VIRTUAL EVENT

Next Generation Protein Therapeutics & Bioconjugates Summit

November 2- 5 2020

Now Delivered 100% Virtually in US Pacific Standard Time (PST)

LOOKING BEYOND ANTIBODIES TO TRANSFORM PROMISING PROTEINS INTO NEXT GENERATION MEDICINE

ADVANCE your innovative biologics with cutting-edge engineering, design and conjugates, PROGRESS to the clinic and ACHIEVE top quality products with analytics and successful workflows.

Featured Speakers

Paul Moore
VP, Cell Biology & Immunology, Macrogenics

Thomas Pillow
Senior Scientist, Genentech

Rakesh Dixit
President & CEO, Bionavigen, Former Vice President, R&D, MedImmune

Dario Neri
Professor, ETH

Christian Klein
Head Oncology Programs, Roche Innovation Center Zurich

Steven Nadler
Vice President of Research, Aro Biotherapeutics

AntibodyEng365 #PROTEINSUMMIT

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Simply log onto the digital platform, browse the agenda and tune into the sessions that interest you the most.

Plus, content will be available on demand so you can catch up on anything you might have missed at your leisure.

VIRTUAL NETWORKING

Our virtual platform will enable face-to-face connections via video chat, ensuring you can meet the people that matter most to you.

Create your personal profile to indicate who you are, what you're looking for and who you want to meet. You can filter fellow attendees to find the people most relevant to you and reach out to arrange a video chat. You can even invite other attendees to join the meeting in real time - so if you want to bring your product experts or sales representatives at a crucial moment, they can join the conversation instantly.

Our networking platform will make it easy to connect with the right people - helping you to have the conversations that matter with the people who matter to you..

Day One • Monday, November 2, 2020

8:50 **Conference Welcome**

9:00 **Chairperson's Opening Remarks**

9:10 **KEYNOTE: Immune-empowered Antibodies and Bispecific Molecules for Oncology: Bench to Bedside**

Clinical stage programs covering the following will be presented in context of case studies:

1. Leveraging innate and adaptive tumor immunity through Fc engineering (e.g. margetuximab)
2. Dose and schedule optimization of CD3-based bispecific to maximize therapeutic window (e.g. flotetuzumab)
3. Bispecific DART® molecules to enable dual checkpoint pathway blockade (e.g. MGD013: PD-1 x LAG3)

Paul Moore, VP, Cell Biology & Immunology, **Macrogenics**

9:30 **LIVE Q & A with Paul Moore**

9:50 **KEYNOTE:Cancer Wars: The Rise of Antibody Drug Bioconjugates**

- Challenges and Opportunities in development of antibody drug bioconjugates (ADBC)
- Lessons learned from successful and failed antibody drug bioconjugates
- Five rights of the best class ADBC
- Cancer Immunotoxins
- ADBC for non-oncology indications: pros and cons
- Antibody-oligonucleotides-conjugates: value proposition

Rakesh Dixit, President & CEO, **Bionavigen**

10:10 **LIVE Q & A with Rakesh Dixit**

10:30 **Spotlight Presentation**

10:50 *Networking Coffee Break*

NOVEL PROTEIN DESIGNS R & D TO CLINICAL

11:30 **Conjugated Proteins: A Rational Design for Mitigating Clearance Mechanisms and Altering Biodistribution**

Many people assume that PEGylation or albumination etc. will automatically increase the half-life of a protein. Whereas that is frequently true when kidney clearance requires simple increase in size, many proteins such as the blood factors are big enough that they are not cleared by the kidneys. Arbitrarily putting a PEG on these does not guarantee increased half life. Therefore I want to focus on first understanding a clearance mechanism. If you mitigate clearance you will get half life extension.

Mary Bossard, Principal Fellow, **Nektar Therapeutics**

11:50 **Engineering design and Lessons Learned from a Novel Bispecific Receptor-mAb Fusion**

Inhibiting more than one signaling pathway by engaging different cell surface receptors can provide additional therapeutic benefit in various diseases. This can be achieved either through combination therapies or through dual targeting with bispecific molecules. We will share lessons learned from a format that permits receptor engagement as well as antibody binding; effectively combining two different modalities into one functional molecule.

