PRE-CONFERENCE DISCUSSION DAY | TUESDAY, SEPTEMBER 17

Chaired by:

Patrick Baeuerle
Managing Director
MPM Capital

Dr. Patrick A. Baeuerle is the co-founder of six MPM oncology start-ups. He has taken on a leadership role in one MPM portfolio company and serves on the board of directors and scientific advisory boards at several other portfolio companies.

Prior to joining MPM, Patrick was Vice President, Research, and General Manager of Amgen Research Munich GmbH, where he was responsible for the development of BiTE antibody Blincyto®, which was approved in 2014 in less than three months by the U.S. FDA for therapy of relapsed/refractory acute lymphoblastic leukemia. He has also served as Chief Scientific Officer for Micromet, Inc., and earlier headed small-molecule drug discovery at Tularik Inc., a publicly traded biotechnology company also acquired by Amgen (AMGN). Prior to this, he was Professor and Chairman of Biochemistry and Molecular Biochemistry at the Medical Faculty of Freiburg University, Germany, where he did groundbreaking research on transcription factor NF-kappaB.

Patrick is the recipient of the European Molecular Biology Laboratory's 2019 Lennart Philipson Award in recognition of his many contributions to the development of cancer immunotherapies. To date, he has published 240 PubMed-listed papers that have been cited more than 69,800 times. He has a Hirsh index of 126 and was rated Germany's most frequently cited biomedical scientist of the decade (1990-1999), and among the top 50 worldwide (1990 to 1997).

Patrick holds a Ph.D. in Biology from the University of Munich and performed post-doctoral research with Dr. David Baltimore at the Whitehead Institute at MIT. He is also an Honorary Professor of Immunology of the Medical Faculty at the University of Munich.

Pioneering the Next Generation of CD3 Bispecifics

Patrick Baeuerle Managing Director **MPM Capital**	**9.00**	**Chair's Opening Remarks**
David DiLillo Senior Staff Scientist **Regeneron**	**9.15**	**Benchmarking T Cell-Redirecting Therapies for Cancer: Comparing CD3-Bispecifics and CAR T Cells** • Two competing platforms exist for redirecting T cells to recognize and kill tumors: Bispecific antibodies and chimeric antigen receptor (CAR) T cells • 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
	9.45	**Speed Networking**
	10.30	**Morning Refreshments**
David DiLillo Senior Staff Scientist **Regeneron** **Tariq Ghayur** Senior Research Fellow **AbbVie** **Eugene Zhukovsky** CSO **Biomunex**	**11.00**	**Panel Discussion: Contrasting Bispecific Therapeutics & CAR-T Approaches** • Evaluating "off-the-shelf" vs personalized therapies • Understand how these contrasting approaches each manage safety for on target off tumor toxicities • Investigating differences in terms of solid and liquid tumour targeting • Are these therapeutics considered cures or just bridging therapies to the next breakthrough?
Rick Austin Senior Director, Biology Research **Harpoon Therapeutics**	**11.30**	**TriTAC: A Tri-Specific T Cell Engaging Platform for the Treatment of Solid Tumors** • TriTAC molecules contain three antibody domains: an anti-CD3 domain to bind to T cells, an anti-target domain to bind antigens on tumors cells, and an anti-albumin domain to provide half-life extension. • TriTAC molecules have potent directed T cell killing activity in vitro and in vivo • HPN424, a TriTAC molecule targeting PSMA, is being tested in a Phase I clinical trial. • HPN536, a MSLN targeting TriTAC, is in development

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Pioneering the Next Generation of CD3 Bispecifics

