Antibody Engineering & Therapeutics Europe

European Meeting of the ANTIBODY SOCIETY

11-13 June, 2019
Postillion Hotel Amsterdam, Amsterdam, The Netherlands

BRINGING YOU THE LATEST SCIENCE, TECHNOLOGIES AND PARTNERS NEEDED TO ACCELERATE NEXT GENERATION ANTIBODIES TOWARDS COMMERCIAL SUCCESS

Keynote Luminaries to Inspire Your R&D Efforts

Lgr5 Stem Cell Based Organoids and Their Applications in Cancer Research

Hans Clevers, M.D., Ph.D.
Professor of Molecular Genetics,
Hubrecht Institute, *The Netherlands*

Mining the Immune Repertoire of Mice with Fully Human Immunoglobulin Loci for Therapeutic Human Antibodies

Allan Bradley, Ph.D.
Chief Scientific Officer,
Kymab Limited, *United Kingdom*

Antibody Therapeutic Developments, Pipeline and Progress at MedImmune

Jane Osbourn, Ph.D.
Vice President, Research and Development and Site Leader,
MedImmune, *United Kingdom*

Bispecific Antibodies and Beyond: The Magic Bullet Revisited

Ton Logtenberg, Ph.D.
President and CEO,
Merus N.V, *The Netherlands*

Produced by the Organizers of the Antibody Engineering & Therapeutics San Diego Event

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THE INDUSTRY'S EUROPEAN MEETING FOR ANTIBODY AND PROTEIN THERAPEUTIC SCIENCE, TECHNOLOGY AND NETWORKING

SCIENCE

Accelerate your pipeline of antibody and protein therapeutics to market by applying best practices and lessons learned from case studies and new data presentations from global industry leaders working across the entire spectrum of antibody discovery and development.

TECHNOLOGY

Bring your product to market by meeting leading product and service providers showcasing exciting antibody technologies in our poster and exhibit hall.

NETWORKING

Connect with industry and academic scientists and executives from Europe and around the world focused on antibody and protein therapeutic discovery and development during luncheons, cocktail receptions and networking breaks. Networking has never been easier with the included conference app that allows you to view the attendee list and schedule meetings before, during and after the event.

Tuesday, 11 June, 2019 • Pre-Conference Workshops*

*Additional registration fee applies. See the pricing page or visit the website for more details.

08:00 *Registration and Coffee*

Morning Half-Day Workshop • 08:40-12:15

Workshop A: Bispecific Antibodies: New Strategies and Case Studies

08:40 **Workshop Moderator's Remarks**

Aran Labrijn, Ph.D., Principal Scientist, Antibody Research and Technology, **Genmab,** *The Netherlands*

08:45 **Bispecific Antibodies: History and (Future) Promises**

Since the concept of a man-made bispecific antibody was originally described (almost 60 years ago), many technical and conceptual advances have led to the extensive bispecific antibody landscape known today. A short historical perspective will be given, including discussion of the different bispecific antibody classes, the unique opportunities for dual-targeting and the (current) challenges facing the (pre-) clinical development of bispecific antibodies.

Aran Labrijn, Ph.D., Principal Scientist, Antibody Research and Technology, **Genmab,** *The Netherlands*

09:15 **Bispecific Target Discovery by High Throughput Functional Screening of Hundreds of Combinations of Different Target Pairs**

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 in functional human cell assays large numbers of bispecific antibodies. 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.

Laura Starkie, Ph.D., Principal Scientist, Bispecific Target Discovery, **UCB,** *United Kingdom*

09:45 **The Use of Unbiased Screens to Identify Bispecific Antibodies with a Unique Mode of Action**

Target-based drug discovery based on disease modelling and pathway analysis mainly focusses on a design approach for bispecific antibodies. Our strategy uses an unbiased approach with a functional readout that allows the discovery of bispecific antibodies with unique features and biology. The process of functional screening to lead bispecific antibody of several of our clinical candidates will be described in this presentation.

Cecile Geuijen, Ph.D., Vice President, Oncology, **Merus,** *The Netherlands*

10:15 *Networking Refreshment Break*

10:45 **The Immunology Underlying CD3-bispecific Antibody Treatment**

Immunotherapy of cancer with CD3-targeting bispecific antibodies (CD3 bsAb) is a very promising strategy, also for solid malignancies. Xenograft mouse models often fail to fully recapitulate the natural tumor microenvironment, and therefore we investigated the immunological consequences of CD3 bsAb therapy in fully immune-competent mouse tumor models.

Thorbald van Hall, Ph.D., Associate Professor, Medical Oncology, **Leiden University Medical Center,** *The Netherlands*

11:15 **Dual Targeting Approach Using Complementary Hemi-Bodies**

Antigens suitable for T cell redirecting strategies against cancer are scarce. Consequently, we developed an antibody derivative, which comes in two complementary halves and addresses antigen combinations instead of single molecules. Each half contains an antigen specific scFv fused to either the VL or VH domain of an anti-CD3 antibody. When these two hemibodies bind their respective antigens on a cancer cell, they reconstitute "on target" the original CD3-binding site to engage T lymphocytes.