Bernhard Sielaff, Principal Research Scientist II, **Abbvie**

12:10 **Spotlight Presentation**

12:30 **LIVE Q & A with Speakers from Session**

11:00 *Lunch Break*

2:00 **XTENylated Protease Activated T cell engagers: XPATS - A novel format to mitigate the on-target, off-tumor problem**

XPATs are conditionally active T cell engagers that are activated by high protease activity in the tumor microenvironment. Unstructured polypeptides provide long in vivo half-life and universal masking, while protease release linkers enable unmasking in the tumor microenvironment. In vitro activity of XPATs is attenuated >10,000-fold relative to unmasked forms. Masking provides >100-fold safety benefit in primate studies.

Volker Schellenberger, CTO, **Amunix**

2:20 **New Technologies To Advance Bispecific Antibodies From Research Into Early or Clinical Development**

Christoph Spiess, Principal Scientist, Antibody Engineering, **Genentech**

2:40 **KEYNOTE: An Overview of Daichi Sankyo's ADCs: Preclinical and Clinical updates on DXd-based ADCs**

Daiichi Sankyo has developed a DXd-based antibody-drug conjugate (DXd-ADC) technology. DXd is an exatecan-derivative, a potent DNA topoisomerase I inhibitor which causes cancer cell death. The technology enables us to produce ADCs to which a potent payload is connected via a cleavable peptide-based linker with potential for a high drug-to-antibody ratio. The linker of DXd-ADCs is selectively cleaved by lysosomal enzymes such as cathepsins that are upregulated in tumor cells. DXd-ADCs showed preferable pharmacokinetic profiles: a high stability of the drug-linker in plasma and a short systemic half-life of the payload, and potent antitumor activity in preclinical studies. In addition, DXd released in target-antigen expressing tumor cells defuses across cell membranes due to its high membrane permeability, which could lead to cytotoxicity in neighboring tumor cells regardless of their target antigen expression. Recently, the FDA approved trastuzumab deruxtecan (T-DXd, DS-8201), a HER2-targeting DXd-ADC, for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. This presentation will describe updated preclinical and clinical data on safety, pharmacokinetics, and antitumor activity of DXd-ADCs including DS-8201, U3-1402, and DS-1062.

Jun Hasegawa, Senior Researcher, **Daichii Sankyo**

3:00 **LIVE Q & A with Speakers from Session**

3:30 *Networking Reception*

**Program subject to change*

PLENARY SESSION

9:10 **KEYNOTE Webinar: Update on applications of CrossMab Technology for the Generation of Bispecific Antibodies for Cancer Immunotheray**

Bispecific antibodies have gained major interest as they enable novel mechanisms-of-action and therapeutic applications that cannot be achieved using conventional monospecific antibodies. CrossMab technology has emerged as one of the most versatile antibody engineering technologies in industry over the past decade, and 14 bispecific antibodies using CrossMab technology have entered into clinical trials. In this presentation an overview of the development of bispecific CrossMab antibodies at Roche will be given with a focus on their application for cancer immunotherapy. This will cover T cell bispecific antibodies, tumor-targeted co-stimulatory antibody fusion proteins as well as bispecific antibodies targeting immune checkpoint inhibitory receptors on T cells.

Christian Klein, Head Oncology Programs, Department Head Cancer Immunotherapy Discovery 3, **Roche Innovation Center Zurich,** *Switzerland*

9:30 **LIVE Q & A with Christian Klein**

9:50 **KEYNOTE: Optimising ADCs Through Choice of Antibody, Site, Linker and Payload**

As the technology around ADCs improves and expands, there arises a diversity of variables resulting in a complex choice. I will present several case studies on how we have approached optimizing the efficacy and safety of an ADC through tuning of the various ADC components.

Thomas Pillow, Senior Scientist, **Genentech**

10:10 **LIVE Q & A with Thomas Pillow**

10:30 **Spotlight Presentation**

10:50 *Networking Coffee Break*

OVERCOMING COMMON COMPLEX PROTEIN DRUG CHALLENGES

11:30 **Antibody-guided enzyme replacement therapy for lysosomal diseases**

Conventional enzyme replacement therapies (ERT) for many lysosomal diseases suffer from insufficient delivery to affected organs. Antibody-guided ERT is a new approach that utilizes antibody-enzyme fusion proteins to address this problem. The antibody moiety recognizes transmembrane proteins involved in lysosomal trafficking that are also preferentially expressed in cells most affected in a particular disease. We show superior efficacy of antibody-guided ERT as a protein therapeutic or gene therapy in models of lysosomal diseases.