	12.00	**Lunch & Networking**
Volker Schellenberger President & CTO **Amunix**	**1.00**	**XPAT-T Cell Engagers: A Novel Format to Mitigate the On-Target, Off-Tumor Problem** • XPATs represent a novel format of highly-selective bispecific T cell engagers that are activated by proteases in the tumor microenvironment • XTENylation provides long in vivo half-life and universal masking applicable to any antibody. • T cell activation of XPATs is attenuated >10,000-fold prior to local proteolysis in the tumor microenvironment
Victor Levitsky VP, Immuno-Oncology **Molecular Partners**	**1.30**	**Development of Poly-Specific T-Cell Engagers & Immunomodulatory Molecules Using the DARPin Technology Platform** • The DARPin technology provides a versatile platform for generation of polyspecific, multifunctional biotherapeutics with excellent biophysical and easily controlled pharmaco-dynamic characteristics , low, if any, immunogenicity and desired biological properties • Several DARPin based drug candidates are successfully progressing through different stages of pre-clinical and clinical development
	**2.00**	**Roundtable Discussion: Evaluating the Criteria Essential to Success in the Increasingly Competitive CD3 Bispecific Field** Collectively discuss CD3 targeting approaches and share experiences in overcoming key challenges. Gain insights and perspectives from stakeholders at a range of different stages of development in the field and benchmark your progress against a variety of companies and organizations
Patrick Baeuerle Managing Director **MPM Capital**	**2.45**	**Chair's Closing Remarks**
	3.00	**Close of Discussion Day**

"The World Bispecific Summit is a critical, focussed conference that brings together the leaders in a field that represents the frontiers of the next generation of therapeutic biologics!"

Lathrop & Gage LLP

"Focused on topics that matter. Top speakers. The best conference in the field in my opinion"

Glenmark

"Great speakers, great networking and stimulating discussions!"

Sanofi

PRE-CONFERENCE WORKSHOPS | TUESDAY, SEPTEMBER 17

Workshop A — 9.00-12.00PM

Enhancing the Translatability of Immuno-Oncology Therapeutics

An unprecedented range of immuno-oncology combination approaches are currently under investigation, but without robust preclinical validation backing the mechanism of action of these strategies, many of these studies will fail to reach their clear potential. This interactive workshop will share how the efficacy of immuno-oncology agents can be investigated in translational culture systems, providing you with the valuable tools to enhance your immuno-oncology work.

Attend this workshop to gain valuable insights into:

- A novel ex vivo human system to investigate immuno-oncology agents
- How models can replicate a more natural and translationally-relevant tumor microenvironment
- Insights into the mechanistic data that can be generated from translational systems and how this can enhance immuno-oncology clinical development

Prasad Adusumilli
Deputy Chief and Director,Mesothelioma Program
Memorial Sloan-Kettering Cancer Center

Workshop B — 1.00-4.00PM

Innovative Discovery & Delivery Approaches for Bispecifics for Infectious Disease Indications

Developing bispecifics for infectious diseases is challenging, but the potential rewards for success are huge, given the global unmet need in many of these indications. An increasing amount of bispecific development is taking place outside oncology, using new enabling technologies to tackle the complex challenges inherent to infectious diseases applications is critical to success.

Attend this workshop to gain valuable insights into:

- Case studies outlining protein engineering innovations to develop and adapt formats to complex biological contexts
- Investigating new gene-encoded methods for in vivo delivery using non-viral synthetic DNA to enable to body to produce bispecifics
- Understanding the flexibility and range of different bispecific designs able to be delivered using this approach
- The future promise of bispecifics in addressing unmet medical need in the infectious disease space

Jonathan Lai
Professor, Biochemistry
Albert Einstein College of Medicine

Ami Patel
Researcher
Wistar Institute

"All of the speakers were excellent. Their professional knowledge and experiences will be a great help in the development of our pipelines"

Jichul Lee, Research Director, SG Medical

8.20 **Chair's Opening Remarks**

Jonah Rainey
VP
Gritstone Oncology

Enhancing the Selectivity of Bispecifics in Solid & Liquid Tumor Indications

8.30 **Designing T-cell Engagers for Better Therapeutic Windows**

- Sequence-based antibody discovery using transgenic human IgG rodents
- Engineering, optimizing and selecting multi-specific leads for desired biology
- Considerations in selecting the efficacy and potency of T-cell engagers for liquid and solid tumor targets
- Designing the next generation of safer therapeutic bi- and multi-specific T-cell engagers