Gernot Stuhler, M.D., Immunotherapy Lab, **University Hospital Würzburg,** *Germany*

11:45 **J-chain Based Bispecifics: IgM CD20xCD3**

Bruce Keyt, Ph.D., Chief Scientific Officer, **IGM Biosciences, Inc.,** *USA*

12:15 *Close of Workshop A*

12:20 *Luncheon Provided for Full-Day Workshop Attendees Only (Those registered for both workshop A and workshop B)*

Afternoon Half-Day Workshop • 13:40-17:15

Workshop B: Antibody-drug Conjugates (ADCs): New Strategies and Case Studies

13:40 **Workshop Moderator's Remarks**

Esther Breij, Ph.D., Director of Translational Research, **Genmab,** *The Netherlands*

13:45 **Insights into Conjugation Processes Employed in the Development of Therapeutic ADCs**

Conjugation strategies are of great importance in the successful design and development of effective ADCs. The impact of current conjugation technologies on ADC stability, therapeutic index and pharmacokinetics will be discussed. Additionally, challenges and advancements in techniques for chemical modification of antibodies will be explored.

Justyna Mysliwy, Ph.D., Bioconjugation Team Leader, **Iksuda Therapeutics Ltd.,** *United Kingdom*

14:15 **Challenges in Process Development of Antibody-drug Conjugates (ADCs)**

Synthon's ADC technology aims to create ADCs having an optimal therapeutic window, balancing the effect of potent cell-killing agents on tumor cells versus healthy cells. Case studies will be presented of various ADCs in development together with challenges which are observed during conjugation, purification and manufacturing.

Guy de Roo, Ph.D., Principle Scientist, **Synthon Biopharmaceuticals BV,** *The Netherlands*

14:45 **The Pyrrolobenzodiazepine (PBD) Dimer Class of ADC Warhead**

The rationally designed PBD dimers have emerged as an important class of ADC warhead which exert their activity through forming highly cytotoxic DNA interstrand cross-links in the DNA minor groove. This presentation will describe how an understanding of structure activity relationships has enabled this flexible platform to be tailored to individual requirements in novel ADCs..

John A. Hartley Ph.D., Professor of Cancer Studies, **University College London** and Director of Pre-clinical Development, **Spirogen Ltd,** *United Kingdom*

15:15 *Networking Refreshment Break*

15:45 **Preclinical Development of Enapotamab Vedotin - Opportunities in Treatment Resistant Solid Cancers**

The presentation will provide an overview of the preclinical anti-tumor activity of enapotamab vedotin in (treatment-resistant) preclinical models for melanoma and NSCLC.

Esther Breij, Ph.D., Director of Translational Research, **Genmab,** *The Netherlands*

16:15 **Development of Highly Potent Pyrrolobenzodiazepine Based ADCs from Bench to Clinic: Challenges and Lessons Learned** NEW DATA

Pyrrolobenzodiazepine (PBD) dimers represent a promising new class of toxins for the development of antibody drug conjugates (ADCs). More than a dozen PBD-based ADCs are currently in various stages of clinical development for the treatment of various malignancies. This presentation will highlight some experiences when developing PBD-based ADCs from bench to clinic.

Patrick H. van Berkel, Senior Vice President, Research and Development, **ADC Therapeutics,** *United Kingdom*

16:45 **ADC Technologies, Strategies to Improve Therapeutic Index and Efficacy**

Today's ADCs utilize different antigen targets, conjugation technologies, and payload warheads of various mechanisms such as tubulin inhibitors, DNA damaging, topoisomerase inhibition, or DNA polymerase II inhibitors. The main challenge remains to reach desirable efficacious doses due to the toxicity profile. Advanced methods to improve therapeutic index, including increasing ADC hydrophilicity, are presented.

Juhani Saarinen, Chief Executive Officer, **Glykos Finland Oy**

17:15 *Close of Workshop B*

Wednesday, 12 June, 2019 • Main Conference • Keynote Presentations

07:30 *Registration, Breakfast and Exhibit/Poster Viewing*

08:15 **Chairperson's Remarks**

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

08:20 **Lgr5 Stem Cell Based Organoids and Their Applications in Cancer Research**

Stem cells are the foundation of all mammalian life. Stem cells build and maintain our bodies throughout life. Every organ in our body is believed to harbor its own dedicated stem cells. These adult stem cells replace tissue that is lost due to wear and tear, trauma and disease. Adult stem cells are highly specialized and can only produce the tissue in which they reside; they ae 'multipotent'. Examples are bone marrow stem cells that make all blood cells, skin stem cells and gut stem cells. Even the brain is now known to harbor its specialized stem cells. The adult stem cells allow us to live 80-90 years, but this comes at a cost: they are the cells that most easily transform into cancer cells. We have identified a gene (lgr5) that marks a series of known and novel adult stem cells, in organs such as the gut, the liver, the lung and the pancreas. We have learned to grow these stem cells in a dish into mini-versions of the human organs from which they derive. This so called organoid technology opens a range of avenues for the study of development, physiology and disease, and for personalized medicine. In the long run, cultured mini-organs may replace transplant organs from donors and hold promise in gene therapy.

Hans Clevers, M.D., Ph.D., Professor of Molecular Genetics, **Hubrecht Institute,** *The Netherlands*

08:55 *Keynote Questions*

09:00 **Antibody Therapeutic Developments, Pipeline and Progress at MedImmune**

Putting antibody therapeutic development into context – the past, present and future. The presentation will exemplify the development of antibody therapeutics over the past 25-30 years and the classic challenges overcome; current pipeline examples from the MedImmune portfolio; and future capabilities that are beginning to unfold, including in silico design and phenotypic selections.

