AsiaTIDES: Oligonucleotide & Peptide Therapeutics

February 21-23, 2017
The Westin Miyako Kyoto
Kyoto, Japan

THE PREMIER EVENT IN ASIA FOR ACCELERATING PROMISING OLIGONUCLEOTIDE AND PEPTIDE MOLECULES FROM RESEARCH TO COMMERCIALIZATION

Global Experts Help Accelerate Your Molecules to Market

Synthesis and Biological Activity of New DNA Analogues
Marvin Caruthers, Ph.D.
University of Colorado, USA

A RaPID Way to Discover Bioactive Pseudo-Natural Peptides for Therapeutic Uses
Hiroaki Suga, Ph.D
University of Tokyo

Multifunctional Envelope-type Nano Device for Nanomedicines
Hideyoshi Harashima, Ph.D.
Hokkaido University, Japan

- Hear the Latest Groundbreaking Oligo and Peptide Science to Improve Your R&D and CMC Strategies
- Form Successful Business Collaborations with Oligonucleotide and Peptide Leaders from Around the World
- Optimize the Drug-Like Properties and Improve the Delivery of Your Molecules
- Implement CMC and Analytical Techniques to Improve Efficiencies and Cost-Savings in Your Manufacturing Operations

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ASIA'S PREMIER MEETING TO ACCELERATE PROMISING MOLECULES FROM RESEARCH TO COMMERCIALIZATION

ACCELERATE YOUR PRODUCT TO MARKET

Hear case studies, best practices and lessons learned from global oligonucleotide and peptide developers currently in preclinical and phase 1/2/3 clinical trials. Ensure product approval by hearing regulatory guidance and roadmaps to successful IND/IMPD submissions from industry leaders.

MEET YOUR NEXT PARTNER AT ASIATIDES

Connect with 250+ oligonucleotide and peptide leaders across Asia, Europe and North America during networking lunches, dinners and cocktail receptions.

EVALUATE NEW TECHNOLOGIES AND SERVICES

Improve your process development, analytical and manufacturing efforts by meeting with 20+ global technology leaders in the exhibit hall. The exhibit hall also features peer-submitted posters that contain new and unpublished research from global scientists working across all phases of oligonucleotide and peptide development.

Call for Posters

Limited space is available for poster presentations at this event.
If you have new results/data on topics relevant to this conference, we encourage you to submit your poster abstract online at www.AsiaTIDESevent.com. The deadline to submit your abstract is January 24, 2017 and you must be a registered attendee in order to present a poster..

Meet the AsiaTIDES 2017 Scientific Advisory Board

Hiroaki Suga, Ph.D., Professor of Chemistry, School of Science**,** University of Tokyo, *Japan*

Osamu Sato, Executive Director, R&D Planning Department, Daiichi Sankyo, *Japan*

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Mimoun Ayoub, Ph.D., Director, Global Tides, Lipids and Carbohydrates & Injectables, CordenPharma International, *Switzerland*

PRE-CONFERENCE WORKSHOPS Tuesday, February 21, 2017 • 8:00am-12:00pm

Workshop #1: ROADMAP TO A SUCCESSFUL IND/IMPD SUBMISSION FOR OLIGONUCLEOTIDE THERAPEUTICS – DEFINING AND MANAGING CMC ACTIVITIES

Workshop Leaders:

G. Susan Srivatsa, Ph.D., President, **ElixinPharma,** *USA*
Thomas Rupp, Owner & Principal, **Thomas Rupp Consulting,** *Germany*
Additional Speaker:
K.S. Chin, Global Business Director, **Hongene Biotechnology Ltd.,** *China*

Workshop will achieve the following:

This highly strategic, introductory workshop will address starting material considerations, manufacturing challenges and Quality Control activities to support a successful IND/IMPD submission towards initiation of clinical studies for oligonucleotide therapeutics. Participants will gain broad understanding of the regulatory CMC requirements for oligonucleotide therapeutics in the US, Europe, Canada and Asia.

Who Should Attend:

Anyone interested in preclinical/clinical development of oligonucleotide therapeutics including scientists in R&D, manufacturing, quality control, quality assurance, project management, business development and regulatory affairs.

General Workshop Overview:

- Regulatory expectations: CMC overview & considerations around IMPD filing
- Manufacturing: Amidites as starting materials
- Manufacturing: General synthesis chemistry and purification
- Analysis: Specific considerations for conjugates, single strand & duplex molecules

Workshop #2: ACCELERATING PEPTIDES INTO HUMAN STUDIES: DRUG DEVELOPMENT AND REGULATORY CONSIDERATIONS

Workshop Leaders:

Bruce Morimoto, Ph.D., Executive Director, Applied Translational Medicine, **Celerion,** *USA*
Robert Hagopian, Director Business Development, **PolyPeptide Group,** *USA*
Duu-Gong Wu, Ph.D., Senior Director of CMC/Regulatory Consulting, **PPD** and Former **FDA CDER** Deputy Division Director, New Drug Chemistry Division II, *USA*

Workshop will achieve the following:

This practical, introductory workshop will address early drug development of peptide therapeutics. A detailed discussion of moving peptide therapeutics from discovery to clinical trials will include a description of strategies for early clinical development, including GMP synthesis, analytical controls and specifications; formulation strategies; pharmacokinetics and toxicology study designs and requirements; and the regulatory framework for preparation of IND-IMPD dossiers. Participants will gain a basic understanding of the considerations and requirements for taking a peptide therapeutic into first-in-human clinical trials.

