NEW TECHNOLOGIES, R&D ADVANCES AND CLINICAL DATA TO HELP YOU FAST-TRACK NEXT-GENERATION THERAPEUTICS TO MARKET

Antibody Engineering & Therapeutics ASIA is produced by **KNect365,** the same organizers as Antibody Engineering & Therapeutics US (San Diego) and Antibody Engineering & Therapeutics EUROPE (Amsterdam). Bringing together renowned industry and academic scientists working in the areas of antibody and protein engineering and therapeutic development, this conference provides you with the latest information about antibody-related technologies and preclinical and clinical data on antibody, ADC, bispecific and immuno-oncology programs from around the world.

Register now to learn about cutting-edge scientific advances in the field and to find the partners you need to accelerate your next-generation antibodies towards commercial success.

SCIENCE

Accelerate Your Product to Market

Hear case studies, best practices and lessons learned from global antibody, protein, ADC and Immuno-oncology developers currently in preclinical and phase 1/2/3 clinical trials.

TECHNOLOGY

Evaluate New Technologies and Services

Improve your discovery, preclinical and clinical development by meeting with global technology leaders and service providers in the exhibit hall. The exhibit hall also features peer-submitted posters that contain new research from global scientists working in antibody and protein therapeutic development.

NETWORKING

Meet Your Next Partner at Antibody Engineering & Therapeutics ASIA

Connect with antibody, protein, ADC and immune-oncology leaders across Asia, Europe and North America during networking lunches, poster sessions, dinners and cocktail receptions.

PRE-CONFERENCE WORKSHOP • Tuesday, February 26, 2019 • 9:00am-12:45pm

Enabling Technologies in Antibody Discovery and Therapeutic Development

8:00 **Registration and Coffee**

9:00 **Workshop Moderators' Opening Remarks**
Sai Reddy, Ph.D., Assistant Professor, **ETH Zurich,** *Switzerland*
David Johnson, Ph.D., Founder and CEO, **GigaGen,** *USA*

9:15 **Genomics and Yeast Display for Antibody Discovery and Engineering**
David Johnson, Ph.D., Founder and CEO, **GigaGen,** *USA*

9:45 **Antibody Design and Engineering through Integration of Computational and Experimental Methods**
Over the last decade there have been significant advances in computational protein design methods, high throughput protein characterization, and availability of antibody repertoire data. Convergence of these methods enable structure-guided design and engineering of antibodies. Here we discuss, through examples, application of computational and experimental methods for lead antibody discovery.
Karthik Viswanathan, Ph.D., Director, Research, **Visterra, Inc.,** *USA*

10:15 **Rational Selection of Antibody Clones**
In silico sequence analysis is useful for the rational selection of developable, manufacturable, and "designable" clones. By using our high-resolution antibody modeling protocol which proved competitive at antibody modeling assessment II, we have recently found that one can identify the clones which are relatively easy for successful optimization. Molecular simulation and informatics approaches revealed such "design-ability" corresponds to structural versatility of CDR-H3.
Hiroki Shirai, Ph.D., Executive Fellow, Modaility Research Laboratories, **Astellas Pharma,** *Japan*

10:45 *Networking Refreshment Break*

11:15 **Rapid Functional Interrogation of the Immune Repertoire – Next Generation Antibody Discovery**
Numerous disruptive technologies, from NGS of BCRs to bottom-up serum Ig proteomic, have been developed to study B cell repertoires in the past decade. At Pfizer, we are further pushing the boundary of technologies to enable fast and comprehensive interrogation of functionally relevant, antigen specific B cells from both peripheral and bone marrow compartments through the use of proprietary high-throughput automation, novel single cell technology and deep sequencing.
Gabriel WC Cheung, Ph.D., Senior Director, BioMedicine Design, **Pfizer,** *USA*