Andrew Baik, Staff Scientist**, Regeneron**

11:50 **KEYNOTE: Experimental and Computational Methods For Generating and Engineering Antibodies with Drug-like Properties**

Peter Tessier, Albert M Mattocks, Professor of Pharmaceutical Sciences, **University of Michigan**

12:10 **Spotlight Presentation**

12:30 **LIVE Q & A with Speakers from this Session**

1:00 *Lunch Break*

CHARACTERIZATION FOR YOUR COMPLEX MOLECULES

2:00 **Ultrafast identification and stability characterization of site-specific conjugates**

This presentation will highlight new methods that allow identification and characterization of large number of antibody variants simultaneously without the need of high throughput robotics. The described novel approaches provide a versatile platform to uncover new conjugation sites for site-specific ADCs and monitor their biotransformation.

Sayumi Yamazoe, Senior Research Investigator, **Bristol-Myers Squibb**

2:20 **Analytics, both, biochemical and physical stability testing for Bispecifics and Fusion proteins**

Eric Falcone, Scientist II, Pharmaceutical Development, **Alexion**

2:40 **Developability Assessment and Biophysical Characterization of Antibody and Bispecific Drug Molecules at the Discovery Stage**

- Factors which may impact the developability of monoclonal antibodies and various formats of bispecific antibodies will be reviewed
- The talk will outline a selection process which enable the design, triage, and optimization of antibody leads with optimal physicochemical properties before they reach the development phase, thereby reducing the level of risk failure and reducing development time to FIH.
- The physico-chemical characterization, candidate screening, and optimization and early developability assessment of candidate molecules will be discussed.
- Correlations between analytical and biophysical assay endpoints will be discussed

Laurence Fayadat-Dilman, Senior Director, Protein Sciences, **Merck**

3:00 **LIVE Q & A with Speakers from the Session**

Day Three • Wednesday, November 4, 2020

PLENARY SESSION

9:00 **Chairperson's Opening Remarks**

9:10 **KEYNOTE: Cancer Therapy Using Antibody-Cytokine Fusion Proteins**

Engineered cytokine therapeutics are gaining importance for the treatment of cancer and of chronic inflammation.

In this lecture, I will present preclinical and clinical progress for the development of innovative products, that offer unprecedented activity and selectivity for the treatment of serious human conditions.

In particular, I will focus on strategies to achieve "activity on demand"

Dario Neri, Professor, **ETH**

9:30 **LIVE Q & A with Dario Neri**

9:50 **KEYNOTE: Centryn Conjugates for Selective Targeting of Functional Payloads**

Steven Nadler, Vice President of Research, **Aro Biotherapeutics**

Centyrins are small 10kD stable protein domains capable of binding with high potency and selectivity to many target proteins. Importantly, centyrins are capable of delivering various payloads including siRNA and toxins in a cell type specific manner. We will discuss our work using a centyrins for specific intracellular delivery of various payloads including KRAS siRNA.

10:10 **LIVE Q & A with Steven Nadler**

10:30 **Spotlight Presentation**

10:50 *Networking Coffee Break*

FUTURE DRUG CHALLENGES

11:30 **Tumor-Targeted Immune-Stimulating Antibody Conjugates (ISAC): a New Class of Immuno-Oncology**

The clinical success of cancer immunotherapies has reinvigorated the discovery for novel immune stimulants. Selective activation of the innate immune system to generate an adaptive immune response has long been a goal for drug discovery. Systemically delivered small molecule Toll-like receptor (TLR) agonists have been vigorously pursued in the clinic but have suffered from undesirable side-effects, mainly attributed to the inherent mode of action. To overcome these liabilities, we developed an immune-stimulating antibody conjugate (ISAC) platform. ISACs are tumor-targeting monoclonal antibodies that systemically deliver a powerful innate immune-stimulating agent directly to the tumor microenvironment. Pre-clinical data will be presented demonstrating an adaptive immune response leading to durable T cell mediated tumor clearance and surveillance through TLR7/8 agonism. The structure-based design of novel TLR7/8 agonists will be presented. Bolt's approach to this new class of immuno-oncology therapeutics demonstrates the promise of the ISAC platform

