

# RNA OLIGONUCLEOTIDES: EMERGING CLINICAL APPLICATIONS

NATIONAL INSTITUTES OF HEALTH  
HILTON HOTEL, ROCKVILLE, MARYLAND  
DECEMBER 15-16, 2011

## AGENDA

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*Thursday, December 15, 2011*

8:15 AM      **Welcome and Introductions**

8:30 AM      **Keynote Address: Overview of short interfering RNA (siRNA) and  
microRNA (miRNA)**

**Presenter:**      Phillip Sharp, Ph.D., Massachusetts Institute of  
Technology, Cambridge, MA

9:00 AM      **Session I: Overview of Current Clinical Approaches using siRNA**

- *Current and Proposed Clinical Applications of siRNAs*

**Presenters:**      Jared Gollob, M.D., Alnylam Pharmaceuticals,  
Cambridge, MA

James Thompson, Ph.D., Quark Pharmaceuticals, Inc.,  
Boulder, CO

Thomas Schlupe, Sc.D., Calando Pharmaceuticals, Inc.,  
Pasadena, CA

10:15 AM      **Break**

10:30 AM      • *Oligonucleotide Approaches for Neurodegenerative Diseases*

- Antisense regulation of splicing (e.g., exon skipping/inclusion)
- Sequestering of RNA repeats

**Presenters:**      Eric Hoffman, Ph.D., George Washington University  
School of Medicine, Washington, DC

Charles Thornton, M.D., University of Rochester,  
Rochester, NY

11:10 AM **Panel Discussion – Speakers Session I**

**Moderator:** Yuman Fong, M.D., Recombinant DNA Advisory Committee Chair, Memorial Sloan-Kettering Cancer Center, New York, NY

**Discussion Questions:**

- What has been learned about biodistribution of siRNAs when delivered by systemic or local administration?
- What has been learned about the persistence of oligos and their physiologic effects?
- What has been learned about immune or inflammatory responses and what models are best for predicting such responses?
- How has the potential for off target activity been addressed?
- What assays and animal models are available and what are their strengths and limitations?
- What are the key challenges that need to be addressed to move the field forward?

**Panelists:** Beverly L. Davidson, Ph.D., University of Iowa, Iowa City, IA

Michael Templin, Ph.D., Marina Biotech, Bothell, WA

12:40 PM **Public Comment**

12:50 PM **Lunch**

1:40 PM **Session II: microRNA Mechanisms of Action and Potential Clinical Applications**

- *Considerations for Exploiting miRNA in Therapeutic Applications*
  - Different effects in different cellular contexts
  - Different approaches: miRNA augmentation, mimicry, suppression

**Presenter:** David Bartel, Ph.D., Massachusetts Institute of Technology, Cambridge, MA

2:10 PM • *Potential Therapeutic Approaches in Different Clinical Contexts*

- Oncology

**Presenters:** Judy Lieberman, M.D., Ph.D., Children’s Hospital Boston, Boston, MA

Joshua Mendell, M.D., Ph.D., University of Texas  
Southwestern Medical Center at Dallas, Dallas, TX

Frank Slack, Ph.D., Yale University, New Haven, CT

- Cardiovascular disease

**Presenters:** Gerald Dorn, M.D., Washington University School of  
Medicine in St. Louis, St. Louis, MO

Carlos Fernandez-Hernando, Ph.D., New York  
University, New York, NY

3:55 PM      **Break**

4:10 PM      • *Potential Therapeutic Approaches in Different Clinical Contexts (Continued)*

- Infectious diseases

**Presenters:** Bryan Cullen, Ph.D., Duke University Medical Center,  
Durham, NC

Michael Hodges, Ph.D., Santaris Pharma A/S, Denmark

- Immunology/Inflammation

**Presenters:** Mark Boldin, Ph.D., Beckman Research Institute of  
the City of Hope, Duarte, CA

5:20 PM      **Questions**

5:30 PM      **Adjourn**

**Friday, December 16, 2011**

8:00 AM • *Development of Preclinical Models, Supporting Technologies, and Tools*

- Delivery and preclinical models
  - Predictive animal models (broad spectrum, epigenetic, long-term effects)
  - Pharmacokinetic studies

**Presenters:** John Rossi, Ph.D., Beckman Research Institute of the City of Hope, Duarte, CA

Andrew Miller, Ph.D., King's College London, London, England

- Technologies and tools for the assessment of oligonucleotide specificity
  - Bioinformatics infrastructure
  - Tools for unbiased screening for target site validation

**Presenters:** Julja Burchard, M.S., Merck & Co., Inc., West Point, PA

Morten Lindow, Ph.D., Santaris Pharma A/S, Denmark

10:00 AM **BREAK**

10:15 AM **Panel Discussion – Speakers Session II**

**Moderator:** Natasha Caplen, Ph.D., National Cancer Institute, National Institutes of Health, Bethesda, MD

**Discussion Questions:**

- To what extent can one use bioinformatics and high-content-screens like microarrays or proteomics to detect and document specificity, or lack thereof, for oligos intended for therapeutic use?
- What assays and animal models are being used to model the effect of knockdown or augmentation of miRNAs?
- What are the delivery challenges for miRNA modulators and how do they compare to siRNA?
- What potential long-term or epigenetic effects should be considered for miRNA modulating therapy?
- To what extent do we believe the clinical experience with siRNAs will inform the clinical application of miRNAs and what may be the key differences?

- What are the key unanswered research questions that need to be addressed to facilitate clinical development?

**Panelists:** David Bartel, Ph.D., Massachusetts Institute of Technology, Cambridge, MA

Judy Lieberman, M.D., Ph.D., Children’s Hospital Boston, Boston, MA

John Rossi, Ph.D., Beckman Research Institute of the City of Hope, Duarte, CA

12:30 PM **Public Comment**

12:40 PM **Lunch**

1:40 PM **Session III: Regulatory Issues**

- FDA Regulatory Oversight of RNA Oligonucleotides

**Presenter:** Robert Dorsam, Ph.D., Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD

- Regulation of RNA Oligos – One Company’s Experience in the US and Abroad

**Presenter:** Sara Nochur, Ph.D., Alnylam Pharmaceuticals, Cambridge, MA

2:15 PM **Panel Discussion – Speakers Session III**

- Are there regulatory science questions for evaluation of RNA oligonucleotides that are not shared by other small molecule drugs?

3:00 PM **Closing Remarks**

3:10 PM **Adjourn**