AsiaTIDES: Oligonucleotide & Peptide Therapeutics

February 26-28, 2019
Hilton Tokyo Bay Hotel
Tokyo, Japan

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

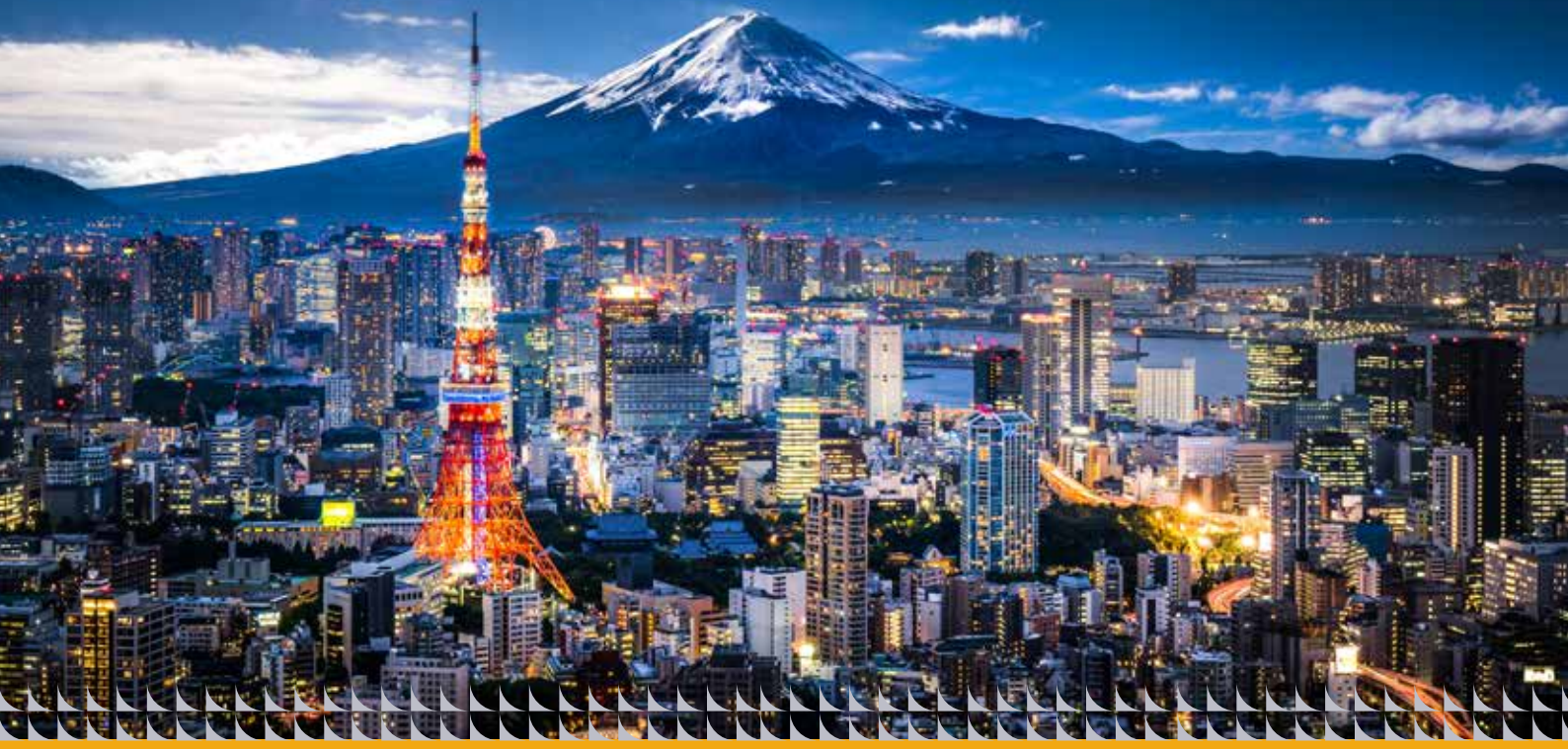
Top Companies Share Strategies to Accelerate Your Therapeutics

The Discovery of Semaglutide
Jesper Lau, Ph.D.
Vice President, Protein & Peptide Chemistry, Novo Nordisk A/S, *Denmark*

RNAi Therapeutics Delivered
Muthiah (Mano) Manoharan, Ph.D.
Senior Vice President of Drug Discovery, Alnylam Pharmaceuticals

New Strategies and Technologies in Oligonucleotide Therapeutic Development
Thazha P. Prakash, Ph.D.
Executive Research Fellow, Ionis Pharmaceuticals Inc.

Optimizing the Properties of Antisense Nucleic Acid Therapeutics
Chandra Vargeese, Ph.D.,
Senior Vice President, Head of Drug Discovery, WAVE Life Sciences



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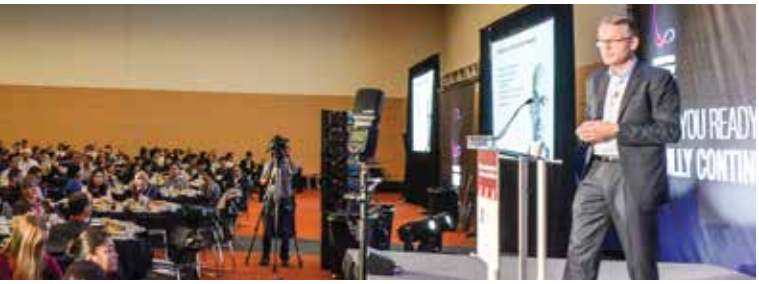
APPLY THE LATEST INNOVATIONS IN OLIGONUCLEOTIDE AND PEPTIDE DEVELOPMENT

SCIENCE

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.

