AsiaTIDES: Oligonucleotide & Peptide Therapeutics

February 27-March 1, 2018
Westin Miyako Kyoto
Kyoto, Japan

THE ONLY EVENT IN ASIA BRINGING TOGETHER SCIENCE, TECHNOLOGIES AND PARTNERS TO ACCELERATE OLIGONUCLEOTIDE AND PEPTIDE MOLECULES TO MARKET

Keynote Presentations

Transforming Daiichi Sankyo into a Global Pharma Innovator: Updated Directions and Future Vision of R&D
Junichi Koga, Ph.D.
Head of R&D Division, Executive Officer, Daiichi Sankyo, *Japan*

Recent Progress in the Discovery and Development of Macrocyclic Peptides
Patrick Reid, Ph.D.
Chief Scientific Officer, PeptiDream, Inc., *Japan*

Delivering Biopharmaceuticals across Biobarriers: Opportunities and Challenges in Drug Development
Ekkehard Leberer, Ph.D.
Senior Director, R&D Alliance Management, Sanofi and Scientific Managing Director, COMPACT Consortium, Innovative Medicine Initiative, *Germany*

Stunning Clinical Effectiveness of RNA/ENA Chimera Antisense Oligonucleotide (AO85) against Dystrophin Exon 45 in DMD Patient
Yasuhiro Takeshima, M.D., Ph.D.
Professor, Department of Pediatrics, Hyogo College of Medicine, *Japan*

Register by 9 February and Receive a $100 USD Savings

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APPLY THE LATEST INNOVATIONS IN OLIGONUCLEOTIDE AND PEPTIDE DEVELOPMENT

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 300+ oligonucleotide and peptide leaders across Asia, Europe and North America during networking lunches, poster sessions, dinners and cocktail receptions.

EVALUATE NEW TECHNOLOGIES AND SERVICES

Improve your discovery, clinical, 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 The exhibit hall also features peer-submitted posters that contain new and unpublished research from global scientists working across all phases of oligonucleotide and peptide development.

PRE-CONFERENCE WORKSHOPS • TUESDAY, FEBRUARY 27, 2018 • 9:00am-1:00pm

Workshop #1: Accelerating Oligonucleotides to IND and Beyond

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

Speakers:

Making Drugs out of Oligonucleotides: Role of Chemical Modifications

Muthiah (Mano) Manoharan, Ph.D., Senior Vice President of Drug Discovery, **Alnylam Pharmaceuticals,** *USA*

Process Development and Early Stage Development– Lessons Learned from a Few Cases Studies

Companies moving to clinic for the first time with oligonucleotides usually face a lot of questions. In this presentation, we will address those questions with respect to the CMC parts of an IND/IMPD for drug substance and drug product, based on recent experiences.

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

Regulatory Considerations for Oligonucleotide Therapeutics

David T. Lin, Ph.D., Senior Consultant, Biologics Consulting, (Former Chemistry Team Leader and Former Acting Division Director, Division of New Drug Chemistry, **CDER, FDA),** *USA*

Delivery Strategies for Oligonucleotides

Speaker TBA

Workshop #2: An Introduction to Peptide Therapeutic Development: Strategies for Moving to the Clinic, CMC and Beyond

Workshop Moderators:

Christopher A. Rhodes, Ph.D., *President & CEO,* **Drug Delivery Experts,** *USA*

Bruce H. Morimoto, Ph.D., Vice President, Scientific Affairs, **Celerion,** *USA*

Speakers:

Regulatory Considerations for Peptide Therapeutics

Duu-Gong Wu, Ph.D., Senior Director, Regulatory Consulting, **PPD** (and Former Deputy Division Director of Division of New Drug Chemistry, **CDER, FDA),** *USA*

Formulation Considerations for Peptide Therapeutics

Christopher A. Rhodes, Ph.D., President and CEO, **Drug Delivery Experts,** *USA*

Bioanalytical Strategies for Peptides

Rafiq Islam, Senior Director, Bioanalytical Services, **Celerion,** *USA*

Analytical Characterization of Peptides

Speaker TBA

MAIN CONFERENCE • PLENARY KEYNOTE SESSION • TUESDAY, FEBRUARY 27, 2018

1:55 **Chairperson's Remarks**

Osamu Sam Sato, Ph.D., Executive Director, R&D Planning Department, **Daiichi Sankyo Co., Ltd.,** *Japan*

2:00 **Transforming Daiichi Sankyo into a Global Pharma Innovator: Updated Directions and Future Vision of R&D**

Junichi Koga, Ph.D., Head of R&D Division, Executive Officer, **Daiichi Sankyo,** *Japan*

2:30 **Recent Progress in the Discovery and Development of Macrocyclic Peptides**

PeptiDream will present some of its recent progress in the discovery and development of therapeutics arising from its PDPS technology. PDPS technology has proven to be a powerful hit finding platform effective against almost any target. PeptiDream has evolved to turn those initial constrained peptide hit candidates into peptide therapeutics, small molecule therapeutics, and peptide-drug conjugates.