Jane Osbourn, Ph.D., Vice President, Research and Development and Site Leader, **MedImmune,** *United Kingdom*

09:35 *Keynote Questions*

09:40 *Networking Refreshment Break and Exhibit/Poster Viewing*

10:20 **Mining the Immune Repertoire of Mice with Fully Human Immunoglobulin Loci for Therapeutic Human Antibodies**

Mice with immunoglobulin gene repertoires constructed from human variable genes use conserved evolutionary mechanisms to elaborate an almost infinite repertoire of diverse and highly evolved antibodies. By implementing massively parallel sequencing of the B cell compartments and reconstructing the evolutionary history of every B-cell, rare therapeutic antibodies can be identified. Iterative screening of family members enables the identification of antibody-drugs with ideal biological activities and biophysical properties.

Allan Bradley, Ph.D. Chief Scientific Officer, **Kymab Limited,** *United Kingdom*

10:55 *Keynote Questions*

11:00 **Bispecific Antibodies and Beyond: The Magic Bullet Revisited**

Since monoclonal antibodies have proven to be successful therapeutics, technological advances have created new generations of antibody-based therapeutics. Among these, bispecific and other multivalent formats hold the promise of purveying improved targeting, novel modes of action and exciting new biology based on target combinations. This presentation focuses on recent advances of technologies and clinical trials exploring these new antibody formats.

Ton Logtenberg, Ph.D., President and CEO, **Merus N.V,** *The Netherlands*

11:35 *Keynote Questions*

11:40 **The Antibody Society Student/Postdoc Poster Competition Award Presentation**

11:50 Scientific Briefings

Synthetic DNA Technologies Enable Antibody Discovery and Optimization

Utilizing its proprietary DNA writing technology to create oligo pools, genes, and synthetic libraries, Twist Pharma, a division of Twist Bioscience, provides the biotechnology industry with an end-to-end antibody discovery solution. This solution includes (1) a panel of high diversity synthetic antibody libraries, (2) a proprietary human anti-GPCR antibody phage display library focused on this validated target class, and (3) a Twist Antibody Optimization (TAO) platform for antibody affinity and developability optimization.

Aaron Sato, Ph.D., Chief Scientific Officer, **Twist Bioscience,** *USA*

When the Power of Nature and Technology Meet: Overcoming Tolerance by Combining Repertoire Sequencing with Single-Cell Screening

Functional information about antibodies from single-cell screens can be combined with large datasets obtained from the same sample analyzed in parallel with repertoire sequencing. Overlaying these two datasets drastically expands the diversity of functionally annotated antibody sequences from a single campaign. We show how this combined approach can be applied to the discovery of antibodies against poorly immunogenic and highly homologous targets for therapeutic applications.

Jens Ruschmann, Ph.D., Senior Scientist and Project Lead, **AbCellera,** *USA*

12:20 *Networking Lunch and Exhibit/Poster Viewing*

13:30 Scientific Briefings

Computational Approaches for Optimizing the Developability of Biotherapeutics

mAb candidates often present liabilities for developability, such as aggregation-prone regions or poor solution behavior. We optimized an integrin α11 binding mAb using homology modeling and rational design where reducing hydrophobic surface patches improved HIC behavior. Retrospective data analysis demonstrates that 3D descriptors and multi-parameter models can screen candidates and enrich libraries with favorable developability properties for ranges of biotherapeutics.

Nels Thorsteinson, Scientific Services Manager, Biologics, **Chemical Computing Group,** *Canada*

Build Better Biologics with Machine Learning and Synbio

This presentation will showcase how ATUM combines recent developments in genome engineering, automation, big data and product analytics to increase efficiency of engineering and developability of biologics and cell lines. Cell lines generated using the LeapIn® transposase combined with optimized vector constructs, proprietary codon optimization and QSAR-based protein engineering allow for an information rich and efficient optimization of mAbs, bispecifics, CAR-T molecules, and the increasingly complex biologics approaching the market place.

Claes Gustafsson, Ph.D., Co-founder and Chief Commercial Officer, **ATUM**

High Throughput SPR Demonstrates that V-lambda Expressing OmniChickens™ Exhibit Broad Epitope Coverage and Picomolar Affinity

The generation of antibodies to therapeutic targets with high conservation between rodents and humans is a challenge. Because of their increased evolutionary distance from humans compared to rodents, chickens are an ideal species to circumvent this challenge. Here we introduce a new line of OmniChickens™ which express VL1-44. The use of high throughput SPR allowed us to tease out more subtle relationships between antibodies in a given epitope bin. The analysis of large cohorts of antibodies in a single experiment against a model antigen in the different OmniChicken lines is an important metric in assessing the immune repertoire of our birds.

Kathryn Ching, Ph.D., Senior Scientist, **Ligand Pharmaceuticals,** *USA*

Track 1: New Antibody Formats and Effector Functions

14:00 **Co-Chairs' Remarks**

Jeanette L. Leusen, Ph.D., Associate Professor, Head Immunotherapy Group and UMAB Facility, Laboratory for Translational Immunology, **UMC Utrecht,** *The Netherlands*

Matthias Peipp, Ph.D., Professor and Head of Research, Division of Stem Cell Transplantation and Immunotherapy, **Christian-Albrechts-University Kiel,** *Germany*

14:05 **Understanding Fc Receptor: Antibody Interactions for Improved Cancer Therapy**

It is clear that Fc receptors mediate and modulate the efficacy of antibody immunotherapeutics. It is also clear that the tumour microenvironment can regulate Fc receptor expression patterns. In this presentation I will discuss data relating to these two areas and how knowledge gained can help to deliver more effective immunotherapy

Mark Cragg, Ph.D., Chair in Experimental Cancer Biology, Centre for Cancer Immunology, **University of Southampton and Southampton General Hospital,** *United Kingdom*

14:35 **Engineered Fc Domains with Exquisite Selectivity for a Single FcγR**

George Georgiou, Ph.D., Professor, Laura Jennings Turner Chair in Engineering, Department of Chemical Engineering, **The University of Texas at Austin,** *USA*

15:05 **Design of Antibodies for Better Performance**

The half-life of the two most abundant proteins in blood, IgG and serum albumin, is roughly 3 weeks. This has made IgG the natural choice for design of antibody therapeutics, while albumin is increasingly used as a fusion partner. Remarkably, the half-life of these unrelated proteins is prolonged by a common receptor, FcRn. I will present strategies for design of novel albumin and antibody molecules with improved functions that may translate into new biologics.