11:45 **Immune-Profiling of Human B cell Repertoire Using Next Generation Sequencing Technology**
Next-generation sequencing (NGS) has allowed a massive increase in capacity to sequence genomes at relatively low cost and in a short time frame. It has revolutionized multiple aspects of biological research and is actively being adopted into profiling human B cell receptor (BCR) repertoires. Several NGS platforms are currently available, with average read lengths of 75 bp to 8,500 bp and different error rates. Using NGS, we successfully constructed database of BCR repertoire from human volunteers. Afterwards, we developed algorithms for analyzing the diversity, enrichment pattern, accumulation of somatic hyper-mutation in BCR repertoire. Through in silico analysis with machine learning technology we devised strategies to select clones of interest. Now we are actively applying this technology for the analysis of BCR repertoire in cancer patients.
Junho Chung, M.D., Ph.D., Professor, **Seoul National University School of Medicine,** *South Korea*

12:15 **Bispecific Target Discovery by High Throughput Functional Screening**
To exploit the true potential to access novel biology with bispecific antibodies, we have developed technology to facilitate unbiased target pair identification and validation through grid screening large numbers of bispecific antibodies in functional human cell assays. Combination of our antibody discovery capabilities, a novel bispecific screening format and high throughput flow cytometry or imaging enables us to screen thousands of bispecific antibodies to hundreds of antigen combinations and identify new target pairs for a defined patient phenotype. The technology and a specific example application from patient phenotyping to new target pair discovery will be described.
Pallavi Bhatta, Ph.D., Principal Scientist, Functional Screening, **UCB,** *United Kingdom*

12:45 *Close of Workshop*

MAIN CONFERENCE KEYNOTE SESSION • Tuesday, February 26, 2019

1:55 **Chairperson's Remarks**

2:00 **Targets & Therapeutics: Lessons Learned from Humira and other TNF Antagonists**

The presentation will focus on the role of the underlying target biology for developing novel Biologics therapeutics using TNF and TNF antagonists as case study. I will discuss the evolution of Anti-TNF approaches, the history of adalimumab and will start to answer the question how to explain some of the apparent clinical differences between the Anti-TNF agents in clinical use today. In this context the learnings about TNF biology and the mechanism of action of TNF antagonists will be discussed and how those learnings impact the development of novel therapeutics.
Jochen G. Salfeld, Ph.D., Vice President, Global Biologics, **AbbVie Bioresearch Center,** *USA*

2:45 **Drug Discovery Driven by Antibody Engineering Technologies**

Previously, antibody engineering was mainly applied to improve the properties of a parent antibody by methods such as humanization, affinity maturation, stability engineering and half-life extension. Recent advances in antibody engineering have enabled us to conceive and realize novel antibody drug concepts. This presentation describes how antibody engineering technologies can drive the discovery of innovative antibody drugs.
Tomyuki Igawa, Ph.D., CEO and Research Head, **Chugai Pharmabody Research Pte. Ltd.,** *Singapore*

3:30 *Networking Refreshment Break*

4:00 **ADCs, Bispecifics, Cell Therapies and Oncolytic Virus Therapies: Daiichi Sankyo's Innovative Therapeutic Development Progress and Pipeline**

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

4:30 **How We Can Improve the Affinity of an Antibody**

Physicochemical approaches deepen our insights into antigen-antibody interactions. Recently, we have investigated how we can rationally improve the affinity of antibodies for the targets. Here I introduce our recent progress on engineering affinity of antibody based on physical biochemical approaches.
Kouhei Tsumoto, Ph.D., Professor and Director, Department of Bioengineering, Department of Chemistry and Biotechnology, **The University of Tokyo,** *Japan*

5:00 *Close of Day One*

6:00 **Networking Dinner in Tokyo**
Network with fellow Antibody Engineering & Therapeutics Asia attendees from around the world by attending this Networking Dinner event at S Tokyo restaurant. Sign up to attend this optional dinner by selecting this dinner option during registration (additional fee required)