Patrick Reid, Ph.D., Chief Scientific Officer, **PeptiDream, Inc.,** *Japan*

3:00 **Stunning Clinical Effectiveness of RNA/ENA Chimera Antisense Oligonucleotide (AO85) against Dystrophin Exon 45 in DMD Patient**

A modified nucleotide of 2'-O, 4'-C-ethylene-bridged nucleic acid (ENA) has been shown to have high binding affinity for the complementary RNA strand and nuclease resistance. We have identified an 18-mer antisense RNA/ENA chimera against dystrophin exon 45 (AO85) that is able to induce skipping of dystrophin exon 45. Here, we report the clinical effectiveness of AO85 which was administered intravenously in DMD patient.

Yasuhiro Takeshima, M.D., Ph.D., Professor, Department of Pediatrics, **Hyogo College of Medicine,** *Japan*

3:30 *Networking Refreshment Break*

4:00 **Oligonucleotide Manufacturing Capacity – A Shortage Might Soon Turn into an Excess**

In 2015/16, oligonucleotide "oligo" customers experienced capacity constraints resulting in long lead times. Nitto Avecia was the first to respond to timely meet the customer's needs, by opening its new manufacturing facility with up to 1800mmol additional capacity in August 2017. Other CMO's and Biotech's also began building additional capacity which will be operational in the 2018 to 2020 timeframe. However, disappointing results of some late stage clinical trials during the previous 12 months have drastically reduced the demand for oligo manufacturing capacity for the next few years. It's quite possible the oligo market may soon be faced with excess manufacturing capacity

Detlef Rethage, President, **Nitto Denko Avecia, Inc.,** *USA*

4:30 **Cyclisation of Analgesic Conotoxins as a Tool to Modulate Folding, Potency and Biopharmaceutical Propertiest**

Conotoxins from the venoms of marine cone snails have attracted considerable attention as leads for the development of novel analgesics, following the registration of Prialt (ziconotide) a decade ago. This presentation will describe the use of synthetic cyclisation to enhance the biopharmaceutical properties of several classes of conotoxins with the potential for orally delivered analgesic activity.

David Craik, Ph.D., Professor of Biomolecular Structure, Institute for Molecular Bioscience, **University of Queensland,** *Australia*

5:00 **Delivering Biopharmaceuticals across Biobarriers: Opportunities and Challenges in Drug Development**

Biologics such as proteins, peptides and oligonucleotides have a huge pharmacological potential but their widespread therapeutic application has been very limited due to pharmacokinetic and drug disposition limitations at both the tissue and cellular level. The presentation will address these delivery limitations and summarize the work of a European consortium of pharma companies and academic partners to improve nanocarrier-based delivery technologies that can overcome these limitations.

Ekkehard Leberer, Ph.D., Professor of Biochemistry and Senior Director, R&D Alliance Management, **Sanofi,** *Germany* and Scientific Managing Director, COMPACT Consortium, **Innovative Medicines Initiative,** *Belgium*

5:30 *Close of Day One*

6:00 **Networking Dinner in Kyoto**

Network with fellow AsiaTIDES attendees from around the world by attending this Networking Dinner event at Ganko Takasegawa Nijoen, a high-class kaiseki cuisine restaurant in a historic building with an impressive and spacious Japanese garden. Your ticket includes access to an 11 course dinner with free flowing of drinks, including tempura and higher-quality sushi and sashimi and the presence of a Maiko (apprentice geisha). Round-trip transportation from the conference venue will be provided. To purchase a ticket, simply select this option during registration or by emailing register@ibcasia.com.sg ($120 USD fee to attend).

MAIN CONFERENCE • PLENARY SESSION • WEDNESDAY, FEBRUARY 28, 2018

8:00 *Registration and Coffee*

Regulatory Strategies for Oligonucleotide and Peptides

8:40 **Chairperson's Remarks**

9:00 **Regulatory Considerations for the Development of Oligonucleotide Therapeutics in the United States**

The typical factors for development of oligonucleotide products include potency/efficacy, stability in vivo, favorable pharmacokinetics (PK), favorable pharmacodynamics (PD), minimization of off-target effects and safety. However, oligonucleotide drugs fall somewhere between small molecules and large-molecule biologics, creating a new set of unique regulatory challenges. Oligonucleotides are chemically synthesized, and despite the diversity within this class of drugs, there are similarities in approaches for synthesis. This presentation will focus on quality expectations for oligonucleotide products and will explore the application of the quality concerns to oligonucleotide products.