TECHNOLOGY

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 The exhibit hall also features peer-submitted posters that contain new and unpublished research from global scientists working across all phases of oligonucleotide and peptide development.

NETWORKING

Meet Your Next Partner At AsiaTIDES

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

8:00 *Registration and Coffee*

Workshop #1: Accelerating Oligonucleotides to IND and Beyond

Workshop Overview:

This workshop will address early drug development and CMC of oligonucleotide therapeutics. A detailed discussion of moving oligonucleotide therapeutics from discovery to clinical trials will include a description of strategies for early clinical development, including GMP synthesis, analytical controls and specifications; nonclinical, CMC, manufacturing and scale-up and the regulatory framework for preparation of IND-IMPD dossiers. Participants will also gain a basic understanding of the considerations and requirements for taking an oligonucleotide therapeutic into first-in-human clinical trials.

Workshop Agenda:

9:00 **Workshop Co-Moderators' Opening Remarks**
Marc M. Lemaitre, Ph.D., Principal, **ML Consult,** *USA*
Thomas Rupp, Owner & Principal, **Thomas Rupp Consulting,** *Germany*

9:15 **The Chemistry behind Approved Oligonucleotide Therapeutics**
Muthiah (Mano) Manoharan, Ph.D., Senior Vice President of Drug Discovery, **Alnylam Pharmaceuticals,** *USA*

9:45 **Oligo Synthesis Scale-up and Process Related Issues and Troubleshooting**
Thomas Rupp, Owner & Principal, **Thomas Rupp Consulting,** *Germany*

10:45 *Networking Refreshment Break*

11:15 **CMC Oligos - Real World Case-studies**
Marc M. Lemaitre, Ph.D., Principal, **ML Consult,** *USA*

12:00 **Presentation Title TBA**
Florian von der Mülbe, Ph.D., Chief Production Officer, **Curevac,** *Germany*

12:45 *Close of Workshop*

Workshop #2: Accelerating Peptides to IND: Moving to the Clinic, CMC and Beyond

Workshop Overview:

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.

Workshop Agenda:

9:00 **Workshop Co-Moderators' Opening Remarks**
Bruce Morimoto, Ph.D., Vice President, Drug Development-Operations, **Alkahest, USA**
Christopher Rhodes, Ph.D., President and CEO, **Drug Delivery Experts,** *USA*

9:15 **Challenges in Synthesis of the Peptide API**
An overview of solid versus liquid phase peptide manufacturing approaches will be presented. This will be followed by potential challenges including aggregation, scale-up, stability, changes in manufacturing early versus late phase, and other related notes.
Robert Hagopian, Director Business Development, **PolyPeptide Group,** *USA*

10:00 **Analytical Methods, Pre-formulation, and Formulation for Early Phase Development**
The discussion will focus on all aspects of drug product development. We will start with analytical methods required for drug product, including in process controls, QC release methods, and stability, and how they differ from those for drug substance. In addition, we will discuss preformulation and formulation development of peptides to support non-clinical research studies, toxicity studies, and clinical programs. A third topic area to cover will be the selection, design, and development of delivery systems for peptides.
Christopher Rhodes, Ph.D., President and CEO**, Drug Delivery Experts,** *USA*

10:45 *Networking Refreshment Break*

11:15 **IND-enabling, Nonclinical Safety Studies for Peptides: Pharmacokinetics, Bioanalysis and Toxicology**
Peptides bridge small molecules and biologics, not only in their size, but also in specificity and selectivity. These unique properties of peptides require specialized consideration when designing and executing the safety studies to support first-in-human clinical trials. This talk will outline and discuss the pharmacokinetics and bioanalysis of peptides and the design of toxicology studies for peptides.
Bruce Morimoto, Ph.D., Vice President, Drug Development-Operations, **Alkahest,** *USA*

12:00 **Similarities and Differences in the Product Development between a Peptide Drug and a Peptide Biologic in the US**
With the advancement of immunotherapies, the development of peptide therapeutic cancer vaccines and preventive vaccines as biologics has entered new therapeutic areas. The regulation and the process in FDA governing the review and approval these products as biologics under PHS Act are quite different relative to other therapeutic peptides regulated as drugs. The presentation will discuss the similarity and differences in the review process and data requirements between a peptide drug and a peptide biologic.
Duu-Gong Wu, Ph.D., Senior Director, Regulatory Consulting, **PPD** (and Former Deputy Division Director of Division of New Drug Chemistry, **CDER, FDA),** *USA*

12:45 *Close of Workshop*

MAIN CONFERENCE PLENARY KEYNOTE SESSION • Tuesday, February 26, 2019

1:55 **Chairperson's Remarks**

2:00 **RNAi Therapeutics Delivered: Improving Pharmacological Properties of siRNAs**

This presentation will focus on key advances in these areas: 1) LNP mediated delivery and the approval of the first RNAi therapeutic; 2) Advances in GAlNAc conjugates and 3) Chemical modifications for improving the pharmacology of siRNAs.