Jan Terje Andersen, Ph.D., Group Leader and Associate Professor, Department of Immunology, **Oslo University Hospital,** *Norway*

15:35 *Networking Refreshment Break and Exhibit/Poster Viewing*

16:15 **IgA Is a Novel Isotype to Treat Lymphoma and Neuroblastoma, and Is Enhanced by CD47/SIRPa Checkpoint Inhibition**

All mAb immunotherapy in the clinic are of the IgG isotype, but IgA has a distinct mode of action, that might overcome some disadvantages of IgG. We have explored the effectiveness of IgA in preclinical models for lymphoma and neuroblastoma. For neuroblastoma, IgA has the extra advantage that the most important side effect, neuropathic pain is abrogated. Furthermore, we show enhancement of IgA therapy by innate checkpoint inhibition of CD47 or SIRPa.

Jeanette L. Leusen, Ph.D., Associate Professor, Head Immunotherapy Group and UMAB Facility, Laboratory for Translational Immunology, **UMC Utrecht,** *The Netherlands*

16:45 **Boosting Immune Effector Function Using Novel Immunocytokines and Targeted 4-1BB Agonists**

In this presentation an overview of the application of recent antibody engineering technologies to enhance immune effector function of T cell bispecific antibodies using novel generation immunocytokines and targeted immunomodulatory antibody fusion proteins will be given.

Christian Klein, Head Oncology Programs & Department Head Cancer Immunotherapy Discovery, Roche Pharmaceutical Research & Early Development, **Roche Innovation Center Zurich,** *Switzerland*

17:15 **Darpin-based Agents and Intra-tumoral Delivery**

Andreas Plückthun, Ph.D., Professor and Director, Department of Biochemistry, **University of Zürich,** *Switzerland*

17:45 *Networking Cocktail Reception and Exhibit/Poster Viewing*

Track 2: Recent Advances in Immuno-Oncology Approaches

14:00 **Co-Chairs' Remarks**

John Anderson, Ph.D., Deputy Head of Programme and Professor of Experimental Paediatric Oncology, **UCL Great Ormond Street Institute of Child Health,** *United Kingdom*

Paul W.H.I. Parren, Ph.D., Professor, Leiden University Medical Center and EVP, Research & Development, **Lava Therapeutics,** *The Netherlands*

14:05 **Small Molecule Targeting of the CD47 Myeloid Checkpoint**

CD47 serves as a "do not eat me" signal for myeloid cells by binding to the inhibitory receptor signal-regulatory protein alpha (SIRPα). Using a haploid genetic screen, we have identified an enzymatic modifier of the SIRPα binding site on CD47. Both genetic and pharmacological interference with enzyme activity enhances both antibody-dependent cellular phagocytosis and antibody-dependent cellular cytotoxicity of tumor cells. Furthermore, interference with enzyme activity leads to a major increase in neutrophil-mediated tumor cell killing in vivo. These data identify a novel target to interfere with the CD47 pathway, and thereby augment antibody therapy of cancer.

Ton N. Schumacher, Ph.D., Professor of Immunotechnology, **Leiden University** and Principal Investigator, **The Netherlands Cancer Institute,** *The Netherlands*

14:35 **Redirecting T-cells for Cancer Immunotherapyusing Next Generation Bispecific Antibodies and Fusion Proteins** NEW DATA

This talk will discuss a new generation of therapeutic approaches to redirect and enhance T cells attack on cancer cells. The approaches are based on combinations of "off-the-shelf", systemically administered, recombinant proteins that have been engineered to enhance their activity for stimulating T cells in tumors and/or lymph nodes vs. normal tissues.

Pablo Umaña, Ph.D., Head Oncology Discovery, Cancer Immunotherapies, **Roche Innovation Center Zurich,** *Switzerland*

15:05 **Bispecific γδ-T cell Engagers for Cancer Immunotherapy**

Vγ9Vδ2-T cells constitute the largest γδ-T cell subset in human peripheral blood and are powerful anti-tumor immune effector cells that can be identified in many different tumor types. This presentation will discuss bispecific antibodies designed to engage Vγ9Vδ2-T cells and their use for cancer immunotherapy.

Hans van der Vliet, M.D., Ph.D., Chief Scientific Officer, **Lava Therapeutics BV,** *The Netherlands*

15:35 *Networking Refreshment Break and Exhibit/Poster Viewing*

16:15 **CAR-engineering Approaches Using Gamma Delta T Lymphocytes**

Gamma delta T cells combine features of both innate and adaptive immunity and act as a first line of defence against infection. Their role in cancer is less clearly defined but there is strong evidence for their natural residence in the solid tumour niche, and a role in immune surveillance. We have adopted engineering approaches to exploit the capacity of gamma delta T cells to sense cancer and invest them with enhanced effector function through use of chimeric costimulatory receptors.