David T. Lin, Ph.D., Senior Consultant, Biologics Consulting, (Former Chemistry Team Leader and Former Acting Division Director, Division of New Drug Chemistry, **CDER, FDA),** *USA*

9:30 **Regulatory Issues and Challenges during Different Phases of Peptide Product Development in US**

Peptides as chemically-synthesized molecules with biological activities present some unique regulatory challenges during the product development. For peptide products, the approvals for marketing as both drugs and biologics under different laws and regulations and review organizations with US FDA add additional complexities and difficulties during different phases of development in United States. The presentation will discuss: 1) Current regulatory trend in US for the review and approval of peptide products, 2) Different regulatory issues and data requirements for the peptide products to be developed as a drug or biologic and 3) How to navigate the unique regulatory and scientific issues during different phases of peptide development, e.g. to avoid clinical hold.

Duu-Gong Wu, Ph.D. Senior Director, **Regulatory Consulting, PPD** (and Former Deputy Division Director of Division of New Drug Chemistry, **CDER, FDA),** *USA*

10:00 **Novel siRNA Therapeutics for Fibrotic Disease Treatment with Polypeptide Nanoparticle Delivery Technology: Regulatory Experiences in US and China**

Using a proprietary and optimized polypeptide-based delivery technology, we have developed the novel antifibrotic therapeutics with siRNAs targeting both TGFβ1 and Cox-2 simultaneously, for initial indication of skin hypertrophic scar followed with liver fibrosis and other fibrotic conditions. With IND approvals by both US FDA and China CFDA, we have started clinical phase 2a in US and preparing clinical phase 1 in China for our leading drug candidate STP705 (Cotsiranib®) to treat human skin hypertrophic scar. I will discuss the unique advantage of our Polypeptide Nanoparticle (PNP) technology platform for safe and efficient siRNA delivery, and our strategy for advancing multiple clinical studies in both China and USA in near future.

Patrick Y. Lu, Ph.D., President & CEO, **Nanotides Pharmaceuticals, Inc.,** *USA*

10:30 *Networking Refreshment Break with Exhibit and Poster Viewing*

MAIN CONFERENCE • CONCURRENT TRACKS • WEDNESDAY, FEBRUARY 28, 2018

OLIGONUCLEOTIDE TRACK

Preclinical and Clinical Updates

11:10 **Chairperson's Remarks**

William Marshall, Ph.D., President & CEO, **miRagen Therapeutics, Inc.,** *USA*

11:15 **Non-clinical Development of DCR-PHXC for the Treatment of Primary Hyperoxalurias**

Primary hyperoxalurias are closely related genetic disorders resulting in elevated oxalate production in the liver. Excess oxalate accumulates in the urine where it often precipitates with calcium, leading to a variety of symptoms including frequent and severe kidney stone formation, nephrocalcinosis, and kidney failure. We are investigating a potential treatment for all forms of primary hyperoxaluria with a GalNAc-conjugated Dicer-substrate siRNA targeting the enzyme LDHA.

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

11:45 **Discovery and Development of microRNA Targeting Therapeutic Candidates for the Treatment of Hematological Malignancy and Pathological Fibrosis**

MicroRNAs regulate the expression of gene networks that culminate in the control of complex cellular processes. Dysregulation of the expression of certain microRNAs may affect pathways that contribute to disease pathology. We have advanced two product candidates into clinical trials; MRG-106, a LNA antimiR® targeting microRNA-155 in hematological malignancies and MRG-201, a synthetic replacement (promiR) for microRNA-29 in pathological fibrosis. An overview of our latest clinical observations will be presented.

William Marshall, Ph.D., President & CEO, **miRagen Therapeutics, Inc.,** *USA*

12:15 **GalNAc Conjugates for the Advancement of RNAi Therapeutics**

GalNAc Conjugates have revolutionized the field of RNAi therapeutics. Alnylam has advanced many therapeutic programs using this platform technology. The challenges, solutions and human therapeutic applications of GalNAc conjugated siRNAs will be presented.

Muthiah (Mano) Manoharan, Ph.D., Senior Vice President of Drug Discovery, **Alnylam Pharmaceuticals,** *USA*

12:45 *Networking Luncheon with Exhibit and Poster Viewing*

PEPTIDE TRACK

Peptide Discovery and Development

11:10 **Chairperson's Remarks**

11:15 **Genetically-Encoded Chemically-Modified Peptides**

We use genetically-encoded (GE) libraries as starting materials for multi-step organic synthesis. Examples are N-terminal conjugation1 and cyclization of linear peptides2 with simultaneous introduction of glycan entities. We developed the Genetically-Encoded Fragment-Based Discovery (GE-FBD) platform;3 which combines >109 peptides with GE-modifications.4 The talk will describe the progress and challenges in application of GE-FBD platform. References:

1. (a) J. Am. Chem. Soc., 2014, 136, 8149. (b) ACS Chem. Biol., 2012, 7, 1482
2. (a) Chem. Sci., 2016, 7, 3785. (b) Org. Biomol. Chem., 2016, 14, 5539-5545.
3. Ng et al., J. Am. Chem. Soc., 2015, 137, 5248
4. Tjhung et al., J. Am. Chem. Soc., 2016, 138, 32.