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

2:30 **The Discovery of Semaglutide – A Journey from Ala Scan to Structural Design of GLP-1 Analogues**

Since the early clinical findings of using glucagon like peptide-1 (GLP-1) to regulate blood glucose levels in the late 80´s there has been an increasing interest to discover and develop GLP-1 receptor agonists for treatment of type 2 diabetes. The increased non-clinical and clinical understanding of the mechanism of action of GLP-1 and the parallel technical development have now brought the scientific community to a very high level of understanding with structural insight of the interaction of peptides and small molecules with GPCR class B receptors. The discovery of semaglutide is a fantastic example on how technology and biologic understanding have developed in parallel ending with a superior peptide for treatment of diabetes.

Jesper Lau, Ph.D., Vice President, Protein & Peptide Chemistry, **Novo Nordisk A/S,** *Denmark*

3:00 **New Strategies and Technologies in Oligonucleotide Therapeutic Development**

Inability to selectively deliver antisense oligonucleotide (ASO) therapies to ß-cells is a substantial barrier to the development of treatments for ß-cell specific diseases. We show that the GLP1 receptor can be used as a targeting approach for efficient and selective delivery of ASO to pancreatic ß-cells in cells and in animals.

Thazha P. Prakash, Ph.D., Executive Research Fellow, **Ionis Pharmaceuticals, USA**

3:30 *Networking Refreshment Break*

4:00 **Recent Progress in Ribosomal in-vitro Expression of Pseudo-natural Peptides**

This lecture discusses recent progress in ribosomal in-vitro expression of pseudo-natural peptides containing D-amino acid, beta-amino acids, and other exotic amino acids. This method opens a new opportunity to explore novel sequence space of pseudo-natural peptides.

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

4:30 **The Oligo Therapeutics Market Landscape – A 17 Year Retrospective on Market Trends, Deals, Investments and Key Clinical Developments and a Look to the Future**

Over the last 17 years the number of oligo therapeutic programs has grown from roughly 100 programs in 2002 to over 400 in 2018, driven by the emergence of new classes such as siRNA, miRNA, and CRISPR 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 17 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.,** *USA*

5:00 *Close of Day One*

6:00 **Networking Dinner in Tokyo**

Network with fellow AsiaTIDES attendees from around the world by attending this Networking Dinner event at a Tokyo restaurant. Sign up to attend this optional dinner by selecting this dinner option during registration (additional fee required)

MAIN CONFERENCE PLENARY SESSION • Wednesday, February 27, 2019

8:00 *Registration and Coffee*

mRNA Therapeutics

8:55 **Chairperson's Remarks**

Jim Thompson, Ph.D., Head CMC Project Management, **Moderna Therapeutics,** *USA*

9:00 **An Introduction to mRNA Therapeutics**

Jim Thompson, Ph.D., Head CMC Project Management, **Moderna Therapeutics,** *USA*

9:30 **Novel mRNA Immunotherapies**

Due to its unique characteristics, mRNA may be easily employed for potent cancer immunotherapy. The potential of mRNA-based cancer therapeutics will be presented and discussed.

Robert Jabulowsky, Ph.D., Deputy Head of Project Management, **BioNTech AG,** *Germany*

10:00 **Effective Delivery of Therapeutic Proteins by mRNA**

In recent years the field of mRNA therapeutics has expanded significantly. mRNA drugs can fill critical gaps not met by traditional small molecule drugs, available biological treatments, and emerging gene therapies. Our data supports the ability of sequence-engineered chemically unmodified mRNA to achieve ample protein expression.

Nigel Horscroft, D.Phil., Area Head, Molecular Therapy, **CureVac AG,** *Germany*

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

OLIGONUCLEOTIDE TRACK

11:10 **Chairperson's Remarks**

Optimizing Properties of Oligonucleotides

11:15 **From Stereopurity to Precision Medicine: Optimizing the Properties of Antisense Nucleic Acid Therapeutics**

Wave Life Sciences has developed proprietary synthetic chemistry and manufacturing capabilities that we are using to design and produce stereopure antisense oligonucleotides (ASOs) for patients with serious, genetically defined disease. In our evaluation of ASOs that promote RNase H-mediated activity or exon-skipping activity, we have explored the relationships among sequence space, chemical modification and backbone stereochemistry to optimize their pharmacological properties. We have discovered a relationship between the molecular configuration of our ASOs and their activity. We will present data from multiple programs that illustrate how our chemistry platform allows us to optimize ASOs for mechanism (e.g., gene knockdown or splicing), properties in vitro and in vivo, and distribution to an array of tissues.

Chandra Vargeese, Ph.D., Senior Vice President, Head of Drug Discovery, **WAVE Life Sciences,** *USA*

11:45 **The Role of Base Modifications in Folding, Binding and Pharmacology of DNA-based Aptamers**

Base modifications front-loaded into SELEX libraries have expanded the range of proteins for which high-affinity aptamers can be selected. The composition and physico-chemical properties of modified side chains profoundly influence folding, binding, metabolic stability and pharmacokinetic properties of aptamers, with implications for development of new diagnostics and therapeutics.