John Anderson, Ph.D., GOSHCC Professor of Experimental Paediatric Oncology and Honorary Consultant Oncologist, **UCL Great Ormond Street Institute of Child Health,** *United Kingdom*

16:45 **TEGs - αβT cells Engineered to Express a Defined γδTCR – The Next Generation of CAR T**

γδ T cells do frequently not depend on HLA context for tumor recognition, and display potent cytotoxicity toward a surprisingly large array of tumors, while preserving normal tissues. However, this potential is hampered by a huge diversity in activities of individual clones as well as individual receptors expressed by γδT cells. The critical role of γδTCR in determining the specificity of response remains a major unifying feature of γδ T cells. This allows exploiting tumor-specific γδTCRs out of the context of primary γδT cells, thereby overcoming major weaknesses of γδT cells in advanced cancer patients, such as proliferation deficiency or rapid deletion. By utilizing αβT cells engineered to express a defined γδTCR (TEGs) as a next generation of CAR-T the best aspects of the two worlds are combined, such as memory formation and high proliferation capacity of αβT cells, and the broad anti-tumor reactivity of defined γδTCRs.

Jürgen Kuball, M.D., Professor, Department of Hematology, **UMC Utrecht** and Scientific Co-founder and Scientific Advisor, **Gadeta,** *The Netherlands*

17:15 **iNKT Cell Immunotherapy in Allogeneic Stem Cell Transplantation and Blood Cancers**

This presentation will discuss the experimental and clinical observational evidence suggesting that the CD1d-restricted, glycolipid-reactive invariant NKT cells are critical for regulation of acute graft-versus-host disease (aGVHD); specifically, that donor iNKT cells protect recipients of allogeneic stem cell transplantation from aGVHD. It will also provide an overview of the work that demonstrates the potential of iNKT cells as an effective platform for chimaeric antigen receptor-based immunotherapy of cancer that can be sourced from healthy individuals without risk of aGVHD.

Tassos Karadimitris, Professor, **Imperial College London,** *United Kingdom*

17:45 *Networking Cocktail Reception and Exhibit/Poster Viewing*

07:30 *Registration, Coffee and Exhibit/Poster Viewing*

Track 1: Turning Antibody Leads into Drugs

08:25 **Chairman's Remarks**
John McCafferty, Ph.D., Founder and CEO, **IONTAS,** *United Kingdom*

08:30 **Transitioning from Lead Discovery through Pre-clinical/in vivo PoC**
Andy Nixon, Ph.D., Vice President, Biotherapeutics Molecule Discovery, **Boehringer Ingelheim,** *USA*

09:00 **The Use of Bispecific Antibodies to Modulate Anti-Tumour Immune Responses**
Bispecific antibodies are an attractive alternative to cancer treatments combinations. This presentation will discuss F-star's approach to create bispecific mAb². In vitro and in vivo efficacy of F-star bispecific antibodies targeting oncology pathways will be presented.
Francisca Wollerton, Ph.D., Director of Antibody Engineering, **F-star Biotechnology,** *United Kingdom*

09:30 **Human Antibodies for Novel Targets and Underserved Diseases**
Hans de Haard, Ph.D., Chief Scientific Officer, **Argenx,** *Belgium*

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

10:40 **Addressing Antibody Developability by Mammalian Display**
As well as having appropriate binding affinity it is important that clinical drug candidates are non-polyreactive and have optimal biophysical properties allowing formulation at high concentrations. Our mammalian display platform has allowed direct selection from libraries of antibody variants with reduced polyreactivity and aggregation propensity. Addressing developability issues during lead discovery significantly de-risks the future development of antibody drugs.
John McCafferty, Ph.D., Founder and CEO, **IONTAS,** *United Kingdom*

11:10 **True Specificity Is a Critical Development Characteristic in Therapeutic Antibody Development**
UltraHuman Eight has shown for the first time that antibody polyspecificity can be the direct cause of unpredictable side effects in the clinic. Novel insights into identification of off-target binding events and their remediation to create ideal clinical leads with minimised risk will be presented.
Jonny Finlay, CEO, **UltraHuman,** *United Kingdom*

11:40 **Following the Translational Biology in Human Osteoarthritis from Anti-NGF to P75-Fc**
Osteoarthritis remains a considerable burden on society, lacking effective treatment options, so the profound analgesia seen with anti-NGFs was rightly seen as a huge step forward. Unfortunately, side effects have emerged, most noticeably an acceleration of underlying disease. We now understand why this happens and have developed an alternative mechanism based on an endogenous neurotrophin receptor, P75. This molecule is showing dramatic effects in phase I testing in OA patients.
Kevin Johnson, Ph.D., Co-Founder and Partner, **Medicxi,** *United Kingdom*

Track 2: Antibody Therapeutics for Autoimmune and Neurodegenerative Diseases

08:25 **Chairwoman's Remarks**
Marie Kosco-Vilbois, Ph.D., Chief Scientific Officer, **AC Immune SA,** *Switzerland*

08:30 **Combination Depleting mAbs for Th1 and Th17 Cells and Tolerance Induction for Autoimmune 'Cure'**
We have developed excellent mAbs to CCR6 (a Th17/Tfh marker) and CXCR3 (a Th1 marker). We have engineered these mAbs to be depleting and are able to achieve total depletion in mouse models. This results in effective inhibition in disease models, such as rheumatoid arthritis, psoriasis, fatty liver and others. To achieve even better efficacy, we have combined these treatments with metabolite diets (see Marino et al Nature Immunology 2017) which are powerfully immunosuppressive, and Treg inducing. We are working on an ambitious strategy to 'reset' then restore tolerance to auto antigens such that patients can live drug free.
Charles MacKay, Ph.D., Professor, **Monash University,** *Australia*