8:00 *Registration and Coffee*

Design, Engineering and Selection Strategies to Improve Antibody Properties

8:55 **Chairperson's Remarks**

9:00 **Novel Strategies for the Construction of Yeast Surface Display Antibody Fab Libraries and for the Selection of Binders with Prescribed Properties**

A novel streamlined approach for rapid construction of large yeast surface display antibody libraries will be presented that allows for simultaneous introduction of heavy- and light chain diversities into one display plasmid. Moreover, selection strategies for the isolation of antibodies with prescribed properties will be described (e.g epitope coverage, species-crossreactivity).

Stefan Zielonka, Ph.D., Associate Director, Protein Engineering & Antibody Technologies, **Merck KGaA/EMD Serono,** *Germany*

9:30 **Engineering Antibodies in Mammalian Cells by Combining Genome Editing with Next-generation Sequencing**

We have recently established a technique known as homology-directed mutagenesis (HDM), which is able to generate mutagenesis libraries directly in mammalian cells using CRISPR-Cas9. In HDM, we introduce genetic diversity into target proteins (e.g., antibodies) by using single stranded oligonucleotides (ssODNs), which serve as DNA donor templates following Cas9-induced DNA cleavage. We combined HDM with next-generation sequencing, which enables several of the most essential methods of antibody engineering to be performed in directly in mammalian cells expressing full-length IgG.

Sai Reddy, Ph.D., Assistant Professor, **ETH Zurich,** *Switzerland*

10:00 **Assessing the Molecular Properties of mAb Clones at Early Lead Selection Stage in cellulo by Using the ER as a Physiological Test Tube**

Have you selected promising lead mAb clones only to find out later during pre-formulation stage that they have poor solubility issues? How can we avoid costly mistakes of selecting physicochemically unfavorable mAb clones and unknowingly advancing such mAbs in drug discovery/development pipeline? Are there any rational approaches? In this talk, I will illustrate the predictive values of overexpression-induced cellular phenotypes in assessing high concentration solution behaviors of individual mAb clones. By examining the biosynthetic steps of various human IgG mAbs for which prominent solution behavior problems were known (e.g., aggregation, crystallization, gelation, LLPS, cryoprecipitation, viscosity, agitation sensitivity, etc.), we found that condensation-prone IgG mAbs induces three types of prominent cellular phenotypes during mAb overexpression. Apparent correlations between solution behaviors in vitro and biosynthetic events in the endoplasmic reticulum (ER) can be leveraged to identify unfavorable mAb clones that are not suitable for high-level expression and high concentration liquid formulation. Our approach paves the way for a preemptive elimination of unfavorable mAb clones from the lead panel from the very beginning, at an early transient expression testing stage even without protein purification.

Haruki Hasegawa, Ph.D., Principal Scientist, Biologics - Therapeutic Discovery, **Amgen, USA**

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

11:15 **Generating Potent and Selective Inhibitors of Kv1.3 Ion Channel by Fusing Venom Derived Mini Proteins into Peripheral CDR Loops of Antibodies**

Pathogenic T cell effector memory (TEM) cells drive many autoimmune disorders and are uniquely dependent on the Kv1.3 channel. A number of venom derived cysteine-rich mini-protein inhibitors of Kv1.3 are being developed as potential drug candidates, but can suffer from manufacturing difficulties, short half-lives and a lack of specificity. We have developed a novel molecular format wherein a peripheral CDR loop of an antibody has been replaced by a cysteine-rich mini protein. In this novel format, the mini-protein benefits from the half-life of an antibody and the antibody gains additional diversity by the addition of a scaffold which is pre-disposed to blockade of ion channels. We have used this format to develop a panel of low-nM Kv1.3 inhibitors with selectivity exceeding 400-fold on Kv1.1, a close homologue.

