing clinical programs.

Oligonucleotides for Infectious Diseases: An Overview
Daniela Verthelyi, MD, PhD
Senior Staff Fellow, Division of Thereapeutics Proteins, CBER, FDA

FDA Perspectives on the Development of Anti-infective Therapies
Mark J. Goldberger, PhD
Director, Office of Antimicrobial Products
CBER, FDA

Discovery and Development of an siRNA, ALN-RSV01, for Respiratory Syncytial Virus
Akshay K. Vaishnaw MD, PhD
Vice President, Clinical Research
Alnylam Pharmaceuticals, Inc.

AVI BioPharma: Rapid Response to Emerging Infectious Diseases
Pat Iversen, PhD
Senior Vice President of Research and Development
AVI BioPharma

Coley's Experience in Treatment of Hepatitis C
Julie Lekstrom Himes, MD
Vice President, Clinical Research
Coley Pharmaceutical Group, Inc.

PANEL DISCUSSION

5:00-6:00 PM **RECEPTION**

FRIDAY • APRIL 20

7:30-8:30 AM **REGISTRATION AND CONTINENTAL BREAKFAST**

SESSION 5 BREAKOUTS

8:30-10:00 AM SESSION 5A, NONCLINICAL TRACK

General Issues in the ADME Properties of Oligonucleotide Drugs
Session Chairperson
Andrew M. Vick, PhD
Principal Research Scientist: Drug Disposition, Eli Lilly and Company

Oligonucleotide-based compounds continue to hold great promise as novel therapeutic agents designed to alter biological processes utilizing a variety of mechanisms including aptameric binding to specific proteins, sequence specific immunostimulatory adjuvants, and to inhibit the production of various disease-related gene products. An understanding of the principles underlying the ADME properties of oligonucleotides is critical to understanding the biological activity of this class of compounds, and ultimately therapeutic response optimization. This session will review our current knowledge of the pharmacokinetic attributes of oligonucleotide drugs with particular attention given to oligonucleotide metabolism. Further, this session will highlight ADME's expanding value in the discovery and development of oligonucleotide-based therapeutics.

Aptamers: Chemical Modifications and ADME
Renta Hutabarat, PhD
Director of Drug Metabolism and Pharmacokinetics, Archemix Corporation

Immunostimulatory Oligos with Emphasis of Species and Route Differences
Brian Livingston, PhD
Director of Preclinical Research, Dynavax

Single Stranded ASOs with Emphasis on Chemistry Metabolism and PK/PD
Richard Geary, PhD
Vice President of Pharmacokinetics and Drug Metabolism
Isis Pharmaceuticals, Inc.

8:30-10:00 AM SESSION 5B, CMC TRACK

Challenges in Process Development for Oligonucleotide Synthesis
Session Chairperson
Carl M. DeJuliis, PharmD
Associate Director, Worldwide Regulatory Strategy, Pfizer, Inc

Oligonucleotide manufacturing technology has progressed quite a bit in the past few years, with two approved oligonucleotide molecules in the market, and many more in the pipeline. The task of manufacturing low-cost oligonucleotide medicines still remains. This session will address the challenges of synthesizing and scaling up key raw materials as well as the formation and removal of impurities during synthesis and post-synthesis purification. We will also examine the relationship of different process parameters and its predictability by scaled down systems.

The Difference Between Scaling Up and Making Bigger, Challenges in the Scale Up of Oligonucleotide Manufacturing Processes
Paul McCormac, PhD
Director of Process Development, Avecia Biotechnology

Applications of Green Chemistry in Oligonucleotide Synthesis
Yogesh Sanghvi, PhD
President, Rasayan Inc.

New Analytical Method for the Detection of Single Stranded Impurities in Duplex APIs
Huseyin Aygün, PhD
Chief Scientific Officer, BioSpring Gmbh

Manufacturing Oligonucleotide API's – Identification of Process-related Impurities
Kenneth Hill, PhD
Director of Process Development,
Agilent Technologies Inc.