09:00 **Targeting Cell to Cell Spreading of Alpha-synuclein as a Therapeutic Intervention Strategy for Parkinson's Disease (and Other Synucleinopathies)**
Parkinson's disease (PD) is a progressive neurodegenerative disease, caused by intracellular aggregation of the protein alpha synuclein. Recent evidence from in vitro and in vivo models suggests that cell-to-cell spreading of alpha-synuclein is the molecular basis of PD, implying an extracellular state of these aggregates. At AC Immune, we are targeting this mechanism with antibodies, raised through our proprietary platform, to prevent the pathological spread of alpha-synuclein aggregates in PD patients.
Jan Stöhr, Ph.D., Head of Non-AD Proteinopathies, **AC Immune SA,** *Switzerland*

09:30 **Evox Therapeutics: Using Exosomes to Deliver Drugs to New Places**
Exosomes are small nanometer-sized vesicles that all cells continuously secrete and that represent the body's natural mechanism for delivering proteins and nucleic acids safely and effectively from cell to cell. Evox is engineering exosomes to contain a variety of drugs and enabling their delivery to tissues and cells that have previously been inaccessible. Therapeutic applications of this novel drug delivery approach will be presented, with special attention paid to improved efficacy and delivery of biologics, such as antibodies.
Antonin de Fougerolles, Ph.D., CEO, **Evox Therapeutics Limited,** *United Kingdom*

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

10:40 **Developing Therapeutic Antibodies for Alzheimer's Disease**
Developing monoclonal antibodies for Alzheimer's disease and other neurodegenerative diseases poses unique challenges. This presentation with include strategies for antibody discovery approaches and give examples of how we translate data from preclinical models to predict target engagement and inform clinical trial design.
Jasi Atwal, Ph.D., Scientific Manager, **Genentech,** *USA*

11:10 **Updates from An Anti-asynuclein Program**
Allan Jensen, Ph.D., Senior Director, Biotherapeutic Discovery, **H. Lundbeck A/S,** *Denmark*

11:40 **Late Breaking Presentation**

12:10 Scientific Briefing

WuXiBody™, An Innovative and Versatile Bispecific Antibody Format Opens a New Era for Therapeutic Antibody Development

Bispecific antibodies are growing area of biotherapeutics but with many development challenges. Many of the new platforms have limitations in yield, purity, stability, solubility, half-life, and immunogenicity. Thus, a one-size-fit-all solution is still desired. Aiming to solve those issues, WuXi Biologics has generated WuXiBody™, a flexible proprietary bispecific antibody format that can reduce the development time by 6 -18 months.

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

Fixed Light Chain Transgenic Chicken for Bispecific Antibody Discovery

Bispecific antibodies play an important role in the therapeutic antibody space. We engineered an OmniAb® chicken expressing a common light chain, thereby deriving epitope specificity from the heavy chain. This chicken expresses fully human antibodies that undergo affinity maturation in vivo and offers the additional advantage of recognizing highly conserved targets that might otherwise be challenging on a rodent platform.

Phil Leighton, Ph.D., Director of Molecular Biology, **Ligand Pharmaceuticals**

The Three Step Streamlined mAb Process

New modalities of mAbs and cost and time constraints lead to the requirement of a robust, quickly and simply adaptable platform to any mAbs. The three step streamlined mAb process allows saving diafiltration between steps thanks to the flexibility of use of CMM HyperCel sorbent while maintaining a high capacity. The process is described in batch and easily converted to continuous mode

Catherine Allioux, Global Product Manager, **Pall Biotech,** *France*

12:40 *Networking Lunch and Exhibit/Poster Viewing*

13:50 Scientific Briefings

AlivaMab Discovery Services and AlivaMab Mouse: A Case Study in the Rapid, Efficient Discovery of Highly-Potent Neutralizing Antibodies

Experience and proven, scientific- and timeline-based success should drive decision-making when outsourcing your therapeutic antibody discovery project. The experienced and collaborative team at AlivaMab Discovery Services provides comprehensive discovery services based on customized project plans for your therapeutic antibody discovery projects using AlivaMab Mouse, the next-generation human antibody discovery platform of choice for the majority of the world's top 15 pharmas.

Larry Green, Ph.D., CEO, **Ablexis & AlivaMab Discovery Services**

John "Lippy" Lippincott, Ph.D., Vice President of Research, **AlivaMab Discovery Services**

Advancing from Target-to-Lead Candidates in 24 Hours using Beacon Plasma B Cell Antibody Discovery

Anupam Singhal, Ph.D., Senior Manager, Technology Development, **Berkeley Lights**

Therapeutic Antibody Discovery Empowered with Humanized Animal Models

The talk will also present case studies using target humanized mouse models for high-throughput hit screening to accelerate therapeutic antibody discovery to identify antibody candidates without intensive in vitro binding and cell-based function assays for hit and lead screening, so that to shorten antibody discovery time-line and select better antibody candidates with higher affinity and specificity and better in vivo efficacy.