John McCafferty, Ph.D., Founder and CEO, **IONTAS,** *United Kingdom*

Scientific Briefing

11:45 **Uncovering Critical Receptors and Assessing Target Specificity of Biotherapeutics**

Historically, deconvoluting the targets of phenotypic molecules has presented a major challenge in drug development due to the low likelihood of successfully identifying a primary receptor coupled with the high rate of false positive results that could be generated. However, efficient identification of the true cell surface targets of antibodies and other ligands is now possible through the use of highly specific cell microarray screening. Thousands of cDNAs encoding individual full-length human receptors are spotted onto microarray slides and overlaid with human cells. The cells become reverse-transfected, expressing the protein encoded by the vector beneath. Binding of a test ligand to one of these over-expressed cell surface proteins is identified and the specific interaction with the target receptor validated. Extensive cDNA libraries currently cover around 75% of the plasma membrane proteome, with representation from all major sub-classes including GPCRs, receptor kinases, Ig superfamily receptors and ion channels, among others. This presentation describes the use of cell microarray technology in both primary receptor identification and in off-target profiling. Data for a variety of ligands (including antibodies, proteins, peptides, engineered cells and small molecules), will provide examples relevant to lead selection of phenotypic antibodies, the discovery of novel immunotherapy targets and the generation of data which supports safety assessment prior to IND submissions.

Mark Aspinall O'Dea, Ph.D., EMEA Business Development Manager, **Retrogenix,** *United Kingdom*

Delivery Strategies to Overcome Biological Barriers

12:15 **Tumor-Specific Cell-Penetrating Antibodies: Engineering and Applications**

Cell-penetrating biologics are primed to target previously undruggable proteins. However, translating this technology into therapeutic agents remains challenging, due to non-specific tissue distribution. At Orum, we have developed a cell-penetrating antibody, which specifically internalizes into the cytosol of cancer cells and selectively binds to the activated GTP-bound form of various oncogenic Ras mutants. This talk will cover the engineering and application of cell-penetrating antibodies for direct Ras targeting.

Sung Joo Lee, Ph.D., Founder and Executive Officer, **Orum Therapeutics,** *South Korea*

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

1:55 **Chairperson's Remarks**

Yong-Sung Kim, Ph.D., Professor, Department of Molecular Science and Technology, **Ajou University,** *South Korea*

2:00 **RNAntibody as a Therapeutic Option**

The delivery of mRNA is emerging as a promising alternative to the use of recombinant proteins when applied to protein therapies. We demonstrate that mRNA can be used for the delivery of a variety of therapeutic antibodies to treat various indications.

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

2:30 **BBB-Crossing Trojan Horse Bispecific Antibody Targeting Alpha-synuclein for Parkinson's Disease**

Parkinson's Disease (PD) is the second most frequent neurodegenerative disease globally. The main hurdles are the lack of a PD-specific mechanism of action to target and of efficient BBB (blood-brain barrier)-penetration strategies. Immunotherapy against critical targets in the brain has been proposed as a strategy. ABL has harnessed its BsAb platform to develop a bispecific antibody (BsAb) that would first target a PD-specific disease mechanism—namely, the formation of extracellular synuclein aggregates in PD—and maximize BBB penetrance by targeting a novel receptor-mediated transcytosis (RMT) receptor on brain endothelial cells. The result is ABL301, a first-in-class BsAb for PD. ABL301 is a first-in-class BsAb for PD and its main differentiation to others is improved BBB penetration and anti-alpha-synuclein antibody that is highly selective to aggregated alpha-syn. The efficacy was confirmed with various in vitro and in vivo tests in cell- and PD animal models. The main mechanisms include reduction in alpha-syn burden, facilitation of microglial uptake/clearance of alpha-syn aggregates, inhibition of cell-to-cell transmission, reduction in neuroinflammation and increase in neuroprotection. ABL301's BBB shuttle antibody improved BBB penetration, thus resulted in more brain and CSF penetration than anti-alpha-synuclein MoAb. The work conducted with ABL301 underscores ABL's commitment to develop novel, BsAb-based therapeutic strategies to overcome BBB penetrance.