Brian Safina, VP Chemistry, **Bolt Biotherapeutics**

11:50 **COBRA: A Novel Conditionally Active T-Cell Engager Platform**

Maverick has developed a novel recombinant bsAb platform called COBRA™ (Conditional Bispecific Redirected Activation). COBRAs are engineered to enable targeting of more widely expressed and validated tumor cell surface antigens by focusing T cell engagement within the tumor microenvironment. COBRA molecules are designed to bind to target antigen, which may be expressed on both tumor and normal cells, yet not engage T cells unless exposed to a proteolytic microenvironment, which is common in tumors but not in normal healthy tissues. Once bound to the tumor target antigen, protease-dependent linker cleavage allows COBRAs to convert an inactive anti-CD3 scFv to an active anti-CD3 scFv binding domain. Upon conversion, COBRAs are then able to simultaneously co-engage T cells and target antigen, resulting in a potent cytolytic T cell response against the tumor cells.

Danielle Dettling, Senior Director, **Maverick Therapeutics**

12:10 **Spotlight Presentation**

12:30 **LIVE Q & A Speakers from Session**

1:00 *Lunch Break*

2:00 **C'Dot Drug Conjugates (CDCs)**

- Exploring the range of imaging and therapeutic payloads that can be attached to the C-Dot platform
- Sub 10nm conjugates increases the payload capacity but are able to cross the blood brain barrier.

Gregory Adams, CSO, **Elucida Oncology**

2:20 **CXCR4 Heteromers as Targets for Cancer Therapy**

G-protein coupled receptors (GPCRs) often exist and function as heteromers. CXCR4, a GPCR that is overexpressed in various types of cancer and often associated with poor prognosis, forms heteromers with other GPCRs. We are developing anti-cancer therapies by targeting CXCR4 heteromers instead of CXCR4 itself. This approach will be a platform for precision medicine and the solution for existing anti-CXCR4 drugs for cancer therapy by improving the efficacy and safety of the drugs.

SoHui Kim, Scientist, **GPCR Therapeutics**

2:40 **Brain delivery of therapeutic proteins using a novel Fc fragment blood-brain barrier transport vehicle**

Mihalis Kariolis, Senior Scientist, Protein Engineering, **Denali Therapeutics**

3:00 **Live Q & A with Speakers from Sessions**

FUTURE DRUG CHALLENGES

9:40 **Oligonucleotide Therapeutics: Now on Target with Antibody Conjugates**

The widespread use of oligonucleotides as therapeutics has been limited by delivery to target tissues. Local delivery to the eye and the CNS has produced clinical successes and drug registrations. Lipid nanoparticles and ligands for the asialoglycoprotein receptor (ASGPR) have been used effectively to deliver oligonucleotide payloads to liver and are being used in the clinic. However, technologies for delivering oligonucleotides to other cell types and tissues have lagged these approaches. This presentation will explore how Avidity Biosciences are using antibody oligonucleotide conjugates to develop drug candidates for multiple disease indications.

Art Levin, CSO, **Avidity Biosciences**

10:00 **Intein-Mediated Reconstitution of Split-Toxins For Improved Selectivity Cell Ablation**

On- and off-target toxicity limit the application of proteinaceous toxins for selective ablation of cancer cells. We will discuss the possibility of improving the targeting specificity via independent delivery of benign fragments of immunotoxins and their cytoplasmic reconstitution into a functional toxin using split-inteins. Receptor-mediated delivery of engineered split-toxins could provide a platform for precise therapeutic ablation of tumors..

FDmitri Judryashov, Associate Professor, **Ohio State University**

10:20 **Antagonistic antibodies and KO mice used to establish a key role for IL-13 signaling via the type 2 IL-4 receptor in experimental atopic dermatitis**

IL-13 and IL-4 are potent mediators of type 2-associated inflammation such as those found in atopic dermatitis (AD). Induction of two distinct models of experimental AD in Il13ra1-/- mice, (lacking the type 2 IL-4R), revealed that dermatitis was dependent on type 2 IL-4R signaling. Furthermore, IL-13Ra1-neutralizing antibodies we isolated established proof-of-concept for therapeutic targeting of this pathway in AD.