Who Should Attend:

Anyone interested in preclinical/clinical development of peptide therapeutics including scientists in discovery research, manufacturing, project management, drug development, business development and regulatory affairs.

General Workshop Overview:

- Manufacturing and synthesis of peptide API's. Going from discovery to early GMP
- Basic formulation strategies to support nonclinical toxicity and human studies
- Drug development considerations for peptide therapeutics: pharmacokinetics and toxicology
- Preparation of IND-IMPD dossiers and design of first-in-human studies
- Regulatory considerations on peptide drug development and update on US review process

MAIN CONFERENCE Plenary Session • Tuesday, February 21, 2017

Keynote Presentations

1:00 **Chairperson's Remarks**
Ved Srivastava, Ph.D., Vice President, Chemistry**, Intarcia Therapeutics,** *USA*

1:05 **Synthesis and Biological Activity of New DNA Analogues**

Morpholino derivatives having amino, N-methylamino, N,N-dimethylamino, and morpholino substituents as well as phosphate/thiophosphate backbones have been prepared. Moreover certain of these analogues are far more stable as duplexes than unmodified DNA/DNA or DNA/RNA, are active with RNAse H1, and have biological activity twice the control (no lipid) in the 15b dual luciferase assay. Similar results have been observed with the triazoyl and 3'-triazoylphosphonate derivatives. Additionally imidoamidate DNA has been synthesized, forms stable duplexes with complementary, unmodified DNA/RNA, and is positively charged.
Marvin Caruthers, Ph.D., Distinguished Professor, Chemistry and Biochemistry, **University of Colorado,** *USA*

1:45 **A RaPID Way to Discover Bioactive Pseudo-Natural Peptides for Therapeutic Uses**

This lecture presents the technical merits of the RaPID system and recent advances in the discovery of pseudo-natural macrocyclic peptides against various drug targets for therapeutic uses.
Hiroaki Suga, Ph.D., Professor of Chemistry, School of Science, **University of Tokyo**

2:15 **Multifunctional Envelope-type Nano Device for Nanomedicines**

We are developing Multifunctional Envelope-type Nano Device (MEND) to deliver siRNA/miRNA/pDNA for Nanomedicines. MEND is developed on the concept of Programmed Packaging where a delivery strategy is programmed to overcome all the barriers to reach the site of action by controlling bio-distribution as well as intracellular trafficking. In this presentation, recent progresses on controlled intracellular trafficking as well as active targeting system to the Lung/Adipose/Tumors will be presented.
Hideyoshi Harashima, Ph.D., Professor of Pharmaceutics, Faculty of Pharmaceutical Sciences, Laboratory for Molecular Design of Pharmaceutics, **Hokkaido University,** *Japan*

2:45 *Networking Refreshment Break with Exhibit and Poster Viewing*

Plenary Presentations

3:15 **The Oligo Therapeutics Market Landscape – A 15 Year Retrospective on Market Trends, Deals, Investments, and Key Clinical Developments and a Look to the Future**
Over the last 15 years the number of oligo therapeutic programs has grown from roughly 100 programs in 2002 to over 300 in 2015, driven by the emergence of new classes such as siRNA, miRNA, and exon-skipping therapeutics. This presentation will provide an overview of the oligo therapeutic programs currently in development, as well as, an analysis of deal activity and investment trends over the last 15 years. Major market trends across the biotech and pharma space will be examined in relation to the current oligo therapeutic market environment.
Alun Garner, Business Development Manager, Nucleic Acid Solutions Division, **Agilent Technologies, Inc.,** *United Kingdom*

3:45 **Peptide Therapeutics: Paradigm Shift in Potential Treatment for Type 2 Diabetes with Once a Year or Half Yearly Dosing of GLP-1 Mimetic**
Exenatide is currently marketed globally as a twice-daily injection for the treatment of Type 2 Diabetes. Exenatide was subsequently formulated in PLGA microspheres as Bydureon for once weekly injection therapy for type 2 diabetes. Bydureon has its drawbacks including nausea, vomiting and a large needle of 23-gauge. Intarcia's Medici Drug Delivery System™ has the potential to provide continuous and consistent treatment with exenatide, ITCA 650 for once a year or half yearly dosing; and the flexibility of near immediate reversibility. All necessary clinical trials of ITCA -650 are completed and we expect to file for regulatory approvals soon. This presentation will describe the overcoming challenges for peptide optimization and peptide delivery technology including Medici Drug Delivery System™.
Ved Srivastava, Ph.D., Vice President, Chemistry**, Intarcia Therapeutics,** *USA*

4:15 **RNA Therapeutics Harnessing the Potential of Locked Nucleic Acid**
Over the past decades, RNA Therapeutics has developed from concept, clinic to market. The next decades are likely to bring RNA medicines to the maturity of small molecules and biologics given the increased access to genetic information, improved understanding of modalities and disease biology. The development has been hampered by a too simplistic approach to the underlying drug discovery principles resulting in unnecessary attrition rates during development. The lessons learned have resulted in new concepts to conduct drug discovery leading to increases in the productivity of RNA therapeutics. Locked Nucleic Acids are now recognized as a preferred chemistry for RNA Therapeutics. An overview of the initiatives in a maturing pipeline of RNA Therapeutics will be presented in the context of lessons learned from LNA drug discovery case stories.
Bo Rode Hansen, Ph.D., Global Head RTR & GM RICC, RTR (RNA Therapeutics Research), **Roche pRED, Roche Innovation Center Copenhagen A/S,** *Denmark*