Ratmir Derda, Ph.D., Associate Professor, Department of Chemistry, **University of Alberta,** *Canada*

11:45 **Discovery and Development of Synthetic Polymyxins for Targeting Gram-negative 'Superbugs'**

In this presentation, we report on our ongoing pre-clinical polymyxin drug development program, a National Institutes of Health (NIH) funded joint academic-industry collaboration between Monash University (Australia) and The Medicines Company (USA). This program aims to produce new polymyxin peptide clinical candidates with improved safety and efficacy over the currently used drugs, polymyxin B and colistin. Aspects of our novel drug design strategy and lead optimization studies will be discussed. To date a number of promising lead candidates have been identified with significantly improved safety profiles and are being progressed towards clinical evaluation.

Kade Roberts, Ph.D., Senior Research Fellow, Biomedicine Discovery Institute, **Monash University,** *Australia*

12:15 **Polypharmacy through Phage Display: Selection of Glucagon and GLP-1 Receptor Co-agonists from a Phage-Displayed Peptide Library**

An emerging area for the treatment of obesity and diabetes is combinatorial hormone therapies, where single molecule peptides are rationally designed to integrate the complementary actions of multiple endogenous metabolically-related hormones. In this study, we report unimolecular polypharmacy agents selected on phage-displayed peptide libraries (PDL). Co-agonists of the glucagon (GCG) and GLP-1 receptors were identified after sequentially selection on GCGR- and GLP1R-overexpressing cells, showing EC50 ≤ 30 pM on each receptor. These results validate the approach for the discovery of optimized polypharmacology paradigms across several metabolically-related hormones.

Elisabetta Bianchi, Head of Peptide Chemistry, **IRBM Science Park,** *Italy*

12:45 *Networking Luncheon with Exhibit and Poster Viewing*

OLIGONUCLEOTIDE TRACK

Preclinical and Clinical Updates *(continued)*

1:55 **Chairperson's Remarks**
William Marshall, Ph.D., President & CEO, **miRagen Therapeutics, Inc.,** *USA*

2:00 **Clinical Update on DS-5141b an Oligonucleotide Drug for DMD Treatment**
Osamu Sam Sato, Ph.D., Executive Director, R&D Planning Department, **Daiichi Sankyo Co., Ltd.,** *Japan*

2:30 **An Oligonucleotide for the Treatment of Duchenne Muscular Dystrophy (DMD): An Update after Launch**
Speaker TBA, Sarepta Therapeutics, *USA*

Manufacturing, CMC and Purification Strategies

3:00 **New Developments in Oligonucleotide Manufacturing and CMC Strategy**
Blake Unterreiner, Director, Business Development & Customer Relations, Nucleic Acid Solutions Division, **Agilent Technologies, Inc.**

3:30 *Networking Refreshment Break with Exhibit and Poster Viewing*

4:00 **5'-GalNAc-Conjugated Antisense Oligonucleotides: Synthesis and Purification Challenges**
GalNAc-conjugated oligonucleotides represent an exciting approach to antisense therapy. In this presentation, we will discuss the challenges associated with production of these compounds. Solution-phase and solid-phase conjugation strategies capable of generating high-quality product will be presented and compared in terms of yield and purity.
Andrew Rodriguez, Ph.D., Assistant Director, Process Chemistry, **Ionis Pharmaceuticals,** *USA*

4:30 **New Purification Process for Antisense Oligonucleotides**
Recent efforts in oligonucleotide purification development have shown that an all aqueous process can achieve higher purities by employing orthogonal separation mechanisms. Higher purity is obtained by reducing challenging impurities such as N-1, P=O, N+1, without sacrificing yield. Positioning the detritylation step between the columns provides robust reaction control. An example of this process and its capabilities will be presented.
Robert S. Gronke, Ph.D., Senior Principal Scientist, Technical Development, **Biogen,** *USA*

5:00 *Networking Cocktail Reception in the Exhibit and Poster*

6:00 *Close of Day Two*

Meet the AsiaTIDES 2018 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*

Daisuke Takahashi, Ph.D., Senior Principal Researcher, Bio-functional Molecular Chemistry Group, Research Institute for Bioscience Products & Fine Chemicals, **Ajinomoto. Co., Inc.,** *Japan*

Hideaki Sato, General Manager, Technical Support and Marketing, **GeneDesign, Inc.,** *Japan*