8:30-10:00 AM SESSION 5C, CLINICAL TRACK

Oligonucleotides in System Diseases
Session Chairperson
Sanjay Bhanot, MD, PhD
Vice President, Isis Pharmaceuticals, Inc.

This session will provide insight into the issues in developing oligonucleotide therapeutics for chronic diseases like diabetes, cardiovascular disease and muscular dystrophy. The metabolic and cardiovascular drugs show interesting activities and face unique challenges in that there are existing drugs for these indications. In contrast, the agents being used for the treatment of muscular dystrophy use a different mechanism of action (splice inhibition) and may need to be tailored to each patient. How each of these therapeutic agents are being developed provides examples for different regulatory and developmental hurdles.

Developing Antisense Oligonucleotides for the Treatment of Type 2 Diabetes
Sanjay Bhanot, MD, PhD
Vice President, Drug Development, Isis Pharmaceuticals, Inc.

Treating Hypercholesterolemia by Inhibiting the Expression of Apolipoprotein B Expression. Recent Clinical Results and Challenges Ahead
Diane Tribble, PhD
Vice President, Clinical Development, Isis Pharmaceuticals, Inc.

Using Antisense Agents to Alter Splicing in Duchenne's Muscular Dystrophy: Can Antisense Provide Individualized Therapy?
Steve Wilton, PhD
Professor of Molecular Medicine, University of Western Australia

Issues in Antisense: ASO that Alter mRNA Splicing in Duchennes Muscular Dystrophy
Sjef de Kimpe, PhD, MBA
Prosensa BV

10:00-10:30 AM **REFRESHMENT BREAK**

SESSION 6 BREAKOUT SESSIONS

10:30 AM-12:00 PM SESSION 6A, NONCLINICAL TRACK

Specific Issues in ADME
Session Chairpersons
J. Neil Duncan, PhD
Research Fellow, Preclinical PDM, Pfizer, Inc
Joy Cavagnaro PhD, DABT, RAC
Access BIO

This session will cover issues associated with the generation of PK data for ODN drugs, the relevance of such data in deriving PK/PD relationships and the potential impact and utility of different approaches to drug delivery. Bioanalytical strategies are influenced by varied analyte sensitivity and selectivity requirements for different types of ODN necessitating selection of appropriate analytical technologies. The importance of appropriate systemic PK assessment in generation of useful PK/PD relationships, the rationale for initial dose and schedule selection and the application of new delivery technologies to facilitate different routes of administration will also be discussed.

Issues in the Bioanalysis of ODN Molecules. Methodologies Employed: Sensitivity Versus Selectivity Considerations
Rand Jenkins
Director, Research and Development, PPD

Implications and Challenges in PK/PD of ODNs
Huiping Xu, PhD
Clinical Pharmacology, Pfizer, Inc

ODN (Antisense and Antigene) and siRNA Delivery and Targeting
Ram I. Mahato, PhD
Associate Professor, University of Tennessee Health Science Center

10:30 AM-12:00 PM SESSION 6B, CMC TRACK

CMC Regulatory Considerations and Panel Discussion – Part 1
Session Chairpersons
Ramesh Raghavachari, PhD
Chemist, ONDQ/DPE/Branch 7, FDA
James V. McArdle, PhD
Vice President, Chemistry, Manufacturing, and Controls
Archemix Corporation

In this session we will discuss, from the perspective of the regulatory agencies and industry, a number of CMC regulatory concerns, including:

- Establishing meaningful specifications
- Managing stringent yet practical acceptance criteria for impurities
- Proving sequences
- Validating methods for the commercial quality control lab
- Understanding mechanisms of degradation and establishing shelf lives
- Managing changes to synthetic processes and manufacturing routes
- Mitigating risk all the way from an unsettled supply chain through end of shelf life

FDA Perspective
Rao Kambhampati
Senior Regulatory Review Scientist, FDA

CMC Requirements for Oligonucleotides in Europe
René Thürmer, PhD
BfArM – Federal Institute for Drugs and Medical Devices, Germany