4:45 **Exploring Macrocyclic Peptide Cell Permeability: Screening Tools and Design Rules**
Macrocyclic peptides can inhibit intracellular protein-protein interactions to address "undruggable" therapeutic targets. However, their pipeline advancement is hindered by suboptimal membrane permeability. Using cell-active sequences derived from p53, we are generating stapled peptide libraries to understand how peptide properties dictate membrane permeability. Using a variety of screening tools, we aim to develop design rules for advancing therapeutic macrocyclic peptides.
Anthony Partridge, Ph.D., Principal Scientist, Merck Research Laboratories, **MSD International GmbH,** *Singapore*

5:15 *Networking Reception in Exhibit and Poster Hall*

6:15 *Close of Day One*

8:00 *Registration and Coffee*

Regulatory Strategies for Oligonucleotides and Peptides

8:25 **Chairperson's Remarks**
G. Susan Srivatsa, Ph.D., President, **ElixinPharma,** *USA*

8:30 **Update on the Regulatory Expectations for the Quality of Oligonucleotide Products**
The complex and diverse nature of oligonucleotides currently in development (antisense, aptamers, siRNA, oligonucleotide conjugates, messenger RNA, CRSPR) is posing unprecedented challenges in meeting the regulatory requirements for drug quality. This presentation provides a historical overview and evolution of the US, European and other regulatory agencies' review practices of novel oligonucleotide products. Discussion will include emerging trends in the industry to meet current expectations for the characterization and quality control of oligonucleotide drug candidates in early to late stage clinical development.
G. Susan Srivatsa, Ph.D., President, **ElixinPharma,** *USA*

9:00 **Overview of Regulatory Issues of Peptides Drug Product Development in US and Case Studies**
Unlike chemical drugs, synthetic peptides are unique products due to their structural complexities and certain biological properties that resemble to those of biological products. Due to its diverse therapeutic activities and indications, they may be regulated under different laws/regulations and review organizations within US FDA. Furthermore, lack of specific ICH and domestic guidance documents may present additional challenge to the companies in dealing with regulatory issues during the different phases of development program for peptide products in US. The presentation will discuss the unique regulatory issues associated with the CMC and the areas of pharmacology and toxicology, and a few case studies will be presented to highlight the potential pitfalls and challenges for the peptide product development.
Duu-Gong Wu, Ph.D., Senior Director of CMC/Regulatory Consulting**, PPD** and Former **FDA CDER** Deputy Division Director, New Drug Chemistry Division II, *USA*

9:30 **Accelerated Development of Anti-Sense Oligonucleotides for Orphan Indications**
In the development of antisense oligonucleotides (ASO's), positive clinical trial results are leading to a drive to get these treatments to patients very quickly. Many of these ASO's are moving very rapidly from Phase I into late-phase registration trials. In some cases, in-licensing and movement of projects between organizations also compounds the development challenge, as less investment is often made for upfront CMC development. In addition, some ASO's are indicated for orphan indications so limited data are available when setting specifications. The author will share examples from our experience that illuminate some of the difficult choices we face as we rapidly move promising ASO's through development to market.
Robert Gronke, Ph.D., Senior Principal Scientist, Technical Development, **Biogen,** *USA*

10:00 *Networking Refreshment Break with Exhibit and Poster Viewing*

PEPTIDE TRACK

Peptide Discovery, Development and CMC

10:40 **Chairperson's Remarks**
El Djouhar Rekai, Ph.D., Head of Operation Products, **PolyPeptide Group,** *Belgium*

10:45 **Macrocyclic Inhibitors of Human Histone Deacetylase Enzymes**
A number of macrocyclic peptides have proven useful as probes and drug candidates due to their potency against histone deacetylases (HDACs). We present a series of cyclopeptides and their evaluation by HDAC profiling, NMR structure determination, and molecular docking to HDAC crystal structures. This reveals insight into the requirements for potent HDAC inhibition by macrocyclic peptides that disrupt the protein–protein interactions between HDAC enzyme and substrate or co-repressor protein in multiprotein complexes.
Christian Adam Olsen, Ph.D., Professor, Drug Design and Pharmacology, **University of Copenhagen,** *Denmark*

11:15 **Understanding the Structure Activity Relationship of the Nrf2-KEAP1 Protein-Protein Interaction Site Using an Nrf2-neh2 Peptide Library Design Approach**
Mechanisms that activate innate antioxidant responses hold much therapeutic potential in neurodegenerative diseases, such as Huntington's disease, Parkinson's disease, Alzheimer's disease. The Keap1-Nrf2 pathway plays a central role in the protection of cells against oxidative and electrophilic stress. Aided with structure-based tools such as NMR, X-ray crystallography and molecular modeling, structure activity relationship (SAR) studies were performed on the Nrf2, peptide sequence to identify peptide inhibitors of the Nrf2/Keap1 protein-protein interaction and further inspiring medicinal chemistry efforts towards peptidomimetics and macrocyclic inhibitors development.
Elisabetta Bianchi, Head of Peptide Chemistry, **IRBM Science Park,** *Italy*