Omid Vafa
CBO
TeneoBio

9.00 **COBRA: A Novel Conditionally Active Bispecific Antibody that Regresses Established Solid Tumors in Mice**

- We have designed a multivalent sdAb-diabody fusion which converts into a highly potent bispecific redirected T-cell therapeutic upon proteolytic activation
- In vitro assays demonstrate protease dependent linker cleavage increases potency of T cell-mediated killing 200-fold, yielding a therapeutic with sub-picomolar potency
- Administration of MVC-101 in mice with established xenografts resulted in protease cleavage dependent T-cell mediated tumor regressions in multiple tumor models
- MVC-101 has extended half-life in vivo upon administration, and rapid clearance post proteolytic activation, resulting in a therapeutic with improved safety profile over conventional T-cell redirected bispecifics

Danielle Dettling
Director, R&D
Maverick Therapeutics

9.30 **Panel Discussion: Examining & Interpreting Failures in the Field to Enhance Future Development**

In order to succeed in the field, it's as important to learn about failures than successes. Bispecific therapeutics have been around for decades and over 100 formats currently exist, so why aren't there more approved bispecifics? Examining the reasons behind failures will help to move forward with more clarity. This panel discussion will bring together perspectives from organizations who have experienced failures in the development of bispecifics to speak candidly about the underlying issues behind the failure and lessons learnt that can be implemented moving forward. Topics to be discussed include:

- What leads to a program being pulled from the clinic?
- What are early warning signs that have proved good predictors of failures in scale up?
- At which stage are failures typically occurring and why?
- Investigating the relative roles of factors such as manufacturability, toxicity and selectivity

Tariq Ghayur
Senior Research Fellow
AbbVie

Eugene Zhukovsky
CSO
Biomunex

Chris Mehlin
Director, Therapeutic Proteins. Senior Staff Scientist
Fred Hutchinson Cancer Research Center

10.15 **Morning Refreshments & Speed Networking**

CONFERENCE DAY ONE | WEDNESDAY, SEPTEMBER 18

Discovery

Optimizing High-Throughput Screening to Enhance Bispecific Discovery

11.30 Bispecific Target Discovery by High Throughput Functional Screening of Hundreds of Combinations of Target Pairs

- Technology platform to discover novel target pairs by unbiased functional screening with large, diverse, combinatorial panels of bispecific antibodies
- Platform combines 3 key technologies: antibody discovery, a novel bispecific screening format and high content high throughput screening
- The platform is applicable to any disease area
- Example of discovery of novel obligate target pairs will be described for autoimmunity, fibrosis and immuno-oncology

Helene Finney, Head, Bispecific Target Discovery, **UCB**

12.00 Screening in Final Format - Combinatorial High-Throughput Generation & Functional Screening of Bispecific Antibodies in Different Formats

- Protein engineering: robust generation of bispecific antibodies by controlled heavy-chain exchange
- Combinatorial bispecific diversity: generation of binder-format matrices
- Format defines function: screening of bispecific matrices identifies formats with desired function
- Outlook: expansion of an automated HTP bispecific platform

Stefan Dengl, Principle Scientist Large Molecule Research, **Roche**

Translational & Clinical

Building & Executing a Robust Preclinical Strategy

11.30 Bringing the Tumor-Directed CTLA-4 x OX40 Bispecific Antibody, ATOR-1015, Into the Clinic

- ATOR-1015 is a CTLA-4 x OX40 bispecific antibody developed for tumor-directed immunotherapy
- ATOR-1015 binds both targets simultaneously, promoting cell-cell interactions expected to enhance the immune activation
- The mode of action is a combination of regulatory T cell (Treg) depletion and effector T cell activation
- ATOR-1015 has anti-tumor effects in several syngeneic tumor models in mice and improves the response to anti-PD-1 treatment
- A first-in-human phase 1 study has started in patients with advanced solid tumors (NCT03782467)