Nebojsa Janjic, Ph.D., Chief Science Officer, **SomaLogic, Inc.,** *USA*

12:15 **Next Generation Locked Nucleic Acids**

Locked Nucleic Acids (LNA) have come a long way from research tools to clinically validated drug candidates. As we are constantly developing this platform, potential next generation analogues have been identified, showing very promising drug properties. Here we will report our latest observations of backbone modified LNA with a particular focus on thiophosphate modifications, including stereo-defined internucleoside linkages.

Konrad Bleicher, Ph.D., Expert Scientist, **F. Hoffmann-La Roche Ltd.,** *Switzerland*

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

1:55 **Chairperson's Remarks**

2:00 **An Update on the DCR-PHXC Program**

Jennifer Lockridge, Ph.D., SVP, Program Development, **Dicerna Pharmaceuticals, Inc.**

2:30 **Optimizing Delivery of mRNA Therapeutics**

Lipid Nanoparticles are the leading technology for delivery of mRNA therapeutics. This presentation will describe the features of LNP critical for maximizing the therapeutic index of mRNA products.

Peter Lutwyche, Ph.D., Chief Technology Officer, **Genevant Sciences Corporation,** *Canada*

PEPTIDE TRACK

11:10 **Chairperson's Remarks**

Peptide Discovery and Peptide Drug Targets

11:15 **Inhibition and Degradation of Drug Targets Using bioPROTAC mRNAs – A Novel Approach with Broad Therapeutic Potential**

To tackle historically intractable targets, we have developed a platform employing targeted degradation. Specifically, we have engineered fusion constructs involving two components I) mini-proteins/peptides with high-affinity against therapeutic targets linked to II) truncated E3 ligase receptors. These 'bioPROTACs' have proven broadly successful with many constructs showing robust degradation activity. Currently, we aim to apply this technology as research tools and therapeutically by pursuing delivery strategies of bioPROTAC mRNAs.

Jeff Chang, Ph.D., Associate Scientist and Post Doc Fellow, Early Discovery Pharmacology, **MSD Singapore**

11:45 **Plants as Biofactories for Producing Peptide-based Pharmaceuticals**

This presentation will provide an update on our progress using plants to discover novel cyclic peptides and then using crop plants to produce 'designer' cyclic peptides with applications in cancer, multiple sclerosis and cardiovascular disease.

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

12:15 **Genetically Encoded Selection of Novel Cyclic and Bicyclic Architectures**

The talk will describe genetically-encoded (GE) platform for discovery of macrocyclic and macrobicyclic peptides synthesized by aqueous late-stage functionalization of readily-available libraries of peptides displayed on phage. The structure of these chemical post-translational modifications can be encoded in the genome of phage using silent encoding technology. The resulting phage displayed libraries of "unnatural" macro(bi)cyclic peptides could be used to target either proteins or cells and tissues; the latter targets are difficult to address with DNA/RNA or bead-based libraries. Expanded chemical space offers value-added properties such as stability to aggressive protease environment and incorporation of unnatural chemotypes that are known to increase bioavailability.

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

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

1:55 **Chairperson's Remarks**

Peptide Synthesis

2:00 **Intracellular Screening for Selective Antagonists of an Oncogenic Transcriptional Regulator**

Our research focuses on design, intracellular library screening and selection of peptide antagonists with high affinity and selectivity for inhibiting protein-protein interactions implicated in disease. 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 further enhanced by expressing off-target proteins during selection with antagonists downsized and refined using structure-inducing constraints and non-natural sequences.

Jody Mason, Ph.D., Associate Professor, Biochemistry, **University of Bath,** *United Kingdom*

2:30 **Massively Parallel Synthesis and Lead Optimization of Peptidomimetics**

We have developed a maskless photolithography peptide synthesis and screening platform that has been applied both for lead discovery and optimization. Our chemical catalog of over 350 amino acid building blocks combined with rapid library design and robust workflows, allows synthesis of over 18 million unique linear or cyclic peptides in less than 48 hrs on a single glass slide. The process is scalable and large libraries of millions of peptides can be synthesized on demand. We have made incremental upgrades and exploring end-point detection, real-time kinetic interaction, and cell-based phenotypic assays. Here, we will describe the core technology and its application to rapidly and systematically evolve high-affinity, high-specificity binding peptides to protein targets in a reproducible and digitally controlled process. We will demonstrate some case-examples, and recent process upgrades that enable real-time kinetic analysis for thousands of peptide-protein interactions in parallel.

Jigar Patel, Ph.D., Director, Peptide Technologies, **Roche Madison,** *USA*

OLIGONUCLEOTIDE TRACK

Oligonucleotide CMC Strategies

3:00 **Process Development and GMP Manufacturing of DNA Adjuvants**
Satoshi Inoue, Ph.D., Scientist, Research & Development Division, **GeneDesign, Inc.,** *Japan*

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

4:00 **Antisense Oligonucleotide Purification Process: Successes and Challenges During Scale-up**
Recently, our first full scale GMP batch for an antisense oligonucleotide was manufactured in the newly built synthesis suite at Biogen. A four-step purification process was then carried out in the existing flexible volume manufacturing facility that, up until this point, has been used for manufacturing Biogen's protein-based parenterals. This was our first test case to demonstrate that Biogen can manufacture ASOs safely, at scale, and achieve high purity and yield. Results are presented on the scalability of the ASO process from bench to GMP scale, highlighting successes and challenges faced with scale-up of the downstream ASO process.
Robert Gronke, Ph.D., Senior Principal Scientist, Technical Development, **Biogen,** *USA*