11:45 **Therapeutic Proteins Made of D-amino Acids**
Stereochemistry is a fundamental property of proteins. Proteins composed of D-amino acids (D-proteins) are resistant to protease degradation, conferring longer in vivo circulation times, and significantly reduced immunogenicity. Mirror image phage display technology has been used to design D-proteins that bind and modulate a variety of therapeutic targets. Recent progress in the development of D-proteins as a new class of pharmaceutical products will be presented.
Dana Ault-Riche, Ph.D., CEO, **Reflexion Pharmaceuticals,** *USA*

12:15 *Networking Luncheon with Exhibit and Poster Viewing*

OLIGONUCLEOTIDE TRACK

Emerging Developments in mRNA and Genetic Therapy

10:40 **Chairperson's Remarks**
William S. Marshall, Ph.D., President and CEO, **miRagen Therapeutics, Inc.**

10:45 **Stabilized Non-immunogenic Messenger RNA (SNIM® RNA) for Transcript Therapy**
Ethris SNIM® RNA is an enabling platform for "Transcript Therapies" in a broad variety of medical indications, from hereditary or acquired metabolic diseases to regenerative medicine. SNIM® RNA circumvent TLR activation and thus enables repeated administration of mRNA. Because of its precursor function, SNIM® RNA yields sustained protein production within the body and overcomes short duration effects of recombinant proteins. Ethris has developed proprietary delivery systems for pulmonary, systemic and local SNIM® RNA administration and will present preclinical results from its activities. Efficient delivery systems and non-immunogenicity are the keys for making mRNA therapeutics reality beyond oncology applications.
Carsten Rudolph, Ph.D., CEO and President, **Ethris GmbH,** *Germany*

11:15 **LNP for mRNA Delivery: Leveraging Clinical siRNA Delivery Experience to Develop Potent, Well-tolerated Product Candidates**
Arbutus has an industry-leading lipid nanoparticle (LNP) nucleic acid delivery system. siRNA-containing LNP products are currently in clinical development in several indications, and critical information on efficacy and tolerability obtained from these studies has been used to develop optimized LNP for the delivery of mRNA. This presentation will provide an overview of key findings from clinical development of siRNA-containing LNP and describe the progress made by Arbutus in design of mRNA-containing LNP, including a discussion of similarities and differences between siRNA and mRNA delivery systems.
Peter Lutwyche, Ph.D., Chief Technical Operations Officer, **Arbutus Biopharma Corp.,** *USA*

11:45 **Computationally Designed Trans-splicing-based Suicide RNAs Effectively and Selectively Destroy Virus-infected or Cancer Cells in vitro**
We employed computational RNA structure design to improve both on-target activity and specificity of trans-splicing RNA (tsRNA) in a Herpes simplex virus thymidine kinase/ganciclovir suicide gene therapy approach. Rationally designed tsRNAs efficiently triggered death of HPV-16 positive or HCC-derived cells in vitro. Highest specificity and cell death activity was observed with tsRNAs furnished with multiple binding domains targeting one or more pre-mRNA biomarkers. Our observations suggest trans-splicing represents a promising approach to suicide gene therapy.
Volker Patzel, Ph.D., Assistant Professor, Microbiology & Immunology, **National University of Singapore**

12:15 *Networking Luncheon with Poster and Exhibit Viewing*

PEPTIDE TRACK

1:25 **Chairperson's Remarks**
Bruce Morimoto, Ph.D., Executive Director, Applied Translational Medicine, **Celerion,** *USA*

1:30 **Efficiency and Oral Bioavailability of Abeta Oligomer Directed D-Enantiomeric Peptides Developed for Therapy of Alzheimer's Disease**
Small soluble Abeta oligomers are suspected to be the major toxic species responsible for development and progression of Alzheimer's disease (AD). We developed highly potent D-enantiomeric peptide compounds that specifically eliminate Abeta oligomers and improve cognitive performance and stop or slow down neurodegeneration of AD transgenic mice. Data on stability and oral bioavailability clearly support the superiority of D-peptides over L-peptides.
Dieter Willbold, Ph.D., Director, ICS-6 Structural Biochemistry, **Forschungszentrum Jülich,** *Germany*

2:00 **Preclinical Studies on P8, A Novel Alzheimer's Disease-modifying Peptide Drug Candidate**
β-Amyloid (Aβ) accumulation in the brain is widely accepted to be critical to the development of Alzheimer's disease (AD). We previously demonstrated that two small, non-overlapping peptides, P4 and P8, from the PS-1 NH2-terminal domain, can substantially and specifically inhibit the production of total Aβ as well as Aβ40 and 42 in model systems of AD without affecting the catalytic activities of β- or γ-secretase, or the level of APP. These peptides and their derivatives offer new disease-modifying drug candidates for the treatment of AD. We now provide data on the preclinical development of the lead peptide drug candidate P8.
Nazneen Dewji, Ph.D., Associate Adjunct Professor of Medicine, UCSD and President and CEO, **Cenna Biosciences, Inc.,** *USA*