Tina Furebring, SVP, R&D, **Alligator Bioscience**

12.00 A Translational Quantitative Systems Pharmacology Model for CD3 Bispecific Molecules: Application to Quantify T-Cell-Mediated Tumor Cell Killing by P-cadherin LP DART

- A translational quantitative systems pharmacology (QSP) model is proposed for CD3 bispecific molecules capable of predicting trimolecular complex (trimer) concentration between drug, T-cell and tumor cell, and linking it to tumor cell killing
- The model was used to quantify the PK/PD relationship of a CD3 bispecific targeting P-cadherin (PF-06671008). It describes disposition of PF-06671008 in the central compartment and tumor in mouse xenograft models, including binding to target and T-cells in the tumor to form the trimer. The model incorporates T-cell distribution to the tumor, proliferation and contraction
- The model was translated to the clinic and used to predict the disposition of PF-06671008 in patients, including the impact of binding to soluble P-cadherin. The model was also used to predict clinical efficacy of PF-06671008 and to investigate sensitive factors which impact efficacy

Alison Betts, Research Fellow, Translational Modeling & Simulation, **Pfizer**

Manufacturing & CMC

Understanding the Unique Analytical Challenges Bispecifics Pose

11.30 Investigating a Novel Computationally & Structurally Designed Methodology to Generate Bispecifics

- Understanding a new methodology to generate bispecifics using G4 unidirectional drivers
- Creating mutations on the CH3 domain and using them as bait to fish out naturally occurring bispecifics from the hybridoma pool
- Understanding the advantages of this approach, including the significant time savings from screening from the hybridoma pool directly into a bispecific format

Igor D'Angelo, Senior Research Scientist, Molecular Engineering, **Amgen**

12.00 Establishing Effective Cell Line Development & Analytical Approaches to Support the Clinical Development of Bispecific Therapeutics

- Insights from overseeing the whole CMC and manufacturing trajectory – understanding the challenges faced at each stage
- Understanding how to approach cell line development in the bispecific space
- Case study: An in-depth insight into the CMC approaches that support the development of a clinical bispecific candidate

Robert Doornbos, Senior Director, Product Development, **Merus**

12.30 Lunch & Networking

CONFERENCE DAY ONE | WEDNESDAY, SEPTEMBER 18

Pioneering Novel Discovery Approaches

1.45 Facile Production of Bispecific Antibodies for High-Throughput Screening of Antibody Pairs & Personalized Therapy

- Photoreactive antibody binding domains (pAbBDs) can be used for the rapid and site-specific labeling of nearly any 'off-the-shelf' IgG
- Bispecific antibodies can be formed from nearly any two full-length IgG, using pAbBDs, for rapid testing of antibody combinations.
- Anti-tumor antibodies collected from serum can be rapidly converted into T cell-redirecting autoantibodies (TRAAbs)

Andrew Tsourkas, Professor, Bioengineering, **University of Pennsylvania**

2.15 Designing Bi- & Multi-Specific CD3/X Molecules to Match Biology & Clinical Unmet Needs

- Technical challenges for designing bi-/multi-specific biologics have been (or can be) solved
- Key challenges now are to design the right therapeutic molecules to match biology/clinical unmet needs
- Key aspects to consider are: (i) the right target pairs; (ii) position of variable domains, valency of each specificity & linker designs, if needed; and (iii) ensuring that the final therapeutic candidate has the right drug-like and PK profiles
- Some examples of above will be provided

Tariq Ghayur, Senior Research Fellow, **AbbVie**

Insights into the Translatability & Clinical Development of CD47-Targeting Bispecifics