Benny Yang, Ph.D., CSO, Director of Antibody Development Department, **Biocytogen**

Track 1: Bioinformatics and Repertoires in Antibody Discovery and Development

14:20 **Co-Chairs Remarks**

Andrew Martin, D.Phil., Professor of Bioinformatics and Computational Biology, **University College London,** *United Kingdom*

Pierre Bruhns, Ph.D., Director, Unit of Antibodies in Therapy & Pathology and Deputy Director, Department of Immunology, **Institut Pasteur,** *France*

14:25 **Characterizing Autoantibody-producing Cells in Mice and Humans**

Our droplet-microfluidic system and bioassays enable the ex vivo analysis of plasma cells and plasmablasts (collectively Ab-producing cells) at the single cell level. It enables to sort cells based on Ab specificity, and to calculate the rate of secretion and affinity of antibodies from single Ab-producing cells. Functional characterization of antibodies and autoantibodies, and sorting efficiencies will be discussed.

Pierre Bruhns, Ph.D., Director, Unit of Antibodies in Therapy & Pathology and Deputy Director, Department of Immunology, **Institut Pasteur,** *France*

14:55 **Deep Screening of the B cell Repertoire to Discover High Quality Antibodies to Challenging Targets**

Having efficient technologies to discover high quality monoclonal antibodies has never been more important. Many of the well characterised and more straight-forward targets have been addressed and antibody therapeutics have been developed successfully. We are now in an era where the nature of targets has become more challenging and the success criteria for an antibody-based therapeutic is more extensive. In order to overcome these challenges and develop novel antibody-based drugs to these "high-hanging fruit", we employ a novel platform that enables deep and broad sampling of the B cell repertoire to discover potentially rare antibodies with desirable characteristics. We will describe how we utilise state of the art automation and droplet microfluidics to facilitate antibody discovery with reference to a number of challenging targets.

John Silva, Ph.D., Senior Principal Scientist, Antibody Discovery, **UCB,** *United Kingdom*

Track 2: Clinical Developments in Antibody Therapeutics

14:20 **Chairwoman's Remarks**

Kerry A. Chester, Ph.D., Professor of Molecular Medicine, UCL Cancer Institute, **University College London,** *United Kingdom*

14:25 **The Scripps CHAVI-ID: Moving HIV Vaccine Design Concepts towards the Clinic**

Dennis R. Burton, Ph.D., Professor, Department of Immunology and Microbiology, **The Scripps Research Institute,** *USA*

14:55 **Targeting Subcellular Trafficking Behavior for the Design of Therapeutic Antibodies**

The use of antibody engineering combined with subcellular trafficking analyses to design therapeutic antibodies in two areas will be discussed: first, the development of engineered antibodies that clear pathogenic antibodies. Second, the design of antibody-drug conjugates (ADCs) that deliver their cytotoxic payload more efficiently to lysosomes within cells, resulting in a potential strategy to circumvent the dose-limiting toxicities that can reduce the therapeutic efficacy of current ADCs.

Sally Ward, Ph.D., Professor, **University of Southampton and Texas A&M University Health Science Center**

Track 1: Bioinformatics and Repertoires in Antibody Discovery and Development *(continued)*

15:25 **From Random Combinatorial Libraries to Collections of Therapeutic Leads – The Evolution of Fully Synthetic Antibody Libraries**

Combinatorial synthetic antibody libraries came a long way from just presenting small random subsets of the immune repertoire to large collections of antibodies with good developability characteristics and broad epitope coverage. The evolution of these libraries and data of projects against difficult targets using our latest library Ylanthia will be presented.

Markus Enzelberger, Ph.D., Chief Scientific Officer, **MorphoSys AG,** *Germany*

15:55 *Networking Refreshment Break and Exhibit/Poster Viewing*

16:25 **Identifying Haemophiliacs with Anti-Factor VIII Antibodies: A Case Study in Repertoire Sequencing Analytics**

The standard treatment for haemophilia A is infusion with replacement Factor VIII, but around 20% of patients develop anti-FVIII antibodies, known as inhibitors. This talk will discuss whether antibody repertoire sequencing (Rep-Seq) can help us predict which haemophiliacs will develop inhibitors. This research will be placed in a broader context: What are the available tools for analyzing Rep-Seq data? And what are the key benefits, challenges and limitations of Rep-Seq?

Adrian Shepherd, Ph.D., Reader in Computational Biology, Birkbeck College, **University of London,** *United Kingdom*

16:55 **30 Years of IMGT: Antibodies from Receptors to Amino Acids, What Have We Learned?**

The creation of IMGT in 1989 marked the birth of immunoinformatics by the official recognition of immunoglobulins (IG) or antibodies and T cell receptors (TR) as 'genes'. A second major breakthrough was the IMGT Collier de Perles for V and C domains, opening new insights on antibody humanization and engineering.

Marie-Paule Lefranc, Ph.D., IMGT® Founder and Director, **University of Montpellier, CNRS,** *France*

17:25 **Extracting Trends from Historical Antibody Developability Data Using Machine Learning**

Antibodies and Biologics are amongst the most potent treatment regimens for a wide range of diseases, including cancers and autoimmune disorders. An important step in assessing liabilities in manufacture involves performing developability assessments (DAS). Novartis has an extensive suite of assays to screen antibodies and biologics for manufacturing liabilities. With extensive efforts to systematically capture and organize these datasets, the time is appropriate to explore the applicability of building machine-learning-based tools to predict the outcome of some important assays on new candidates. This talk will give an overview of Novartis' strategy in building a toolkit involving computational and experimental assays for next-generation developability assessments of antibodies.