2:30 **Discovery and Development of KISS1R Agonists as Clinical Peptide Therapeutics**
Taiji Asami, Associate Director Medicinal Chemistry Research Labs, Pharmaceutical Research Division, **Takeda Pharmaceutical Company,** *Japan*

3:00 *Networking Refreshment Break with Exhibit and Poster Viewing*

3:30 **Human Trials to Combat Zika Virus, Flu and HIV Using Peptide Based Vaccines**
SEEK is a small pharma company focused on the development of peptide vaccines against infectious diseases. Our preclinical portfolio includes vaccines against Chagas, Rotavirus, Hepatitis B and C. Currently we are carrying two Phase IIb human trials testing our broad spectrum influenza vaccine, FLU-v, expected both to be completed in the second half of 2017. In addition, a landmark trial is to be undertaken in collaboration with the NIH in December 2016 to test the ability of a vaccine directed at the saliva of mosquitoes at protecting against mosquito borne diseases such as Zika. As for HIV, a Phase Ib study was completed and talks are underway to move the vaccine into Phase II shortly. The presentation will highlight the peptide selection process, manufacturing and advantages of synthetic peptide vaccines over more traditional ones.
Olga Pleguezuelos, Ph.D., Program Manager, **SEEK,** *United Kingdom*

4:00 **Understanding The CMC of Cocktail Peptide Vaccines**
Although the process of peptide synthesis at any scale has made huge progress, managing the manufacturing of a peptide vaccine is much more complex than a standard API. Producing a peptide vaccine API consisting of multiple epitopes can be a challenge in many aspects: Lengthy CMC consisting of process and analytical development, GMP production and testing of multiple peptides in parallel. Also ICH stability for multiple peptides needs to be monitored. Formulating a cocktail peptide vaccine is very complex. The behavior of each component in the formulation mix adds to the known technical issues associated with peptide stability and aggregation/gelling properties. Different peptides can mutually interact with each other and trigger aggregation through electrostatic interactions. The overall peptide mix ionic charge may also impact the solubility and stability of the vaccine drug product. These aspects need to be investigated during formulation development.
Mimoun Ayoub, Ph.D., Director, Global Tides, Lipids and Carbohydrates & Injectables, **CordenPharma International,** *Switzerland*

4:30 **Highly Efficient Manufacturing Method AJIPHASE® Applying to One-pot Peptide Synthesis and Peptide Conjugated Oligonucleotide**
The practical synthetic method for large scale has been strongly needed in the recent development for peptides. We have developed a novel solution-phase technology AJIPHASE® which employ an efficient one-pot synthesis for large volume of peptides. The efficacy of AJIPHASE® has been proven with the successful synthesis of various peptides in high yield and purity even at large scale. This presentation will describe the technical updates of AJIPHASE® technology and track records of various sequence of peptides.
Daisuke Takahashi, Ph.D., Principal Researcher, Bio-functional Molecular Chemistry Group, Research Institute for Bioscience Products & Fine Chemicals, **Ajinomoto Co. Inc.,** *Japan*

5:00 *Close of Day*

5:30 *Networking Dinner in Kyoto*

OLIGONUCLEOTIDE TRACK

Oligonucleotide Therapeutics: Preclinical and Clinical

1:25 **Chairperson's Remarks**
William S. Marshall, Ph.D., President and CEO, **miRagen Therapeutics, Inc.,** *USA*

1:30 **New Perspectives in LNA Oligonucleotide Therapeutics**
A modelling study has demonstrated that stereo defined internucleoside phosphorothioate (PS) linkages serve as strong determinants for LNA oligonucleotide activity. New pre-clinical data will be presented illustrating how PSs influences and can improve key drug properties of LNA oligonucleotides. The use of PSs in therapeutic oligonucleotides is a "hot topic", and the use of stereo defined vs. random mixture PS will be discussed and placed within the bigger picture of oligonucleotide drug discovery.
Troels Koch, Ph.D., Vice President & Head of Research, RNA Therapeutics, Roche pRED, **Roche Innovation Center Copenhagen A/S,** *Denmark*

2:00 **Pre-clinical Studies of NF-κB Decoy Oligonucleotide for Discogenic Lumbar Back Pain**
One of the highest hurdles for oligonucleotide medicine is the drug delivery to target sites. We attempted a local injection of naked NF-κB Decoy Oligonucleotide into the intervertebral disc to overcome this issue. Furthermore, NF-κB signaling underlies the pathophysiology of discogenic pain. I would like to share our strategy and preclinical data to support the development of NF-κB Decoy Oligonucleotide therapy for this indication.
Yasuhiro Hayashi, Ph.D., Chief Scientist, Drug Discovery Group, R&D Division, **AnGes MG, Inc.,** *Japan*

2:30 **Spherical Nucleic Acids: A Novel and Efficient Approach to Oligonucleotide Therapeutics Development**
Spherical nucleic acids (SNAs) consist of oligonucleotides radially oriented on a spherical lipid bilayer. SNAs show enhanced cellular uptake, and nuclease stability, compared with linear oligonucleotides, and have advantages for local delivery to skin, eye, lung and GI track. Dermal application of a first-in-class anti-TNF-SNA has demonstrated target knockdown without toxicity in a phase 1 clinical trial for mild to moderate psoriasis. Applications of SNAs targeting TLR9 for immune-oncology and as vaccine adjuvants will be presented.
Ekambar Kandimalla, Ph.D., Chief Scientific Officer, **Exicure, Inc.,** *USA*