1.45 Enhancing the Specificity of CD47-Targeting to Improve the Therapeutic Window

- Investigating the rationale behind targeting CD47
- Producing a potent and targeted anti-tumour activity while mitigating against toxicities associated with CD47 targeting
- Improving translatability by utilising in vivo models and patient samples

Emmanuel Normant, Vice President, Preclinical Sciences, **TG Therapeutics**

2.15 Targeting CD47 with a Bispecific Molecule for Superior Efficacy & Better Safety Profile

- Designed a bispecific antibody to prevent anti-CD47 off-tissue toxicity by selectively binding to cancer cells
- The bispecific antibody displayed synergy between two targeted pathways related to innate and adaptive immunity, respectively
- Besides blood malignancies, this molecule has potential in solid tumors as well

Junjian Liu, VP, Head of Drug Discovery & Preclinical Development, **Innovent Biologics**

Enhancing the Developability of Bispecifics

1.45 Understanding the Developability Issues Behind Bispecific Failures

- Contrasting developability issues encountered by a range of bispecific formats
- Understanding developability attributes that can be early predictors of failure
- Investigating a case study highlighting challenges encountered in the development of a bispecific

Nimish Gera, Director of Research & Development, **Mythic Therapeutics**

2.15 Developability of Bispecific Antibodies

- In-silico predictions to assess developability
- In-depth characterization of side products for bispecific antibodies
- Functional assays for lead characterization

Martin Bader, Head of Biochemical & Analytical Research, **Roche**

2.45 Panel Discussion: Investigating Novel Bispecific Designs to Overcome Biological Challenges

- Matching specific biological application to format design
- Investigating approaches to modulate half-life and the effects of this modulation on immunogenicity, efficacy and safety
- Gaining insights from novel format designs and discovery work

Eugene Zhukovsky, CSO, **Biomunex Pharmaceuticals**

Andrew Tsourkas, Professor, Bioengineering, **University of Pennsylvania**

Tariq Ghayur, Senior Research Fellow, **AbbVie**

2.45 Panel Discussion: Enhancing the Translatability & Predictability of Animal Models

- Contrasting in vivo modelling approaches to extract useful data to inform clinical development
- Are in vivo efficacy and safety models sufficient to get good predictions of therapeutic windows?
- Back-translating clinical experience to avoid toxicities in the future

Tina Furebring, SVP, R&D, **Alligator Bioscience**

Emmanuel Normant, Vice President, **Preclinical Sciences, TG Therapeutics**

Alison Betts, Research Fellow, Translational Modeling & Simulation, **Pfizer**

2.45 Panel Discussion: Implementing Strategies to Improve the Developability of Bispecifics

- Understanding the data that needs to be generated to move projects from discovery to early development
- Extracting valuable developability insights from clinical experience – how can we streamline the development of the next generation of bispecifics?
- Bioprocessing innovations to bring down technical hurdles holding back progress in the space

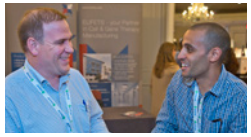
Martin Bader, Head of Biochemical & Analytical Research, **Roche**

Igor D'Angelo, Senior Research Scientist, Molecular Engineering, **Amgen**

Nathan Higginson-Scott, Director, Therapeutic Antibody Technologies, **Pandion Therapeutics**

3.15 Afternoon Refreshments & Scientific Poster Session

The scientific poster session is an ideal opportunity to communicate your new results and expertise to a niche audience of industry experts, get feedback from peers and colleagues in the industry and learn how others in the field have been tackling similar challenges.