Abhinandan Raghavan, Ph.D., Technology Lead (Computational Biology), NIBR Biologics Center, **Novartis Pharma AG,** *Switzerland*

17:55 *Close of Conference*

Track 2: Clinical Developments in Antibody Therapeutics *(continued)*

15:25 **From Discovering Emapalumab to Developing Next Generation Antibody Formats**

We used phage display coupled to upfront functional screening to discover a panel of scFv neutralizing Interferon γ. One of these scFv became the starting point for the development and approval of Emapalumab, the first therapy for the treatment of primary HLH in children. This success prompted us to develop proprietary technologies to generate mAbs for inflammatory conditions but also multispecific antibody-based formats for immuno-oncology.

Nicolas Fischer, Ph.D., Head of Research and Special Projects, **Novimmune SA,** *Switzerland*

15:55 *Networking Refreshment Break and Exhibit/Poster Viewing*

16:25 **Anti-CGRP Antibodies for Migraine Prevention**

Calcitonin gene-related peptide (CGRP) plays a crucial role in the pathophysiology of migraine. By interfering specifically in its pathway migraine attacks can be triggered and attenuated. Monoclonal antibodies against CGRP or its receptor have been developed and proven effective for the preventive treatment of migraine. Several of these antibodies have been approved for their clinical use by regulatory authorities. The presentation will give an overview on the available antibodies regarding the rationale for their development, their mechanism of action and their clinical efficacy.

Jan Hoffmann, M.D., Ph.D., Senior Clinical Lecturer in Neurology, **King's College London,** *United Kingdom*

16:55 **A First in Class IgE Antibody for Cancer Therapy: From Concept to Translation**

We have designed tumour antigen-specific antibodies with IgE Fc regions to harness known effector functions of this class that mediate immune clearance of parasites. Anti-tumour IgE potentiated significant tumour-restricting properties in pre-clinical models and promoted monocyte/macrophage recruitment against tumours. A first-in-class anti-cancer IgE has reached clinical testing, offering opportunities to extend the current IgG-only class of monoclonal antibodies in oncology.

Sophia N. Karagiannis, Ph.D., Reader in Translational Cancer Immunology, Head of Cancer Antibody Discovery and Immunotherapy, **King's College London,** *United Kingdom*

17:25 **Clinical Development of Caplacizumab: An Anti-von Willebrand Factor Nanobody for the Treatment of Acquired Thrombotic Thrombocytopenic Purpura**

Caplacizumab (trade name Cablivi®) is an anti-von Willebrand factor (vWF) Nanobody® produced in Escherichia coli, developed for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP). aTTP is a rare, life-threatening, immune-mediated, thrombotic microangiopathy caused by a deficiency in the processing of vWF, a key protein in hemostasis. Despite the current standard-of-care treatment, consisting of daily plasma exchange (PEX) and immunosuppression, episodes of aTTP are still associated with a mortality rate of up to 20%, with most deaths occurring within 30 days of diagnosis. Caplacizumab blocks the interaction between vWF and platelets and therefore has an immediate effect on platelet adhesion and the ensuing formation and accumulation of the micro-clots that cause the severe thrombocytopenia, tissue ischemia and organ dysfunction in aTTP. Nanobodies are a novel class of proprietary therapeutic proteins based on single-domain antibody fragments that contain the unique structural and functional properties of naturally-occurring heavy chain only antibodies. Caplacizumab received Orphan Drug designation in the EU, USA, Japan, Switzerland and Australia. Cablivi received marketing authorization in the EU and in the US, based on the Phase II TITAN and Phase III HERCULES studies in 220 adult patients with aTTP. In the HERCULES study, treatment with caplacizumab in addition to standard-of-care resulted in a significantly shorter time to platelet count response ($p<0.01$), the study's primary endpoint; a significant reduction in aTTP-related death, recurrence of aTTP, or at least one major thromboembolic event during study drug treatment ($p<0.0001$); and a significantly lower number of aTTP recurrences in the overall study period ($p<0.001$). Importantly, treatment with caplacizumab resulted in a clinically meaningful reduction in the use of PEX and length of stay in the intensive care unit (ICU) and the hospital, compared to the placebo group. In clinical trials, caplacizumab demonstrated a safety profile, consistent with its mechanism of action, with epistaxis, headache and gingival bleeding as the most frequently reported adverse reactions.Caplacizumab represents an important addition to the treatment armamentarium for aTTP as it is the first therapy providing protection from the microthrombosis that is responsible for the morbidity and mortality in this disease.

Bernard Delaey, Ph.D., Regulatory Therapeutic Area Lead, **Ablynx,** *Belgium*

17:55 *Close of Conference*

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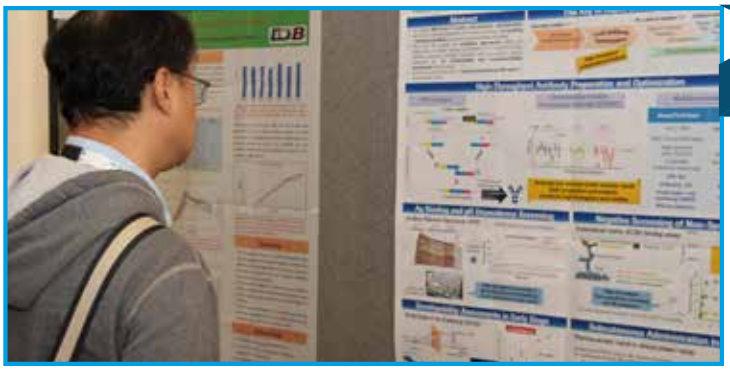

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