Weon-Kyoo You, Ph.D., Vice President and Head of R&D, **ABL Bio,** *South Korea*

Immuno-Oncology

3:00 **Targeting CD47 with Superior Efficacy/Safety Profile**

CD47/SIRPalpha interaction is critical in regulating macrophage function in tumor microenvironment. In recent studies, CD47 blockade had generated promising results in suppressing tumor progression, especially in blood cancers. However, the broad expression profile of CD47 has always been a concern in anti-CD47 approaches. CD47 molecules are highly expressed not only in various of cancers, but also in normal tissues/organs such as brain, bladder, etc. Its level on red blood cells are ubiquitously high, therefore anemia had been frequently observed in preclinical and clinical applications. We designed a bispecific antibody to selectively bind to cancer cells to prevent off-tissue toxicity. Moreover, the bispecific antibody displayed synergy between two targeted pathways related to innate and adaptive immunity, respectively. More detailed data regarding this molecule will be shown in the presentation. In addition, an update on the progress of IBI308, our lead anti-PD1 antibody will be presented.

Junjian Liu, Ph.D., VP, Head of Drug Discovery & Preclinical Development, **Innovent Biologics,** *China*

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

MAIN CONFERENCE • Wednesday, February 27, 2019 (continued)

4:00 **Selection and Development of Potent T cell Receptors for Cancer Immunotherapy**

T cell receptor (TCR)-based immunotherapy is emerging as a promising treatment modality for malignant diseases. Our proprietary target platform XPRESIDENT® discovers human leucocyte antigen (HLA)-bound tumor-associated peptides, while our TCR platform XCEPTOR® generates highly cancer-specific TCRs towards these novel and validated tumor targets. This TCRs are further developed towards adoptive cell therapy applications or engineered into our highly active bispecific TCR scaffold comprising a T cell-engaging antibody for potent redirection and activation of T cells.

Dominik Maurer, M.D., Vice President, Immunology, **Immatics Biotechnologies GmbH,** *Germany*

4:30 **Benchmarking T Cell-Redirecting Therapies for Cancer: Comparing CD3-Bispecifics and CAR T Cells**

The two leading platforms for redirecting a patient's T cells to recognize tumors, CD3-binding bispecific molecules and chimeric antigen receptor (CAR) T cells, both show clinical activity. We have developed pre-clinical in vitro and in vivo models to mechanistically compare these two technologies and will discuss our findings as well as the clinical implications.

David J. DiLillo, Ph.D., Staff Scientist, Immuno-Oncology, **Regeneron Pharmaceuticals**

5:00 **An Anti-PD-1 Antibody with or without FcγRI-Binding Has Profound Impact on Its Biological Functions**

Most of the anti-PD-1 antibodies used in clinical studies are of IgG4 isotype with the S228P mutation ($IgG4_{S228P}$). The functional impact by the interaction of anti-PD-1 $IgG4_{S228P}$ antibody with Fc gamma receptors (FcγRs) is poorly understood. We have systematically studied the impact of FcγRI-engagement to anti-PD-1 antibody by comparing a pair of anti-PD-1 antibodies, BGB-A317/$IgG4_{S228P}$ and BGB-A317/IgG4-variant (abbreviated as BGB-A317), with the same variable regions but two different IgG4 Fc-hinge sequences through in vitro and in vivo functional assessment. The results suggested that FcγRI-binding and crosslinking exerts negative impact on the anti-PD-1 antibody-mediated T-cell stimulation function, potentially, attenuating anti-cancer activities.