Regulatory CMC Considerations for Oligonucleotides
Todd Meyer
Global Biologics, Pfizer, Inc

10:30 AM-12:00 PM SESSION 6C, CLINICAL TRACK

Clinical and Regulatory Challenges of Antisense and Antisense-like Technologies in Clinical Oncology
Session Chairperson
Adrian M. Senderowicz
Medical Offices of Oncology Drug Products, Office of New Drugs, CDER, FDA

The attendees will learn requirements for drug approval in medical oncology. Furthermore, attendees will learn about recent antisense submissions to the FDA and Health Canada. Discussions about these submissions may lead to the incorporation of novel agents from this class in the therapeutic armamentarium. Finally, the attendees will learn about early-stage antisense compounds and recent advances in the preclinical field as well as the future of anti-sense and anti-sense like technologies.

Overview of Clinical and Regulatory Challenges of Antisense and Antisense-like Technologies in Clinical Oncology, FDA Perspective
Adrian M. Senderowicz
Medical Offices of Oncology Drug Products, Office of New Drugs, CDER, FDA

Oligonucleotides in Oncology: Health Canada Perspective Focus on Clinical Trials

Christine Nestruck, MSc, PhD
Assessment Officer
Office of Clinical Trials, Clinical Group 1
Theraeutic Products Directorate
Health Products and Food Branch
Health Canada

Overview of NCI Portfolio and NCI Perspective

Igor Espinoza-Delgado, MD
Senior Clinical Investigator
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute

Antisense and Antisense-like Technologies in Oncology: The Future

Kerry L. Blanchard, PhD, MD
Executive Director, Discovery Biology Research
Eli Lilly and Company

12:00-1:30 PM **LUNCHEON**

SESSION 7 BREAKOUTS

1:30-3:00 PM SESSION 7B, CMC TRACK

CMC Regulatory Considerations and Panel Discussion – Part 2

Session Chairpersons

Ramesh Raghavachari, PhD
Chemist, ONDQ/DPE/Branch 7, FDA

James V. McArdle, PhD
Vice President, Chemistry, Manufacturing, and Controls
Archemix Corporation

In this session we will discuss, from the perspective of the regulatory agencies and industry, a number of CMC regulatory concerns, including:

- Establishing meaningful specifications
- Managing stringent yet practical acceptance criteria for impurities
- Proving sequences
- Validating methods for the commercial quality control lab
- Understanding mechanisms of degradation and establishing shelf lives
- Managing changes to synthetic processes and manufacturing routes
- Mitigating risk all the way from an unsettled supply chain through end of shelf life

Panel Discussion

Todd Meyer
René Thürmer
Rao Kambhampati
Ulrich Granzer
Amit Banjeree
Lilian Radesca
Dieter Deforce
Susan Srivatsa

1:30-3:00 PM SESSION 7C, CLINICAL TRACK

Oligonucleotides – Emerging Therapies in Treatment of Retinal Diseases

Session Chairperson

Peter Hnik, MD, MHSc
Chief Medical Officer, iCo Therapeutics, Inc.

This session will provide pre-clinical and clinical review of experience with oligonucleotides in the eye. Potential advantages in treatment of retinal diseases will be discussed as well as feedback from regulatory agencies on potential issues with these compounds during the regulatory process.

Tolerability and Pharmacokinetics of Antisense Oligonucleotides Administered by Intravitreal Injection in Animal Models

Scott Henry, PhD, DABT
Vice President, Toxicology, Isis Pharmaceuticals, Inc.

Targets for Oligonucleotide Therapies for Retinal Diseases

Karl G. Csaky, MD, PhD
Associate Professor of Ophthalmology
Director, Ophthalmic Unit DCRI, Duke University Medical Center

Local Protein Expression Systems in the Eye

Lisa L. Wei, PhD
Director, Preclinical Sciences, GenVec, Inc.

iCo-007, a VEGF "+" Agent for Potential Treatment of Diabetic Macular Edema, Diabetic Retinopathy and Age-related Macular Degeneration

Peter Hnik, MD, MHSc
Chief Medical Officer, iCo Therapeutics Inc.