4:30 **NittoPhase® HL, High Loading Polymeric Solid Support for Efficient and Cost-Effective Oligonucleotide Synthesis**
When it comes to "Therapeutic Oligonucleotide manufacturing" performance and quality of the solid support matter. In this presentation, quality and performance of NittoPhase® HL is discussed and advantages of this cGMP manufactured solid support in comparison with other solid supports are discussed.
Mohammad Ahmadian, Ph.D., Senior Director, **Kinovate Life Sciences, A Nitto Company,** *USA*

5:00 **Utilizing NMR for Oligonucleotide Characterization**
Thomas Brown, Senior Scientist – Oligonucleotides, **Intertek Pharmaceutical Services,** *United Kingdom*

5:30 *Networking Cocktail Reception with Poster and Exhibit Viewing*

Media Partner

JBA Japan Bioindustry Association

PEPTIDE TRACK

3:00 **A New Scenario for Disulfide Peptide Synthesis Based on Npys Chemistry**
Chemistry based on 3-nitro-2-pyridinesulfenyl (Npys) group gave us a new scenario on disulfide peptide synthesis. Two topics will be discussed in the lecture, i.e., new solid- or no-solid-supported Npys-sulfenates (Npys-OR) as disulfide bond-forming agents and solid-phase-assisted disulfide ligation method. The latter actualizes intriguing "disulfide-driven cyclic peptides synthesis".
Yoshio Hayashi, Ph.D., Professor, Department of Medicinal Chemistry, **Tokyo University of Pharmacy and Life Sciences,** *Japan*

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

Optimizing Peptide Properties

4:00 **Peptide Drug Discovery Case Study: Appropriate Screening for ADME Properties and Pseudo Allergic Reactions at An Early Stage is Key to Success**
The key to success for development of peptide therapeutics is to use an appropriate screening funnel to correctly drive the SAR at the early stage of the project. This presentation will address important issues to consider in peptide development, namely: subcutaneous and plasma metabolism with in vitro/in vivo correlation to optimize bioavailability; potential reactions of peptide induced pseudo-allergy; immunogenicity; oligomerization and aggregation tendencies.
Raffaele Ingenito, Ph.D., Senior Scientist, Peptide Chemistry, **IRBM Science Park,** *Italy*

4:30 **Beyond Antibodies: Targeting VEGF-A and PD-1 with Synthetic D-proteins**
Small proteins have historically been under-utilized as human therapeutics because they are rapidly metabolized, have short half-lives and can be neutralized by anti-drug immune responses. However, proteins composed entirely of D-amino acids ("D-proteins") are resistant to proteases, have longer half-lives and significantly reduced immunogenicity. These properties also enable D-proteins to better penetrate tissues and solid tumors. Because D-proteins are chemically manufactured they can be engineered in ways not possible using biologic manufacturing. Mirror image phage display technology has been used to create D-proteins that are potent inhibitors of VEGF-A, an important therapeutic target for treating cancer and eye diseases. D-protein inhibitors of PD-1, an important immune-oncology target, have also been developed. Therapies combining VEGF-A and PD-1 inhibition have resulted in improved clinical outcomes for liver, lung and kidney cancers. This presentation will focus on the development of D-protein inhibitors to VEGF-A and PD-1.
Dana Ault-Riche, Ph.D., CEO, **Reflexion Pharmaceuticals,** *USA*

5:00 **Of Peptides and PANDAS: Innovative Preclinical Assessment Tools for Safety and Efficacy of Protein and Peptide Therapeutics**
The FDA recently released a new draft guidance defining the equivalence of a rDNA peptide product and a synthetic peptide product. The draft guidance enables generic manufacturers of peptide drugs to file an Abbreviated New Drug Application (ANDA) for synthetic peptide drug products that refer to listed drugs of rDNA origin. Since the processes for manufacturing the generic and reference drug (RLD) are not equivalent, peptide drugs can be associated with impurities. Impurities can result from changes in the sequences due to deletions, insertions, integration of incorrect amino-acids and modifications and also impurities related to the synthetic production. The FDA draft guidance requires manufacturers to prove that the synthetic peptide product does not contain impurities that have an increased affinity for major histocompatibility complexes and potential for engaging immune response, which may drive undesired anti-drug antibody development. We have used both immunoinformatics-driven analysis and in vitro validation assays to perform immunogenicity risk assessment of peptide generics. This combination of in silico and in vitro tools is referred to the PANDA assay which can be used to support generic peptide drug equivalency in an ANDA application. This presentation will provide insight as to the process of performing the PANDA assay, illustrating the process with two case studies (such as Calcitonin and Teriparatide).
Annie De Groot, M.D., Professor (Research) and Director, Institute for Immunology and Informatics, **University of Rhode Island and Founder,** CEO and CSO, **Epivax, Inc.,** *USA*

5:30 *Networking Cocktail Reception with Poster and Exhibit Viewing*

8:40 **Chairperson's Remarks**

Regulatory Strategies for Peptides and Oligonucleotides

8:45 **Regulatory and Clinical Development Strategy for Peptides in the Era of ICH; Oligonucleotide Products - Comparing the Regulatory Environment in US and China**

The content of this presentation includes an illustration of combined regulatory and clinical development strategies for peptides among ICH countries by taking advantage of new ICH guidelines such as E17 MRCT guideline. It will also compare the regulatory environment for oligonucleotides in the US and China.