Kang Li, Ph.D., SVP, Head of Biologics, **BeiGene Co. Ltd.,** *China*

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

6:30 *Close of Day Two*

MAIN CONFERENCE • Thursday, February 28, 2019

7:45 *Registration and Coffee*

8:10 **Chairperson's Remarks**

Antibody-Drug Conjugates

8:15 **Development of Novel Payloads for Oncology ADC Applications**

A limited number of natural product families have been successfully utilized as ADC payloads. Selection of the novel ADC warhead is a challenging process. One of the challenges is often to determine the appropriate linker attachment position on a molecular scaffold, where no SAR or very limited SAR data exists. Another challenge is synthetic linker incorporation into original natural product to enable rapid assessment in ADC format. The aim is to avoid labor, time and resource intensive total synthesis or protection/deprotection strategies. We will discuss several natural product families and focus in particular on the development of novel linker attachment strategy to α-amanitin and evaluation of corresponding ADCs in vitro and in vivo.

Julia Gavrilyuk, Ph.D., Associate Director, Discovery Chemistry, **AbbVie Stemcentrx,** *USA*

8:45 **Creating Next Generation ADCs with Industry Leading DAR Precision and Plasma Stability**

LegoChem Biosciences (LCB) has developed a novel, next-generation site-specific antibody-drug conjugates (ADCs) platform which enables the generation of homogenous ADCs with specifically defined number of payload only at the intended sites on the antibody employed. LCB presents an enzymatic conjugation platform and a proprietary cleavable linker chemistry which overcome limitations of existing ADC approaches including heterogeneity and demonstrate unprecedented plasma stability and efficient and traceless payload release only within the cancer cells.

Jeiwook Chae, Ph.D., Chief Business Development Officer, **LegoChem Biosciences,** *South Korea*

9:15 **Development of Antibody-Drug Conjugates (ADCs) Utilizing DDS and Molecular Imaging**

Antibody-drug conjugate (ADC), as the next generation of antibody therapeutics, is a combination of an antibody and a drug connected via a specialized linker. ADC has four action steps: (1) systemic circulation, (2) the enhanced permeability and retention (EPR) effect, (3) penetration within the tumor tissue, and (4) action on cells, such as through drug delivery system (DDS) drugs. An antibody with a size of about 10 nm has the same capacity for passive targeting as some DDS carriers, depending on the EPR effect. In addition, some antibodies are capable of active targeting. A linker is stable in the bloodstream but should release drugs efficiently in the tumor cells or their microenvironment. Thus, the linker technology is actually a typical controlled release technology in DDS. Here, we focused on molecular imaging. Fluorescent and positron emission tomography (PET) or single photon emission computed tomography (SPECT) imaging is useful for the visualization and evaluation of antibody delivery in terms of passive and active targeting in the systemic circulation and in tumors. To evaluate the controlled release of the ADC in the targeted area, a mass spectrometry imaging (MSI) with a mass microscope as a new type of matrix-associated laser desorption/ionization (MALDI)-MSI analyzer, to visualize the drug released from ADC, was used. Currently, we are also developing a new drug imaging method using electrospray ionization (ESI)-MSI. Now, we have succeeded in developing several ADCs against refractory cancer. Amongst them, anti-IL-7R-ADC has a unique mode action of mechanisms (MOAs), 1) anti-steroid-resistance and 2) anti-homing activity. It can be used for immunoregulation in both lymphoid malignancy and autoimmune diseases. Thus, we will present our recent work of ADC development utilizing DDS and molecular imaging.

Masahiro Yasunaga, M.D., Ph.D., Unit leader, Division of Developmental Therapeutics, Exploratory Oncology Research & Clinical Trial Center, **National Cancer Center,** *Japan*

9:45 *Networking Refreshment Break with Exhibit and Poster Viewing*

10:15 **Development of CCAP Method to Modify Antibody Site-specifically**

CCAP (chemical conjugation by affinity peptide) is a technology to modify antibody/protein site-specifically using affinity peptide to target antibody/protein. For antibody modification, we employed a disulfide-linked peptide composed of 17 amino acids which recognize the marginal region between CH2 and CH3 of Fc in human IgG. The 8th Lys residue of the peptide was modified with DSG (disuccinimidyl glutarate) and used for the modification of Fc to form the covalent linkage with the side chain of Lys 248 on Fc. This reaction proceeded rapidly and quantitatively to produce one or two adducts. This site-specific modification system of antibody through the affinity peptide connected with the functional ligands was applied for the generation of highly functional antibody conjugates including ADC (Antibody-drug conjugate), antibody diagnostic drug for PET imaging or bivalent antibody therapeutics.