Robert Hagopian, Director Business Development, **PolyPeptide Laboratories,** *USA*

Yasuhiro Hayashi, Ph.D., Chief Scientist, Drug Discovery Group, R&D Division, **AnGes MG, Inc.,** *Japan*

Yusuke Kohno, Vice President, **Jitsubo Co Limited,** *Japan*

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

Shawn Lee, Ph.D., President and CEO, CPC Scientific, **USA and China**

Patrick Lu, Ph.D., Founder, President and CEO, **Sirnaomics, Inc.,** *USA*

Michael McGinley, Manager- Core Products, **Phenomenex,** *USA*

Bruce Morimoto, Ph.D., Executive Director Applied Translational Medicine, **Celerion,** *USA*

El Djouhar Rekaï, Head of Peptide Products Operation, **PolyPeptide Group,** *Belgium*

G. Susan Srivatsa, Ph.D., President, **ElixinPharma,** *USA*

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

Mimoun Ayoub, Ph.D., Industry Expert

PEPTIDE TRACK

Peptide Discovery and Development *(continued)*

1:55 **Chairperson's Remarks**

2:00 **Intracellular Screening for Specific Peptide Antagonists of Proteins**
We use Protein-fragment Complementation to identify peptide antagonists of therapeutically relevant targets that include the oncogenic Activator Protein-1 transcriptional regulator, and β-amyloid / α-synuclein proteins implicated in AD/PD. Target-specificity is increased by expressing off-target proteins during selection. Antagonists are downsized and refined using structure-inducing constraints and non-natural sequences.
Jody Mason, Ph.D., Senior Lecturer in Biochemistry, **University of Bath,** *United Kingdom*

Control Strategies for Peptide Impurities and Peptide Manufacturing Learnings

2:30 **Synthetic Therapeutic Peptide – Challenges with Quality Standard and Impurities**
USP develops and publishes standards which are recognized in the Federal Food, Drug and Cosmetic (FD&C) Act since it was first enacted in 1938. U.S. Pharmacopeia (USP) has official monographs and reference standards (RS) for synthetic, recombinant, naturally-derived therapeutic peptides under 40 amino acids in length and insulin products. USP Therapeutic Peptides Expert Panel was formed in 2013 to evaluate quality attributes for synthetic peptide therapeutics based on currently available regulatory guidance and expectations. Quality attributes recommended by the Panel, has been incorporated during modernization of monographs for older peptide products. Compendial requirements for new monographs are aligned to the panel recommendation. The presentation will describe USP's current synthetic peptide program and our continued effort to set quality standards for this product class incorporating the Expert Panel's recommendations on the quality attributes. Compendial challenges such as impurities are illustrated using case studies. Additionally, future standardization opportunities are outlined.
Ranjan Chakrabarti, Ph.D., Vice President, Biologics & Biotechnology, **United States Pharmacopoeia-India**

3:00 **Oral Peptide Development/CMC: Learnings from Scaling up API and Reducing Costs for Peptide Manufacturing**
Major consumable costs for peptide manufacturing include the cost of protected amino acids, coupling reagents, and solvents. At smaller scales, labor and manufacturing facility expenses dominate manufacturing cost. However, at larger scales acquisition and disposition of solvents dominate cost. The relative costs and advantages of solid phase, solution phase and hybrid solid/solution phase manufacturing of peptides for oral use will be discussed.
Robert Geiger, Ph.D., Vice President of QA and Generic APIs, **AmbioPharm,** *USA*

3:30 *Networking Refreshment Break with Exhibit and Poster Viewing*

4:00 **Higher Molecular Weight (HMW) Peptide Impurities – Control Strategies and Acceptance Criteria**
BACHEM
PIONEERING PARTNER FOR PEPTIDES
For peptide drug substances in early clinical development there is often a very strong focus on fast drug substance supply. Therefore, the development of manufacturing process capabilities and economy as well as purity and impurity profile is performed in parallel. Aggregation-prone peptides implicate additional challenges for process development. Furthermore, it is known that sometimes sub-optimal quality attributes such as poor solubility, a shortened shelf life due to high HMW-content may only become apparent in subsequent drug product formulations. Different methods and strategies are applied at BACHEM to minimize and control HMW species of aggregation-prone peptides during synthetic downstream processing. Focusing on typical process stages, BACHEM's standard approach for optimization of process parameters regarding aggregation is presented within different case studies.
Daniel Samson, Ph.D., Vice President API SPPS, **Bachem AG,** *Switzerland*