Dan Zhang, M.D., Co-Founder & CEO, **Fountain Medical Development,** *China*

9:15 **US Regulatory Update: Peptide and Device Combination Products and the Lessons Learned from the Approval of Oligonucleotide Product, Macugen®**

For the convenience of dose delivery and patience compliance, the peptide therapeutics often come as combination products with either a prefilled syringe or a disposable and non-disposable injector device. Frequently, such a peptide combination product brings different challenges for the development and regulatory review that require the regulatory knowledge of both drug/biologic and device. Also, the recent approval of another oligonucleotide product, Mucagen, represents another milestone among the few approvals in US. The presentation will discuss various regulatory issues related to a device-drug or device biologic combination products and also the lessons learned from the new approval of Macugen oligo product in US.

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

9:45 **Understanding FDA's Draft Guidance for a Generic Product of a Highly Purified Synthetic Peptide that References an Approved Application for a Recombinant Peptide Product**

This recently published draft FDA guidance permits generic synthetic peptides to referencing a marketed drug product of rDNA origin. The draft guidance will be discussed with respect to opportunities and challenges.

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*

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

OLIGONUCLEOTIDE TRACK

10:55 **Chairperson's Remarks**

Delivery Strategies

11:00 **MicroRNA-155 Inhibition by Cobomarsen Demonstrates Encouraging Activity in Hematological Malignancies**

microRNA-155 (miR-155) is an important control point in the regulation of pathways implicated in oncology and inflammatory disease. Its overexpression has been shown to be an indicator of poor prognosis in a variety of hematological malignancies. Cobomarsen (MRG-106), an inhibitor of miR-155, is currently being evaluated in several potential indications, including Cutaneous T-cell Lymphoma (CTCL) and Adult T-cell Leukemia / Lymphoma (ATLL). An overview of our latest clinical observations will be presented.

William S. Marshall, Ph.D., President and Chief Executive Officer, **miRagen Therapeutics, Inc.,** *USA*

11:30 **Emerging RNA Therapeutics: Delivery Approaches for mRNA, siRNA and Beyond**

Delivery is a still key challenge to expand therapeutic application of oligonucleotide therapeutics such as siRNA, ASO and mRNA. AccuRna has unique polymer-based delivery platforms for short chain RNA/DNA and mRNA. In this talk, we will describe how we could apply our delivery platform to expand the possibility of nucleotide therapeutics.

Shiro Akinaga, Ph.D., Director, Chief Scientific Officer, **AccuRna Inc.,** *Japan*

12:00 **siRNA Delivery is Still the Key to Therapeutic Success**

In the past 2 decades we have seen dramatic progress in the adoption of RNAi technologies - from understanding the key criteria for siRNA design to improve function and specificity, to using siRNAs to identify and validate targets driving disease and now their validation as viable therapeutics in their own right. However, while there are many tools that allow digital design of siRNAs that can silence gene targets, many diseases such as cancer require inhibition of multiple genes in parallel and the genes that need to be targeted may change with time and stage of disease. We therefore need vehicles that can deliver more than one siRNA into the same cell concomitantly. Modification of these delivery vehicles with ligands to home to specific cell types in tissues may provide better therapeutic efficacy with a higher safety margin. This presentation will discuss our experiences in identification of multiple siRNAs with synergistic effects, development of delivery vehicles that can carry multiple siRNAs, and early steps we are taking in new screening methods to help rapidly identify and validate functional targeting ligands. The benefits of our delivery vehicles for multiple siRNA delivery and the steps needed to drive these innovations to the clinic will also be discussed.

David M. Evans, Ph.D., Co-founder and CSO, **Sirnaomics Inc.,** *USA*

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

PEPTIDE TRACK

10:55 **Chairperson's Remarks**

El Djouhar Rekaï, Ph.D., Head of Development & Manufacturing Process, **PolyPeptide Group,** *Belgium*

Peptide CMC Strategies

11:00 **Introducing Green and Sustainable Solvents in Liquid Phase Peptide Manufacturing Processes**

The challenge for the pharmaceutical industry is to find ways to develop and manufacture APIs based on environmentally-friendly and efficient processes. The selection of solvents and excess of reagents, together with process design including solvent recycling/VOC emission control are emphasized with the objective to minimize the production of wastes/gas emission while being operationally safe and economical. We will describe an overview of the PolyPeptide Group approach for setting environmentally-friendly, safe and cost-effective processes in liquid phase peptide synthesis. Case studies of successful process development to reach improved green processes will be highlighted.

El Djouhar Rekaï, Ph.D., Head of Development & Manufacturing Process, **PolyPeptide Group,** *Belgium*

11:30 **Peptide Quality Attributes and USP Standards**

United States Pharmacopeia (USP) has official monographs for peptides. To understand and evaluate the current regulatory considerations and expectations, an expert panel was formed. The Panel after detailed deliberation, recommended key Quality Attributes for incorporation in USP standards. Compendial requirements for new monographs are aligned to the panel recommendation. The presentation will describe the Expert Panel's recommendations on the quality attributes with case studies from USP's current synthetic peptide program.