Pioneering Quantitative Models to Predict Optimal Bispecific Properties

Chaired by: 

John Burke
President, CEO & Co-Founder
Applied BioMath

4.15 Utilizing QSP Modeling to Inform Clinical and Nonclinical Development of Zymeworks' Azymetric™ Biparatopic Platforms: Pharmacokinetic/Pharmacodynamic Modeling & Therapeutic Index Estimation

- Inclusion of biparatopic binding stoichiometry drives more precise fit of PK data in cynos and humans
- Development of novel pharmacodynamic parameter to evaluate effective of dose concentration and regimen on efficacy
- Estimated delivery of toxin to four compartments: tumor, on-target organ toxicity and off-target toxicities associated with free toxin and FcGammaR2a binding of the antibody
- Therapeutic index estimation with different doses and dose frequencies

Rupert Davies
Senior Scientist, Preclinical Development
Zymeworks

Gerry Rowse
Director, Toxicology & Pharmacokinetics
Zymeworks

4.45 **Model-Based Approach to Design Bispecific Modalities in Early Discovery**

- Bi-specific antibodies are an attractive modality to modulate multiple targets in a disease indication. Each antigen may exhibit similar or different kinetic values like half-life, internalization rates, and expression rates. Target coverage for each antigen may also differ or be similar
- Understanding your drug targets is critical to building an appropriate drug that specifically binds to and elicits the magnitude and duration of response needed for a particular indication
- Here we used a tiered model-based approach to first determine feasibility of a bispecific antibody to appropriately cover multiple antigen pairs
- Once feasibility was assessed, further modeling was performed to determine ideal affinity ranges for each target in bi-specific format at the site of action. Sensitivity analysis was performed to understand each parameter and its impact on predicted target coverage
- This approach guided teams for informed antibody design, prioritization of experiments, and triaging of challenging antigen pairs

Jennifer Fretland
Head, Drug Metabolism & Pharmacokinetics
Sanofi

5.15 **The Next Generation of T-Cell Redirecting Antibodies**

- Harnessing the immune system has revolutionized cancer treatment
- In particular redirected T-cells can kill tumor cells in therapeutically useful ways
- However, off-target toxicity and lack of sufficient Ag limit the therapeutic potential of these approaches
- Revitope is developing two-component systems composed of conditionally activated T cell Engaging Antibody Circuits (TEAC) that initiate and focus cytotoxic immunity accurately on the tumor
- The core idea of TEAC is to split the anti-CD3 paratope of a bi-specific antibody to separately target each half-paratope to the tumor and only permit reconstitution after protease cleavage of the stabilizing dummy domains.
- TEAC can be tumor-targeted with one or two different solid-tumor antigens (requirement for two antigens (an “AND” gate) that may enable greater tumor-specificity
- The discussion will cover protein engineering considerations, activity measurements and the use of quantitative systems pharmacology modeling approaches aid mechanistic understanding

Werner Meier
CSO
Revitope Oncology

5.45 **Chair’s Closing Remarks**

Jonah Rainey
VP
Gritstone Oncology

“An excellent opportunity to learn about the latest developments in the bispecific antibody field”

Boehringer Ingelheim

CONFERENCE DAY TWO | THURSDAY, SEPTEMBER 19

8.30 Chair's Opening Remarks

Jonah Rainey
VP
Gritstone Oncology

Realizing & Demonstrating the Value of Bispecific Approaches

8.45 Bispecific Antibodies: Evolution & Refinement of their Applications

- The main driver of the success of bispecific Abs is the new biologies they enable
- In addition to well established applications (i.e redirection of immune cells), other applications keep emerging or gaining prevalence (i.e more selective tissue delivery)
- As applications mature, more refined molecules are being developed
- A case study of a more tumor-selective T-cell engager is presented

Diego Ellerman
Principal Scientific Researcher
Genentech

9.15 Exploring the Criteria Under Which Bispecifics are Superior to Antibodies & Antibody Combinations

- Target biology and receptor expression data are key factors in selecting a bispecific versus another therapeutic strategy
- Contribution of cell- and tissue-level antigen expression and bispecific affinity/avidity in driving selectivity and specificity
- Dramatic enhancement of on-target potency through rational selection of antigen, epitope, and bispecific