4:30 **Control of Non-Peptide Impurities in APIs Originated from Materials/ Consumables/Equipment Contact through Process Manufacturing and Storage**
PolyPeptide GROUP
Pharmaceutical industries devote significant efforts to identify, quantify, and minimize level of impurities in drug products and consequently in drug substances (APIs). Chemical compounds can be leached into API from various components used in the manufacturing processes leading to potential adulteration of the API, and potentially affecting safety or efficacy of the drug product. This concern drives manufacturers to develop relevant control strategies. This presentation gives an overview and background of our risk management approach to address extractables / leachables, including elemental impurities, in peptide APIs.
El Djouhar Rekai, Ph.D., Head of Products Operation, **PolyPeptide Group,** *Belgium*

5:00 *Networking Cocktail Reception in the Exhibit and Poster*

6:00 *Close of Day Two*

MAIN CONFERENCE • PLENARY SESSION • THURSDAY, MARCH 1, 2018

8:00 *Registration and Coffee*

Oligonucleotide Market Overview in Japan

8:10 **Chairperson's Remarks**

8:15 **R&D Trend of Oligonucleotide Therapeutics in Japan**
In recent years, the R&D of Oligonucleotide Therapeutics has become very active in Japan. Key players from not only pharmaceutical companies but also venture companies and academic researchers moving towards practical applications have appeared. This presentation will discuss the trends, prospects and expectations for for R&D activity of oligonucleotide therapeutics from the viewpoint of journalist.
Aya Kubota, Deputy Editor, **Nikkei Biotech - Nikkei Business Publications**

8:40 **Chairperson's Remarks**

Delivery and Targeting Strategies

8:45 **Developing mRNA Therapeutics with LNP**
Arbutus' Lipid Nanoparticle (LNP) platform is enabling several early and late stage clinical trials. They are designed to deliver their nucleic acid payloads to sites of disease and have been used to target both viral and endogenous gene targets. Here we describe their application to mRNA payloads.
James Heyes, Ph.D., Vice President, Drug Delivery, **Arbutus Biopharma, Corp.,** *Canada*

9:15 **Arrowhead's TRM™ Delivery System – Potent, Modular and Versatile for RNAi**
Arrowhead's new TRM™ delivery system is designed for RNAi trigger delivery to a variety of tissues, not just the liver. We expect to be in human trials with this new technology in 2018 as we look to expand the boundaries of current RNAi efforts.
Bruce D. Given, M.D., Chief Operating Officer, **Arrowhead Pharmaceuticals, Inc.,** *USA*

9:45 **Enhancing ASO Potency in Extra-Hepatic Tissues**
Oligonucleotide therapeutics represent the third distinct platform for drug discovery in the pharmaceutical industry. Recent advances in targeted delivery have greatly enhanced the potency of oligonucleotide therapeutics for suppressing gene expression in hepatocytes. We have explored strategies to enhance potency of oligonucleotide therapeutics in extra-hepatic tissues such as muscle, endocrine organs and in lymphocytes, which will be presented
Punit Seth, Ph.D., Vice President, Medicinal Chemistry, **Ionis Pharmaceuticals,** *USA*

10:15 *Networking Refreshment Break with Exhibit and Poster Viewing*

MAIN CONFERENCE • CONCURRENT TRACKS • THURSDAY, MARCH 1, 2018

OLIGONUCLEOTIDE TRACK

Oligonucleotide Case Studies

10:55 **Chairperson's Remarks**

11:00 **Advancing LNA Therapeutics**
Recently therapeutic oligonucleotide discovery has seen a shift from paradigms based primarily upon sequence diversity, towards exploiting both sequence and design diversity: Small structural alterations can greatly affect the pharmacological properties of oligonucleotides. More recently, it has been realized that the specific stereo definition of phosphorothioate internucleoside linkages (PS) in LNA oligonucleotides are also strong pharmacological determinants. It will be shown in the presentation that new opportunities for oligonucleotide drug discovery are enabled when collective sets of diversity parameters are exploited.
Troels Koch, Ph.D., VP & Head of Research, RNA Therapeutics, **Roche Innovation Center, Copenhagen,** *Denmark*

11:30 **Use of Advanced siRNAs Targeted to Hepatocytes for the Development of Novel Drugs to Treat Liver-related Disorders**
Conjugation of the N-acetylgalactosamine (GalNAc) moieties to the siRNAs allows precise and highly effective knockdown of various genes in the liver, specifically in hepatocytes, of the vertebrate organisms. We will describe how Silence Therapeutics develops novel therapeutic programs addressing hepatocyte-associated diseases using its proprietary GalNAc-siRNA technology.
Torsten Hoffmann, Ph.D., Chief Operating Officer, **Silence Therapeutics,** *Germany*

12:00 **Asymmetric siRNA Targeting Fibrotic Disorders**
OLX10010, a 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 in lung and eye, such as idiopathic pulmonary fibrosis (IPF) and subretinal fibrosis.
Dong-ki Lee, Ph.D., Professor, **Sungkyunkwan University** and Founder and CEO, **OliX Pharmaceuticals,** *Korea*