Ranjan Chakrabarti, Ph.D., Vice President & Head - Global Biologics Lab and Standards, **United States Pharmacopeia,** *India*

12:00 **Cost Efficient Peptide Purification via ZEOsphere DRP Mixed-Mode Chromatography**

Peptide and Oligonucleotides are important API's for modern pharmaceuticals and have to be produced on preparative scale were costs are under pressure. RPC and IEX are well-established but costly chromatographic modes. ZEOsphere DRP Mixed-Mode materials combines the dual action of strong IEX groups (acidic or basic) and Reversed Phase ligands on the packing surface. ZEOsphere DRP in repulsion-attractive mode shows improved selectivities, leading to substantial lower production costs.

Jurgen Machielse, Business Development Director, **Zeochem AG,** *Switzerland*

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

OLIGONUCLEOTIDE TRACK

1:40 **Chairperson's Remarks**

1:45 **NJA-730, The First Therapeutic Compound from NapaJen's Platform Delivery Technology for aGvHD (acute Graft versus Host Disease) Is in Clinical Stage**

Our platform technology is targeted delivery of oligonucleotide therapeutic compounds to antigen presenting cells using SPG (schizophyllan) as a delivery vehicle. We will introduce NapaJen's platform delivery technology and report progress in Phase 1 trial of NJA-730, a CD40-targeting siRNA complexed with SPG, which shows potent pharmacological activity.

Kenji Arima, Ph.D., Chief Development Officer, **NapaJen Pharma, Co. Ltd.,** *Japan*

Preclinical and Clinical Case Studies

2:15 **Anti-FGF2 Aptamer RBM-007 in Phase I/IIa trials for Wet AMD**

RBM-007 is a novel oligonucleotide-based aptamer with potent anti-FGF2 activity. Intravitreal administration of RBM-007 in animals demonstrated anti-angiogenic and anti-scarring effects, consistent with a therapeutic effect desired in the treatment of wet (exudative) AMD. We have entered phase I/IIa clinical trials last summer in the US.

Yoshikazu Nakamura, Ph.D., President and CEO, **RIBOMIC Inc.**, and Professor Emeritus, **The University of Tokyo**

2:45 **Therapeutic RNA Medicines: The Silence Therapeutics Experience in Haematology and Rare Diseases**

Silence Therapeutics' pipeline focus on hepatocyte-associated diseases. Our most advanced asset, SLN124, is a GalNAc-conjugated siRNA targeting hepatic TMPRSS6. SLN124 reduces serum and tissue iron levels in a rodent model for hereditary hemochromatosis type 1 both as monotherapy and in combination with an oral iron chelator. SLN124 also demonstrates therapeutically relevant, dose-dependent and long-lasting effects on iron stores, erythropoiesis and anaemia in an animal model for beta-thalassemia. The first-in-human study is planned to start in 2019 in beta-thalassemia and myelodysplastic syndrome patients. We actively explore options for fine tuning of GalNAc-conjugated siRNA design such as siRNA modification patterns, end stabilisation, linker chemistry, and the number and location of GalNAc units. Combination of novel design elements are included in siRNA conjugates in pre-clinical stage programs with targets in haematology and rare diseases.

David Horn Solomon, M.D., CEO, **Silence Therapeutics,** *United Kingdom*

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

3:45 **TANGO – Targeted-Augmentation of Nuclear Gene Output – for the Treatment of Genetic Diseases**

Stoke is developing antisense-oligonucleotide (ASO) medicines that target pre-mRNA splicing to increase gene expression for the treatment of genetic diseases. Stoke's technology, TANGO, prevents naturally-occurring, non-productive splicing events, thereby increasing productive mRNAs and full-length proteins. We have built a proprietary bioinformatics pipeline that has identified over 100,000 non-productive splicing events and nearly 3,700 potentially druggable disease-associated genes. ASO screening of prioritized disease targets has yielded potent and gene-specific up-regulation for multiple diseases. One such disease, Dravet syndrome (DS), is a severe childhood epileptic encephalopathy characterized by high seizure frequency, cognitive and motor impairments, and increased risk of SUDEP (sudden unexplained death in epilepsy). DS is caused by mutations in the SCN1A gene leading to haploinsufficiency of the voltage-gated sodium channel alpha subunit (NaV 1.1). We have identified ASOs that significantly increase SCN1A mRNA and NaV 1.1 protein in vivo and demonstrate robust efficacy in a mouse model of Dravet Syndrome. These results indicate that Stoke's technology could provide the first gene-specific, disease-modifying approach to restore NaV 1.1 levels to treat Dravet Syndrome. Stoke's technology offers a pioneering strategy to treat diseases that result from reduced expression or insufficient activity of a gene that contains a non-productive splicing event. As over 50% of genes possess such events, the potential target opportunity is significant and largely untapped.