Yuji Ito, Ph.D., Professor, Department of Chemistry and Bioscience, Graduate School of Science and Engineering, **Kagoshima University,** *Japan*

10:45 **ADC Case Study**

Akiko Zembutsu (Nagase), Ph.D., Senior Researcher, Group I, Biologics & Immuno-Oncology Laboratories, **Daiichi Sankyo Co., Ltd., Japan**

Preclinical and Clinical Case Studies

11:15 **UCB Antibody Engineering: Matching Molecule to Clinical Need**

David Humphreys, Ph.D., Director, Antibody Biology, **UCB-New Medicines,** *United Kingdom*

11:45 **Sponsored Scientific Briefing Opportunity**

This sponsored presentation opportunity is available for companies who have an exciting antibody technology or application that they are interested in sharing during a presentation in the conference sessions. For more information and pricing, please contact Aimee Croke at Tel: +1- 857-504-6697; Email: Aimee.Croke@Knect365.com or Kristin Skahan at Tel: +1-857-504-6730 or kristin.skahan@knect365.com

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

1:15 **Chairperson's Remarks**

Jijie Gu, Ph.D., Head of Target Validation, Immunology Discovery, **Abbvie Cambridge Research Center,** *USA*

1:30 **Generation and Characterization of Novel Bispecific Antibody against TLR2 and TLR4, As Potential Therapeutics for Sepsis**

TLR2 and TLR4 play an important role in innate immune system and are the notable contributors to the pathogenesis of infection-associated sepsis. We have developed a potent anti-TLR2 and TLR4 bispecific antibody for treatment of sepsis. In this presentation, the preclinical data of our TLR2/TLR4 bispecific antibody will be presented.

Masahito Sato, Senior Researcher, **Astellas Pharma, Inc.,** *Japan*

2:00 **Antibody Presentation Title TBA**

Shigeru Iida, Ph.D., Director, Antibody & Biologics Research Laboratories, **Kyowa Hakko Kirin Co., Ltd.,** *Japan*

Bispecific Antibodies and Multi-Functional Biologics

2:30 **Unlocking Cancer Therapy**

The favorable biophysical and immunogenicity properties of DARPin® drug candidates enable the straight-forward generation of multi-functional biologics. We took advantage of this and generated several well-behaved drug candidates that unlock restrictions of current cancer therapy. One example is MP0250, a dual VEGF/HGF inhibitor, for which early PhII clinical data indicate it could help overcoming drug resistance in cancer therapy. Another approach was chosen for MP0310, a FAP-targeted 41BB immune cell modulator, in that it was designed to allow for boosting the efficacy of existing cancer therapeutics, enabling novel treatment options.

H. Kaspar Binz, Ph.D., Vice President and Co-Founder, **Molecular Partners AG,** *Switzerland*

3:00 **A Tetravalent Bispecific Antibody with Strong Activity in Inducing Target Degradation and Tumor Regression**

By targeting multiple disease mediators simultaneously, bispecific antibodies (bsAb) show distinguished clinical benefit compared to monoclonal antibodies (mAbs). Various bsAb structures have been described and several being investigated for clinical usage. We have developed a new bispecific design, named Fabs-in-tandem immunoglobulin (FIT-Ig), in which two Fabs are fused directly in a crisscross orientation without any mutations or use of peptide linkers. This unique tetravalent design provides a symmetrical IgG-like bispecific molecule with correct association of 2 sets of VH/VL pairs, exhibiting excellent drug-like properties, in vitro and in vivo functions, as well as manufacturing efficiency for commercial development. EMB-01 is a FIT-Ig molecule targeting both cMet and EGFR and shows strong tumor inhibition in various PDX tumor models as well as a unique activity in inducing degradation of both target receptors. EMB-01 is current in Phase I development.

