RNA OLIGONUCLEOTIDES: EMERGING CLINICAL APPLICATIONS

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

AGENDA

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
Slide Presentation

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
Slide Presentation

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

Thomas Schluep, 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
Slide Presentation

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
Slide Presentation

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
Slide Presentation

2:10 PM

- *Potential Therapeutic Approaches in Different Clinical Contexts*
  - Oncology

Presenters: Judy Lieberman, M.D., Ph.D., Children's Hospital Boston, Boston, MA
Slide Presentation

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

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

  - Cardiovascular disease

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

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

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
Slide Presentation

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

  - Immunology/Inflammation

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

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
Slide Presentation

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
Slide Presentation

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

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
Slide Presentation

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

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

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**