John Rhoden
Senior Research Scientist
Eli Lilly

9.45 Morning Refreshments & Networking

Discovery

Discovering Novel Bispecific Formats to Address Key Biological Challenges

10.30 SMITEs: Putting Some Teeth into BiTEs

- Two bispecific antibodies used in combination can target the coexpression of antigens in tumors while ignoring a single antigen
- Creating a logical AND gate for T cell activation requires each individual molecule to have little/no activity but the combination to be synergistic
- This kind of approach allows the targeting of antigens with wide expression in healthy tissue
- Bispecific architectures are not "Plug and Play" and require optimization for specific antibodies

Chris Mehlin, Director, Therapeutic Proteins. Senior Staff Scientist, **Fred Hutchinson Cancer Research Center**

Translational & Clinical

Enhancing Efficacy While Maintaining Safety Throughout Preclinical & Clinical Development

10.30 Optimizing the Clinical Development of Bispecifics in Immuno-Oncology

- Understanding the key clinical challenges encountered in the bispecific space
- Investigating strategies to minimise side effects and maximise therapeutic effects
- Sharing case studies investigating bispecific clinical development in immuno-oncology

Jon Wigginton, CMO & SVP, Clinical Development, **MacroGenics**

Manufacturing & CMC

Enhancing Process and Analytical Approaches to Link Discovery Work to Clinical Development

10.30 Early Stage Process & Product Characterization of Bispecific Antibodies – A Road Map from DNA to FIH

- Best practices for product and process characterization of bispecific antibodies in preparation for FIH filings
- Process and analytical development and characterization: How much is necessary for FIH?
- Structure function relationship in early stage development: How to access and control critical quality attributes early and effectively to stream line process and analytical development
- Examples from multiple bispecific CMC programs based on Genmab's DuoBody platform will be discussed

Christian Cimander, Senior Director, CMC, **Genmab**

CONFERENCE DAY TWO | THURSDAY, SEPTEMBER 19

11.00 Modification of the Bispecific Antibody Platform with an IL-15 Cytokine Crosslinker to Create Trispecific NK Engagers (TRiKEs): Efficacy Against Solid & Liquid Tumors

- Lessons learned from the creation of bispecific antibodies engaging NK cells to vastly improve their ability to kill through antibody dependent cell-mediated cytotoxicity (ADCC)
- Investigate a new bioengineered drug whereby the cytokine IL-15 is cross-linked into the BsAb scaffold, creating a new platform whereby NK expansion is maximized while ADCC is promoted
- Discussion of the structure, function, rationale, animal studies, toxicity, and clinical potential of these IL-15 TriKes as they relate to liquid and to solid tumors
- Discussion of effective markers to target against solid tumors
- Discussion of multi-target TriKEs targeting simultaneous tumor markers

Daniel Vallera, Professor, **University of Minnesota**

11.00 Insights from the Preclinical & Clinical Development of a Novel CD3-CD123 Bispecific

- Lessons learned from the development of a novel bispecific T cell engager in AML
- Investigating the unique qualities of this bispecific
- Summarising where this will be an advantage to the field in general

Karl Hsu, AVP, Global Head of Early Development Oncology, **Sanofi**

11.00 Incorporation of Bispecific Screens & Robust Analytical Assessment of Drug-Like-Properties at all Stages of Discovery to De-Risk CMC & Pave the Way for Successful Bispecific Development

- Sharing insights into the development of bispecifics to achieve localized immunomodulation to treat autoimmune and inflammatory diseases
- Highlighting advantages to incorporation of screening in bispecific format early in the discovery process
- Understanding how different tiers of necessary manufacturability assessment can be permeated throughout all stages of discovery for streamlined development and CMC de-risking

Nathan Higginson-Scott, Director, Therapeutic Antibody Technologies, **Pandion Therapeutics**