Chengbin Wu, Ph.D., Chairman & CEO, **Shanghai EpimAb Biotherapeutics,** *China*

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

4:00 **WuXiBody™, An Innovative and Potentially One-size-fits-all Bispecific Antibody Format to Open a New Gate for Therapeutic Bispecific Antibody Development**

Bispecific antibodies are growing to be a new category of therapeutic antibodies. They can bind two different targets or two different epitopes on a target, creating additive or synergistic effect superior to the effect of individual antibodies. A lot of antibody engineering efforts have been put into designing the bispecific formats. Some progress in the field has solved some of the issues, e.g. by introducing mutations in the Fc region, such as "knobs-into-holes", the preferred heterodimeric assembly of two different heavy chains has been accomplished. Many other attempts, such as DVD-Ig, CrossMab and BiTE etc. have also been tried. However, these formats may still have various limitations in yield, purity, stability, solubility, half-life, and immunogenicity. Therefore, there still is great need to design bispecific molecules with desirable developability profile and potentially one-size-fit-all to accommodate different needs of therapeutic bispecific antibody programs. Aiming to solve those issues, WuXi Biologics has generated WuXiBody™, an innovative proprietary bispecific antibody format, which has successfully solved the mismatching problem of Ab chains, contains Fc in the molecule to ensure IgG like long half-life in human and easy purification in downstream, has great flexibility to be engineered as either asymmetric or symmetric format and to accommodate different valence needs of bispecific molecules, and has fully human sequence in the backbone expecting low immunogenicity in human. It can be easily produced like normal IgG from CHO cell with high expression level (up to 16g/L), high purity (>95% from a single step purification), high solubility (>30 mg/ml in PBS), high stability (> 2 weeks at 37 °C in serum) and with normal T1/2 in monkey. The technical details and examples will be presented. This innovative bispecific antibody format will open a new gate for therapeutic bispecific antibody development.

Jing Li, M.D., Ph.D., Senior Vice President, Biologics Discovery, **WuXi Biologics,** *China*

4:30 **ND021, A Novel Multi-Specific Antibody Targeting PD-L1-overexpressing Cancers That Stimulates Antigen-committed CD8+ T cells through Concomitant Engagement of a T cell Costimulatory Receptor**

ND021 leverages Numab's next-generation multi-specific technology to elicit highly potent – but tumor-restricted – agonism of 4-1BB, while concomitantly blocking PD-L1. The trispecific anti-PD-L1/4-1BB/HSA ND021 is designed to avoid dose-limiting hepatotoxicities associated with IgG-mediated 4-1BB activation. Animal data strongly suggest that ND021 eliminates the tolerability/efficacy trade-off associated with stimulation of the costimulatory receptor 4-1BB, while eliciting strong anti-tumor responses.

David Urech, Ph.D., CSO and Co-CEO, **Numab AG,** *Switzerland*

5:00 **Humanized Anti-FIXa/FX Bispecific Antibody for the Treatment of Hemophilia A and Beyond**

Emicizumab is humanized anti-FIXa/FX bispecific antibody, which was approval for prophylactic treatment of persons with hemophilia A with inhibitors. In this presentation, I will introduce how emicizumab was created, its preclinical data and Phase III study data. In addition, novel antibody engineering to further improve the property of emicizumab will be presented.

Yuri Teranishi, Researcher, Lead Optimization Unit, **Chugai Pharmabody Research Pte. Ltd.,** *Singapore*

5:30 *Close of Conference*