3:00 *Networking Refreshment Break with Exhibit and Poster Viewing*

3:30 **Chemical Modification in RNAi Therapeutics**
The modification of double-stranded RNAi molecules plays a critical role in increasing in vivo potency and duration. This presentation will discuss chemical modifications and general design strategies for RNAi therapeutics in Arrowhead's programs, such as ARC-F12 for the treatment of thromboembolic diseases, ARC-LPA for the treatment of cardiovascular disease, and extrahepatic programs such as ARC-HIF2 for the treatment of renal cell carcinoma.
Zhen Li, Ph.D., Vice President, Chemistry and Manufacturing, **Arrowhead Pharmaceuticals,** *USA*

4:00 **Next Generation CpG ODNs and STING Agonists as Multi-Task Immuno-Therapeutics**
Clinical trials using immunostimulatory ODNs or cyclic dinucleotides, particularly agonistic as well as non-agonistic ligands for Toll-like receptors (TLRs) and stimulator of interferon genes (STING), have revealed their therapeutic potential not only as vaccine adjuvants but also as mono-immuno-therapeutic agent such as an anti-tumor agent. I will overview the relevant R&D then provide our recent progress.
Ken J. Ishii, M.D., Ph.D., Senior Researcher, **National Institute of Biomedical Innovation, Health and Nutrition (NIBIOHN),** *Japan*

4:30 **Recent Advances in the Clinical Development of microRNA Targeting Therapeutic Candidates for Hematological Malignancies and Pathological Fibrosis**
microRNA targeting allows for the control of complex biological pathways that could have relevance in the treatment of a variety of diseases. We have advanced two microRNA based drug candidates into human clinical trials. Our translational medicine development strategy is based on early mechanistic proof of concept and progressive de-risking in man. An update of our latest results will be presented.
William S. Marshall, Ph.D., President and CEO, **miRagen Therapeutics, Inc.,** *USA*

5:00 *Close of Day*

5:30 *Networking Dinner in Kyoto*

8:15 *Registration and Coffee*

Delivery Technologies and Strategies

8:40 **Chairperson's Remarks**
Robert Gronke, Ph.D., Senior Principal Scientist, Technical Development, **Biogen,** *USA*

8:45 **FEATURED PRESENTATION: Advances in RNAi Therapeutics**
Muthiah (Mano) Manoharan, Ph.D., Senior Vice President of Drug Discovery, **Alnylam Pharmaceuticals**

9:15 **Non-Viral Gene Delivery Systems by the Combination of Lipid Bubbles and Ultrasound: Applications in siRNA, mRNA, Plasmid DNA**
Microbubbles are cavitated by exposure to ultrasound, generating microstreams or microjets which result in shear stress to cells and the generation of transient pores in the cell membrane. Since this approach can be used to deliver extracellular material such as genes into cells, microbubbles could facilitate ultrasound-mediated gene delivery. We describe ultrasound-mediated delivery systems combined with nano/microbubbles and discuss their feasibility as non-viral vector systems.
Kazuo Maruyama Ph.D., Professor, Faculty of Pharma-Sciences, **Teikyo University,** *Japan*

9:45 **Progress in RNAi-based Therapeutics at Arrowhead Pharmaceuticals**
We are developing RNAi-based therapeutics for a wide variety of indications including chronic hepatitis B virus infection, liver disease associated with alpha-1 anti-trypsin deficiency, thromboembolic diseases, cardiovascular disease and cancer. Key to approaching these diverse indications is safe and efficient delivery of the RNAi trigger molecules. This presentation will focus on the development of the different delivery modalities and how their properties are engineered to fit the particular target indication.
Bruce D. Given, M.D., Chief Operating Officer, **Arrowhead Pharmaceuticals,** *USA*

10:15 *Networking Refreshment Break*

PEPTIDE TRACK

Peptide Delivery, CPPs and Half-Life Extension

10:40 **Chairperson's Remarks**
Christopher Rhodes, Ph.D., President and CEO**, Drug Delivery Experts,** *USA*

10:45 **Cyclotides – Ultrastable Cell Penetrating Peptides**
This presentation will provide an update on progress in the field of grafted cyclotides as therapeutics with particular reference to their ability to penetrate cells and block intracellular targets with relevance to cancer.
David Craik, Ph.D., Professor of Biomolecular Structure, Institute for Molecular Bioscience, **University of Queensland,** *Australia*

11:15 **Intracellular Delivery System Based on Cell-penetrating Peptides**
Arginine-rich cell-penetrating peptides (CPPs), including HIV-1 Tat (48-60) and oligoarginine, can be efficiently internalized by cells. Therefore, the CPPs have been widely used as carriers for intracellular delivery. I will be discussing cellular uptake mechanisms of the CPPs and introducing techniques for intracellular delivery of biologically functional molecules (e.g. proteins, peptides, and nucleic acids) by usage of the CPPs.
Ikuhiko Nakase, Ph.D., Special Lecturer (Tenure Track Lecturer), Nanoscience and Nanotechnology Research Center, **Osaka Prefecture University,** *Japan*