12:30 *Networking Luncheon with Exhibit and Poster Viewing*

1:40 **Chairperson's Remarks**

1:45 **Pushing RNA Targeting Drug Development in China Towards Clinical Stages**
Over the years we have established a comprehensive platform for siRNA drug development in Kunshan, China and through our intramural research and high end collaborations with world leaders in the sector such as Ionis and Quark, we have been able to not only add the antisense dimension to our drug pipeline, but also push the first siRNA drug into the clinical stage. This combinatoric strategy will allow as to advance 3-4 RNA targeting drugs into IND or clinical stages over the next 12-18 months.
Zicai Liang, Chairman and CEO**, Suzhou Ribo Life Science Co. Ltd.,** *China*

2:15 **Recent Advances in RNAi Therapeutics at Arrowhead Pharmaceuticals**
In the presentation, Arrowhead Pharmaceutical's new hepatic delivery platform TRiM will be presented. Recent in vivo data in rodents and NHP for ARO-AAT and ARO-HBV will be discussed. ARO-AAT is for the treatment for a genetic disorder, alpha-1 antitrypsin deficiency (AATD), and ARO-HBV is for the treatment of hepatitis B. DMPK data in these two programs will also be disclosed.
Zhen Li, Ph.D., Vice President, Chemistry and Manufacturing, **Arrowhead Pharmaceuticals,** *USA*

PEPTIDE TRACK

Peptide Development and Peptide Delivery

10:55 **Chairperson's Remarks**
Bruce H. Morimoto, Ph.D., Vice President, Scientific Affairs, **Celerion,** *USA*

11:00 **I/O, CBP501 Combo Clinical Trial: Rationale and Updates**
Update on CBP501, a 12aa d-type peptide. It binds calmodulin, increases cytotoxicity of platinum, induces tumor immunogenic cell death, suppresses M2 macrophages, reduces cancer stem cells, and suppresses epithelial-to-mesenchymal transition. A Phase Ib study for the triple drug combination of CBP501, cisplatin and anti-PD1 antibody is ongoing.
Takumi Kawabe, M.D., Ph.D., President & CEO, **CanBas Co., Ltd.,** *Japan*

11:30 **Development of Cancer Peptide Vaccines: Can Cancer Peptide Vaccines Survive?**
Yasuhide Uejima, Ph.D., General Manager, CMC & QA, **BrightPath Biotherapeutics, Co., Ltd.,** *Japan*

12:00 **Peptides as Medical Devices**
3D Matrix has developed the self-assembling peptide platform technology and we successfully obtained the CE marking certificate for one surgical hemostatic agent based on the technology of PuraMatrix®. In this presentation we will introduce our recent progress from the viewpoint of CMC.
Naoki Yamamoto, Ph.D., Business Development, **3D Matrix, Ltd.,** *Japan*

12:30 *Networking Luncheon with Exhibit and Poster Viewing*

1:40 **Chairperson's Remarks**
Bruce H. Morimoto, Ph.D., Vice President, Scientific Affairs, **Celerion,** *USA*

1:45 **Exploring Stapled Peptide Permeability Using p53 as a Model System**
Stapled peptides can inhibit intracellular protein-protein interactions to address "yet-to-be-drugged" therapeutic targets. However, their pipeline advancement is hindered by suboptimal membrane permeability. Using cell-active sequences derived from p53, we have generated a library of several hundred stapled peptides to understand how peptide properties dictate membrane permeability. We will describe insights gained and novel screening tools.
Anthony Partridge, Ph.D., Principal Scientist, Early Discovery Pharmacology, Translational Medicine Research Centre, **Merck Sharp & Dohme,** *Singapore*

2:15 **Applications of Biodegradable Silica in Parenteral Delivery of Peptides**
Biodegradable silica polymer matrix provides a versatile tool for controlled release of parenteral therapeutics. Peptides and proteins are easily and effectively encapsulated in nanoporous silica using the sol gel process which preserves the biological activity of these molecules. Because the drug release is based on adjustable matrix surface erosion, very accurate zero-order release profiles can be obtained. Using this technology, it is possible to administer peptides in a controlled manner even for several months.
Lasse Leino, Ph.D., Adjunct Professor and CEO, **DelSiTech Ltd.,** *Finland*

OLIGONUCLEOTIDE TRACK

2:45 **Antibody-Mediated Delivery of siRNAs to the Muscle**
We explored the applicability of antibodies as a targeting ligand of siRNAs. In a mouse model of Peripheral Artery Disease (PAD), which is a kind of muscle wasting disease, the treatment with antibody conjugated myostatin-targeting siRNA by intramuscular injection resulted in significant silencing of myostatin and hypertrophy of the gastrocnemius without any changes in the body or heart weight, which was translated into the recovery of running performance. This is the first data that myostatin inhibition therapy caused an improvement in running performance in PAD mice.
Tsukasa Sugo, Ph.D., Principal Scientist, Innovation and Entrepreneurship, Pharmaceutical Research Division, **Takeda Pharmaceutical Company Limited,** *Japan*