1:30-3:00 PM SESSION 7D, CLINICAL TRACK

Use of ODN TLR9 Agonists as Vaccine Adjuvants: Clinical Experience

Session Chairperson

Nathalie Garçon, PharmD, PhD
Vice President, Research and North America Research and Development, GlaxoSmithKline Biologicals

This session will cover pre-clinical and clinical experience of TLR9 agonist oligodeoxynucleotides that have been tested clinically as adjuvants to infectious disease and cancer vaccines. Potential advantages over currently available adjuvants will be discussed as well as feedback from regulatory agencies on potential issues with these compounds during the regulatory process.

Experience with a CpG Oligonucleotide as an Adjuvant to a Prophylactic Hepatitis B Vaccine in Healthy Volunteers and HIV-infected Patients

Heather L. Davis, PhD
Senior Vice President Pharmacology R&D
Coley Pharmaceutical Group, Inc.

Experience with a CpG Adjuvant in Malaria Vaccines

Ruth D. Ellis, MD, MPH
Staff Clinician, Malaria Vaccine Development Branch
NIAID/NIH

Characterization of Next Generation Anthrax and Influenza Vaccines Utilizing Immunostimulatory Oligonucleotides as Adjuvants
Brian Livingston, PhD
Director, Preclinical Research, Dynavax Technologies Corp.

Cancer Vaccine Trials with CpG Adjuvant: The Ludwig Institute/Cancer Research Institute Experience
Eric W. Hoffman, PharmD
Director, Office of Clinical Trials Management, Ludwig Institute for Cancer Research

Regulatory Considerations for Use of Oligonucleotides in Vaccine Formulations
Maria Baca-Estrada, PhD
Chief, Bacterial Vaccines Division, Centre for Biologics Evaluation, Biologics and Genetic Therapies Directorate, Health Canada

3:00-3:30 PM **REFRESHMENT BREAK**

3:30-3:45 PM KEYNOTE ADDRESS

FDA's Critical Path and the Promice of New Science
Douglas C. Throckmorton, MD
Deputy Director, CDER
FDA

3:45-5:30 PM SESSION 8

Nonclinical and Clinical Next Steps
Session Chairperson

David H. Schubert
Vice President, Regulatory Affairs and Global Quality Assurance
Coley Pharmaceutical Group, Inc.

Led by discussants, this plenary session will review with health authorities and industry expert panel the challenges and issues associated with the nonclinical and clinical development of ODN-based therapeutics brought forth in this conference. Panel Members will discuss and propose next steps in the further development of therapies using these new drug classes.

Nonclinical Discussant
Arthur A. Levin, PhD
Senior Vice President of Drug Development, Isis Pharmaceuticals, Inc.

Clinical Discussant
Paolo Renzi, MD
Professor University of Montreal
Chief Scientific Officer and Founder
Topigen Pharmaceuticals Inc.

Panel Member Discussion
FDA Representatives
Sally Seymour
Abigail Jacobs
David Jacobson-Kram

HPFB Representatives
Agnes Klein
Jim Gallivan
Christine Nestruck

Academic Representatives
Steve Wilton
Sally Wenzel

Industry Representatives
Art Levin
Art Krieg
Douglas Kornbrust

5:30-5:45 PM CLOSING REMARKS

5:45 PM CONFERENCE ADJOURNED

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Industry and Health Authority Conference on: Oligonucleotides-based Therapeutics

Event ID #07010

DoubleTree Hotel and Executive Meeting Center Bethesda, Bethesda, MD, USA

APRIL 19-20, 2007

Co-sponsored by DIA, FDA, Health Canada, and Oligonucleotide Therapeutics Society

Register online or fax this page to +1-215-442-6199

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Meeting I.D. # 07010 – April 19-20, 2007
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