11:45 *Networking Luncheon*

12:55 **Chairperson's Remarks**
Christopher Rhodes, Ph.D., President and CEO, **Drug Delivery Experts,** *USA*

1:00 **Strategies for Sustaining Exposure of Peptide Therapeutics: Case Studies**
The talk will describe recent advances in sustained release formulation and conjugation approaches for peptides. Case studies will be used to describe pharmacokinetics data generated in preclinical and clinical studies to identify development candidates.
Christopher Rhodes, Ph.D., President and CEO**, Drug Delivery Experts,** *USA*

1:30 **PEGylation Strategy for Long-Acting Peptide Therapeutics**
A major problem with peptides is their short half-life, which is impractical as a therapeutic option, thus it becomes necessary to develop long-acting peptides. PEGylation is a commonly utilized technique for this purpose but steric hindrance from high molecular weight PEG can lead to a dramatic biological activity loss of rather small molecular peptides. Unlike existing PEGylation, we developed a novel PEGylation method by balancing between PEG size and shape, resulting in a long duration without loss of action and reduced adverse effects in humans.
Kang Choon Lee, Ph.D., Haengdan Distinguished Professor, Drug Targeting Laboratory, **SungKyunKwan University (SKKU),** *South Korea*

OLIGONUCLEOTIDE TRACK

Oligonucleotide Delivery

10:40 **Chairperson's Remarks**
Bob Brown, Ph.D., CSO and SVP, Research, **Dicerna Pharmaceuticals,** *USA*

10:45 **NanoFect™; Novel Delivery System of Nucleic Acid Drug for Cancer Therapy Using Micellar Nanoparticle Technology**
NanoFect™ is novel delivery system for nucleic acid drugs, based on micellar technology. In xenograft model systemic treatment of NanoFect™ showed well targeted gene pharmacodynamics and tumor growth inhibition. Active targeting system of NanoFect™ using antibody showed further enhancement of delivery efficiency. In this presentation the potential cancer therapy of NanoFect™ will be discussed.
Sei Yoshida, Senior Scientist, **NanoCarrier Co., Ltd.,** *Japan*

11:15 **Development of Lipid Nanoparticles for Nucleic Acid Delivery**
Our expertise on liposomal formulation technologies led us to develop lipid nanoparticles (LNPs) for nucleic acid therapeutics. LNPs showed potent and durable RNAi-mediated gene-silencing in rodents and non-human primates. We would also discuss particle stability of LNPs (long-term storage stability) as pharmaceutical dosage form.
Yuta Suzuki, Principal Researcher, **Eisai Co., Ltd., Japan**

11:45 *Networking Luncheon*

Oligonucleotide Manufacturing

12:55 **Chairperson's Remarks**
Bob Brown, Ph.D., CSO and SVP, Research, **Dicerna Pharmaceuticals,** *USA*

1:00 **Manufacturing, Process Development and Scale up for siRNA and Peptide forming Nanoparticles**
STP705 is a nanoparticle drug product consisting of 2 siRNA and 1 peptide. This product combines several challenges regarding CMC and offers a nice insight on both peptides and oligonucleotides manufacturing challenges. The presentation intends to cover all topics in a Module 3 CMC IND submission.
Marc M. Lemaitre, Ph.D., Chief Operating Officer, **Sirnaomics, Inc.,** *USA*

1:30 **AJIPHASE® - A Challenge for Oligonucleotide Synthesis in Solution-Phase**
One attractive option to fulfill the increasing demand for therapeutic oligonucleotide is solution-phase synthesis, because this approach is readily scalable. We have reported solution-phase based AJIPHASE® technology for peptides, PMO and GMP manufacturing was successfully conducted. This technology was successfully applied also to oligonucleotide synthesis using phosphoramidite approach. In this presentation, the process development including impurity suppression will be described.
Ken Yamashita, Ph.D., Researcher, **Ajinomoto Co., Inc.,** *Japan*

PEPTIDE TRACK

Peptide Manufacturing and CMC

2:00 **Single to Multiple Disulfide Bridge-rich Peptides: A Perpetually Evolving Approach in Process Development and Scale-Up**

The large abundance of bioactive single and multiple cystine-rich scaffold peptides in nature has fostered the pharma and biotech industry to move from exploration to exploitation of those complex molecules. Over the last decade, the number of disulfide bridges in peptides evaluated in clinical studies has continuously been growing, leading the manufacturers to deeply reconsider their approach of chemical route / process selection and scale-up. We propose an overview of our strategy for setting an optimized, safe and cost effective process of single / multiple disulfide bridge peptides.

El Djouhar Rekai, Ph.D., Head of Operation Products, **PolyPeptide Group,** *Belgium*

2:30 *Networking Refreshment Break*

3:00 **Setting Specifications for Therapeutic Peptides in Clinical Development**

For peptide drug substances in early clinical development there is often a very strong focus on fast drug substance supply. Therefore, development of manufacturing process capabilities and process economy, purity and impurity profile is performed in parallel. According to our experience, additional quality attributes such as salt form / counter ion, water content or small organic impurities are typically outside the scope of an early development program. The peptide counter ion for example might impact the shelf life of the API, causing stability issues in solution and as a solid. Sometimes sub-optimal drug substance quality attributes may only become apparent in subsequent drug product formulations. On the other hand, late-phase changes of quality attributes typically encounter pushbacks from different stakeholders, but still may be advantageous. Hence, a phase appropriate setting of specifications is crucial because both regulatory and practical challenges have to be managed in a time and risk based approach. The presentation will discuss examples from a contract manufacturer's point of view regarding different aspects of peptide drug substance CMC development.