3:15 *Networking Refreshment Break with Exhibit and Poster Viewing*

Oligonucleotide CMC Strategies

3:45 **AJIPHASE® Process Development Focusing on Impurity Suppression**
To address the rising demand of oligonucleotide drugs, we have been developing a unique and novel solution-phase synthesis, AJIPHASE®. The significant difference between AJIPHASE® technology and solid-phase synthesis is that our technology can show the reaction detail in each step by direct analysis. This presentation will highlight the elucidation of side reaction in AJIPHASE® and suppression of the impurities to obtain high purity oligonucleotides.
Taisuke Ichimaru, Researcher, Bio-functional Molecular Chemistry Group, **Ajinomoto Co. Inc.,** *Japan*

4:15 **Case Story: What Does It Take to Integrate LNA Phosphoramidite Specialty Building Blocks into the Supply Chain?**
The chemical complexity of oligonucleotides drug candidates has increased significantly over the past years. This puts a special focus on the quality of the novel starting materials that are chemically complex and are sources of impurities in the final API. In addition, all these factors put extra pressure on the design of a robust supply chain for the novel building blocks spanning from initiation to drug development.
Christoph Rosenbohm, Ph.D., VP and Head of Discovery Operations, **Roche Innovation Center Copenhagen,** *Denmark*

4:45 *Close of Conference*

PEPTIDE TRACK

2:45 **Peptide Delivery: How Nanosystems Can Help Address Present and Future Challenges**
Peptides have become very attractive drugs in the last decades, due to their selectivity, their high bioactivity and low toxicity. These drugs have been successfully developed for the treatment of major diseases like type 2 diabetes and cardiovascular disorders, various types of cancer and multiple sclerosis. Due to their poor stability in extreme pH conditions, their enzymatic degradation and poor absorption across epithelial membranes, as well as their short plasma half-life, peptides remain difficult-to-administer drugs. At the present time, they are predominantly administered via injection, using sustained-release (SR) formulations mainly based on polymer matrices slowly releasing the peptide over months. These formulations have become the most successful injectable peptide formulations on the market. However, the use of alternative routes of administration, like the oral route or the transmucosal route, is likely to increase in the future, due to the pain and invasiveness of injections, as well as disposal issues associated with used needles and relatively complicated injection protocols. Low bioavailability due to limited permeability through the membranes remain a key challenge for these alternative delivery routes. In addition, new challenges have emerged recently, related to the need for intracellular delivery of peptides to new targets in cancer treatment and to the crossing of the blood-brain barrier (BBB) for peptide delivery to the brain. Then, in this context, nanodelivery systems (e.g. nanotubes, nanoparticles or nanocapsules) can provide appropriate solutions to address present and future challenges of peptide delivery, especially as regards SR formulations and delivery systems crossing cellular membranes (either intestinal epithelium or BBB) or entering cells to target intracellular receptors. This paper will present various successful nanosystems for peptide delivery that have entered the clinic or even progressed to the market, and discuss prospective approaches mainly focused on the crossing of membranes.
Joel Richard, Ph.D., Senior Vice President, Peptides Development, General Manager, **OctreoPharm Science GmbH** and Head of Pharm. Dev. Dreux Site, **IPSEN,** *France*

3:15 *Networking Refreshment Break with Exhibit and Poster Viewing*

3:45 **Update on Advances in Oral Delivery of Peptides**
The various technologies and strategies for oral delivery of peptides will be discussed. In addition, data available from literature examples will be used to provide concrete examples for the pharmacokinetics profile achieved with each technology. Finally, new technologies that show some promise for oral delivery will be discussed.
Christopher A. Rhodes, Ph.D., President & CEO, **Drug Delivery Experts,** *USA*

4:15 **Functional Peptide-modified Exosomes for Intracellular Delivery of Therapeutic Molecules**
Exosomes are naturally occurring nanomaterials and could potentially represent the next generation of biological tools for delivering therapeutic molecules. However, the low cellular targeting efficacy and insufficient release of exosomal contents inside the cytosol can hinder their application. I will be discussing novel techniques that were developed to effectively target receptors and enhance cytosolic release of exosomal contents via biofunctional peptides that were modified on exosomal membranes.
Ikuhiko Nakase, Ph.D., Special Lecturer (Tenure Track Lecturer), NanoSquare Research Institution, **Osaka Prefecture University,** *Japan*

4:45 *Close of Conference*

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