11.30 Targeting Bispecific Biologics to Disease Tissues

- Considering the opportunity offered by modular biologics to target drug biology locally to disease tissues
- Examining molecules that exemplify this idea in a range of indications including:
  - Renal fibrosis
  - Immunocytokines
  - Rheumatoid arthritis
  - Immuno-oncology
- Understanding the unique selectivity that comes from integrating conditional and targeted approaches

Andrew Goodearl, Senior Director, **AbbVie**

11.30 Preclinical Safety Assessment of Bispecific Antibodies

- Lack of tumor-restricted antigens is the primary barrier to the development of bispecific antibodies for the treatment of solid tumors
- Avidity-based design greatly enhances the selective killing of HER2/CD3 T-cell dependent bispecific antibody
- Preclinical safety evaluation of bispecific antibody should be designed on a case by case base

Sara Santagostino, Scientist-Pathologist, Safety Assessment, **Genentech**

11.30 ADAPTIR Bispecifics Platform: Excellent Manufacturability, Extended Half-life and ability to Perform Multiple Novel Mechanisms of Action for Treatment of Multiple Diseases

- ADAPTIR Bispecific platform is capable of generating candidates with unique and different mechanisms of actions for treatment of both cancer and autoimmune diseases
- ADAPTIR bispecific platform has excellent manufacturability characteristics to meet clinical and commercial needs
- ADAPTIR platform has extended half-life to improve on dosing protocols for patient convenience

Jane Gross, CSO, **Aptevo Therapeutics**

12.00 Lunch & Networking

Mapping Out the Bispecific Landscape

1.00 Review of the Bispecific Landscape

- Insights into the evolving bispecific clinical landscape
- Contrasting bispecific development in solid tumor and haematological indications
- CD3 and beyond: Investigating key bispecific targets
- Evaluating the reasons behind discontinuations – what are the key roadblocks?

Letrishka Anthony
Senior Analyst, Beacon
Hanson Wade

CONFERENCE DAY TWO | THURSDAY, SEPTEMBER 19

1.30 **Mastermind Discussion: Uniting Discovery, Translational, Clinical and Manufacturing Perspectives to Enhance the Future of Bispecific Drug Development**

Following the individual tracked elements of the agenda, this session facilitates in-depth discussions between participants from different perspectives in an informal environment. After splitting into small groups, discuss the unique challenges you are facing and collaborate on future strategies to improve the effectiveness of bispecific drug development. Discuss issues such as:

- Reflecting on the unique challenges encountered in the development of bispecifics at every stage
- How can siloes between departments be broken down to improve communication?
- How can outsourcing relationships be improved to ensure internal and external processes and standards are aligned?

2.15 **Afternoon Refreshments & Networking**

Discovering Effective Checkpoint Modulator Combinations

2.45 **Design Fitting Bispecifics for Immune Oncology**

This presentation will cover various applications of DART and TRIDENT molecules to leverage anti-tumor immunity framed in the context of optimal molecular design. Therapeutic approaches and associated aspects covered in the talk will be:

- Redirected T-cell killing: lessons learned from the clinic and approaches to optimize therapeutic response
- Dual checkpoint blockade: PD-1 x LAG3 and PD-1 x CTLA4 – from concept to clinic
- Incorporating immune co-stimulation: tumor conditional CD137 pathway activation including concomitant checkpoint blockade

Paul Moore
VP, Cell Biology & Immunity
MacroGenics

3.15 **Bispecific Technology for Igniting T Cell Activation through T cell Engagers, Checkpoint Blockade & Cytokines**

- Clinical experience with CD3 engagers
- Targeting checkpoint blockade and costimulation
- Potency tuned IL-15 to sustain T cell activation and improve therapeutic index

Raphael Clynes
VP, Translational Biology
Xencor

3.45 **Chair's Closing Remarks**

Jonah Rainey
VP
Gritstone Oncology

4.00 **Close of Day Two & End of World Bispecific 2019**

"Provides an excellent overview of the bispecifics field, and brings people of the field together for stimulating discussions and future research"

Roche