Daniel Samson, Senior Director API Manufacturing**, Bachem AG,** *Switzerland*

3:30 **Impurities in Peptide Manufacturing**

For any API the understanding and control of the impurity profile is of paramount importance. The impurity profile of an API is the rather complex result of the API itself, including storage, stability and salt selection, the processing decisions, and the selection and the quality of the starting materials. With examples, this presentation will show that following a systematic approach it is possible to predict and eventually control the impurity profile effectively. Ultimately, the use of such approaches in the development of an API are extremely valuable for making the best informed decisions at the right time during the development.

Jon Holbech Rasmussen, Ph.D., Director, Global Development, **PolyPeptide Group,** *Sweden*

4:00 **Shionogi's Challenges on Impurity Control in Peptide API Process Development using QbD Approach**

In the development of peptide API, no guidelines and regulations have been shown clearly yet, defining the quality/specifications of the target peptide API. On the other hand, requirements for quality controls of API have been complexed these days, such as quality risk management, and control of mutagenic impurities defined by the ICH M7 guideline. In this presentation, I will show you some of our challenges toward the appropriate control strategies of impurities, especially mutagenic impurities.

Youhei Takagi, M.D., Subgroup Leader, Chemical R&D Center, Chemical Development Department, CMC R&D Division, **Shionogi & Co., Ltd.,** *Japan*

4:30 *Close of AsiaTIDES*

OLIGONUCLEOTIDE TRACK

2:00 **PANEL DISCUSSION: Addressing Supply Chain Challenges in Oligonucleotide Manufacturing**

- Quality of amidites and other reagents (supports, solvents): what is the consensus? Is more purity necessary?
- Scale-up - Are we ready for production of tons of oligonucleotides in a few years?
- Can we build a communication including the sponsors?
- What are the specificities of the Asian situation, if any?

Moderator:

Marc M. Lemaitre, Ph.D., Principal, **ML Consult,** *USA*

2:30 *Networking Refreshment Break*

Oligonucleotide Preclinical and Clinical Progress

3:00 **Comprehensive Evaluation of Plasma Protein Binding to Antisense Oligonucleotides**

Binding to plasma proteins is essential for the broad distribution within the body observed for phosphorothioate (PS) modified oligonucleotides. However, surprisingly little is known about the interaction with many plasma proteins besides serum albumin. We developed a fluorescence polarization assay and evaluated 25 of the most abundant plasma proteins. Some of the investigated proteins have binding constants in the low nanomolar range, while others do not bind at all. We report how oligonucleotide backbone, nucleobases, sugar modifications and flexibility influence the binding to key plasma proteins. Additionally, we demonstrate how modulation of binding properties can influence oligonucleotide potency in animal models.

Hans Gaus, Ph.D., Director of Structural Biology, **Ionis Pharmaceuticals, Inc.,** *USA*

3:30 **Update on Preclinical Development of GalXC RNAi Conjugates**

Bob Brown, Ph.D., CSO and SVP, Research, **Dicerna Pharmaceuticals,** *USA*

4:00 **Development of Novel RNA Targeting Therapeutics**

Silence Therapeutics develops targeted RNA-based therapeutics for serious diseases of high unmet medical need. The company recruits several technological platforms to allow down- or up-regulation of mRNA levels in various tissues and cell types. We will present a report on our current work with hepatocyte-targeting GalNAc-conjugated siRNAs, in particular selection and optimization of proprietary molecules, as well as tests in vitro and in vivo with various disease relevant targets.

Dmitry Samarsky, Ph.D., Chief Scientific Officer, **Silence Therapeutics,** *USA*

4:30 **Asymmetric siRNA Targeting Fibrotic Disorders**

OLX101, cell-penetrating asymmetric siRNA (cp-asiRNA) targeting connective tissue growth factor (CTGF), effectively reduces target gene expression as well as expression of fibrotic markers in animal model study. Preclinical as well as clinical study update of OLX101 in anti-skin scar will be presented. In addition to skin scar, OLX101 has a potential to be developed as therapeutics targeting various fibrotic disorders. We will present animal proof-of-concept study result of OLX101 in other fibrotic diseases, such as idiopathic pulmonary fibrosis (IPF).

Dong-ki Lee, Ph.D., Professor, Sungkyunkwan University and Founder and CEO, **OliX Pharmaceuticals,** *Korea*

5:00 *Close of AsiaTIDES*

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****Networking Dinner:* Wednesday, February 22, 2017 • 5:30pm • Restaurant TBD in Kyoto • $120

Hotel/Venue Information

The Westin Miyako Kyoto

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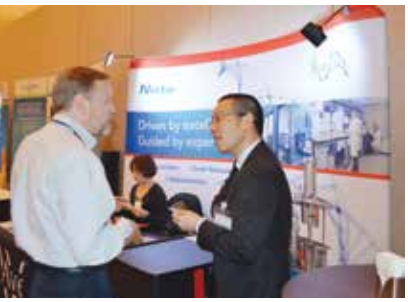

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