Huw Nash, Ph.D., Chief Operating Officer and Chief Business Officer, **Stoke Therapeutics,** *USA*

PEPTIDE TRACK

1:40 **Chairperson's Remarks**

1:45 **Linear and Convergent Approaches to Peptide Synthesis - A Comparison from A Manufacturer's Point of View**

Peptides can be synthesized using liquid phase peptide synthesis (LPPS), solid phase peptide synthesis (SPPS), and combinations thereof, i.e. fragment condensation or ligation. The shorter peptides used in fragment condensations or ligations are themselves accessible via the mentioned synthesis techniques. Fragment condensations are classically carried out in solution with C-terminus activated chemically or enzymatically. Larger fragments can also be ligated by native chemical ligation (NCL). On the other hand, state-of-the-art SPPS conditions are suitable for the synthesis of long peptides. All the mentioned approaches have pros and cons; the selection of the synthesis route depends on the peptide sequence, the target specifications, time-to-market for development, and last but not least the manufacturer: SPPS, LPPS and hybrid approaches differ significantly in the number of unit operations and the complexity of the required equipment trains. Manufacturer's capabilities and platform knowledge play a major role in route selection. In addition, cost of goods, process efficiency, maximum output at peak demand, and green chemistry considerations (e.g. solvent consumption, reaction conditions, waste reduction, replacement of hazardous chemicals) are frequently discussed in this context. In this presentation linear vs. convergent approaches for peptide synthesis are compared and pros and cons are discussed from a manufacturer's point of view.

Daniel Samson, Ph.D., Vice President API SPPS, **Bachem AG,** *Switzerland*

Preclinical and Clinical Case Studies

2:15 **ESCAPE-NA1 and FRONTIER: Two Complementary Phase 3 Trials to Demonstrate the Safety and Efficacy of NA-1 in Acute Ischemic Stroke**

The development of a safe and effective treatment for stroke is one of the greatest challenges in biomedical sciences. NA-1 is a novel neuroprotective peptide that acts by disrupting protein interactions with PSD-95 in the brain. ESCAPE-NA1 is a pivotal Phase 3 underway in 8 countries trial to assess the safety and efficacy of NA-1 in reducing disability in stroke victims who are candidates for endovascular thrombectomy. FRONTIER is a Phase 3 trial in which NA-1 is administered by paramedics in the ambulance to subjects with suspected stroke within 3 hours of onset.

Dave Garman, Ph.D., Chief Technology Officer, **NoNO, Inc.,** *USA*

2:45 **The Orally Available Clinical Stage All-D-enantiomeric Peptide PRI-002 Reverses Cognition Deficits and Decelerates Neurodegeneration in Transgenic Alzheimer's Mouse Models**

PRI-002 proved to eliminate already formed, toxic Aβ oligomers and to reverse cognitive deficits even in old-aged transgenic Alzheimer's disease (AD) mice with full blown pathology and deficits, even by oral administration. PRI-002 is fully blood-brain-barrier penetrable and demonstrated successful target engagement. I will summarize successful in vivo proof-of-concept in four treatment studies in three different transgenic animal models in three different laboratories. I will report first clinical data for PRI-002.

Dieter Willbold, Ph.D., Director, ICS-6 Structural Biochemistry, **Forschungszentrum Jülich,** *Germany*

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

3:45 **Development of a Peptide Vaccine for the Induction of Epitope-specific Antibodies**

FunPep has developed chimeric peptide vaccines composed of B-cell and T-cell epitopes. The peptide vaccine elicits high-titered and high-affinity antibodies that are able to recognize the target protein without co-treatment of any adjuvants. In this presentation I will introduce our recent progress from the viewpoint of preclinical studies.

Hideki Tomioka, Ph.D., Member of the Board and Director, Research & Development, **FunPep Co., Ltd.,** *Japan*

OLIGONUCLEOTIDE TRACK

4:15 **Latest Clinical Results from an Oligonucleotide in Development**
Osamu Sato, Ph.D., General Manager, Sakigake-Projects; DS-5141 and DS-1647 and Senior Executive Advisor for Head of R&D, **Daiichi Sankyo Co., Ltd.,** *Japan*

4:45 **Asymmetric siRNA Targeting Fibrotic and Ocular Disorders**
OLX10010, an anti-fibrotic 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 OLX10010 in anti-skin scar will be presented. In addition to skin scar, OLX10010 has a potential to be developed as therapeutics targeting various fibrotic disorders. We will also present preclinical study data of OLX10010 in other fibrotic diseases in lung and eye, such as idiopathic pulmonary fibrosis (IPF) and subretinal fibrosis.
Dong-ki Lee, Ph.D., CEO, **OliX Pharmaceuticals,** *South Korea*

5:15 *Close of Oligonucleotide*

PEPTIDE TRACK

4:15 **Osseotide, A Synthetic, Selective Osteogenic Peptide for the Treatment of Osteoporosis**
Mineralization in mammalian cells is accomplished by concerted regulation of protein-based extracellular matrix (ECM) components, such as non-collagenous proteins and collagen fibrils in hard tissue such as bone and teeth. Synthetic collagen-binding motif (CBM) peptide mimicking osteopontin, named as Osseotide, has been developed to selectively target osteoblast differentiation, which is clear contrast to current therapy targeting osteoclast. The peptide increased osteogenic differentiation while arresting adipogenic differentiation. In ovariectomized (OVX) mice, estrogen deficiency induced osteoporosis and increased fat tissue deposition. Significant bone loss by osteoporosis was restored by the treatment of Osseotide, evident by well-developed bone structure and bone formation. In addition, significant decrease in total fat and subcutaneous fat was observed in the Osseotide treated group, which is similar extent to that treated by estradiol or PTH. Taken together, these results suggest that the Osseotide could be an effective therapeutic agent for osteoporosis due to its selective targeting osteogenic differentiation.
Yoon Jeong Park, Ph.D., Professor, Seoul National University and Chief Technology Officer, **NIBEC,** *South Korea*

4:45 *Close of Peptide Track*

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