Itai Benhar, Head of Antibody Engineering Lab, **Tel-Aviv University**

10:40 **Bioanalytical Methods Addressing Rising Complexity of Novel Modalities and Novel Delivery Routes for Biotherapeutics**

Increasing complexity of novel therapeutic modalities requires sophisticated bioanalytical methods for their pharmacokinetic assessment with additional consideration given to potential catabolism of complex biotherapeutics and its impact on therapeutic index. Moreover, novel routes of administration of biologics impart additional complexity as the consequence of modifications to the API as well as various formulation components. This presentation will highlight some of the bioanalytical challenges encountered as well as the solutions employed to address them.

Anton Rosenbaum, Head of Regulated Bioanalysis and OMICS by LC-MS, Integrated Bioanalysis, Clinical Pharmacology & Quantitative Pharmacology, **AstraZeneca**

11:00 **LIVE Q & A with Speakers from Session**

11:30 *Networking Coffee Break*

MANUFACTURING STRATEGIES FOR BIOCONJUGATES

12:00 **Recent Analytical Characterization of a Site-Specific ADC**

Abstract Coming Soon

Nicole Schiavone, Senior Scientist, **Pfizer**

12:20 **Antibody Conformational Changes and Aggregation with Peptide Conjugation**

Gary Ren, Lawrence Berkley National Labs

12:40 **LIVE Q & A with Speakers from Sessions**

1:00 *End of Conference*

ON DEMAND CONTENT

These ON-DEMAND presentations will be available to view 24 hours a day starting October 26th for 30 Days We Encourage You to View as Many of these On-Demand Presentations at Possible Prior to the "Live Event" Dates of November 2 -5, so that you can fully participate in the live keynote Q&A, speaker panel discussions and other live topic networking activities….see WATCH LIVE schedule showing all the live activities you can participate in on November 2 – 5.

SBT6050, a HER2-Directed TLR8 ImmunoTAC™ Therapeutic, is a Potent Human Myeloid Cell Agonist with Tumor-Localized Activity

Clinical development of systemically administered myeloid cell agonists has been hindered by acute toxicities due to peripheral activation of the targeted cell types. Intratumoral administration, the route of delivery typically used for innate immune/myeloid cell agonists, is limited by tumor accessibility and a dependence on abscopal responses. SBT6050, a novel therapeutic comprised of a potent toll-like receptor (TLR) 8 agonist conjugated to a HER2-directed monoclonal antibody, is designed for systemic delivery with tumor-localized activation of human myeloid cells.

Unlike other endosomal TLRs, such as TLR7 and TLR9, TLR8 is highly expressed in the human myeloid cells prevalent in tumors, including conventional DCs and macrophages. Agonism of TLR8 in human myeloid cells activates a broad spectrum of anti-tumor immune mechanisms. These activities cannot be replicated by potent agonists for other endosomal TLRs or with clinical agents that only weakly engage TLR8, such as resiquimod. Studies with human immune cells show that SBT6050 potently induces, in a HER2-dependent manner, multiple anti-tumor immune activities, including proinflammatory cytokine and chemokine production, inflammasome activation, direct activation of DCs and indirect T and NK cell cytolytic activity. This activity is dependent upon the ability of the Fc domain of the antibody to engage Fcg receptors on the surface of myeloid cells, facilitating delivery of the TLR8 agonist payload. Our data indicate the favorable profile of SBT6050 is likely due to activation of endosomal TLR8 by efficient delivery of the TLR8 agonist in conjugate form and TLR8's unique expression profile.

Systemic delivery of a SBT6050 surrogate in mice shows robust single agent efficacy in multiple mouse tumor models. In contrast to observations with small molecule TLR agonists, the SBT6050 surrogate does not induce peripheral cytokine production in mice at effective dose levels, consistent with the localized activity of the molecule. Collectively, these data support the development of SBT6050 for patients with HER2-expressing tumors. More broadly, the data presented here describe a novel therapeutic modality that allows for systemic administration of immune modulators with tissue-localized activity.

Sean W. Smith, Senior Director, Chemisty, **Silverback Therapeutics**

Hydrophilic Monodisperse Polysarcosine Drug-linker Platform: Towards Next-Generation Antibody-Drug Conjugates

"Hydrophobicity masking" chemical modifiers can be orthogonally embedded into drug-linker constructs of ADCs. These hydrophilic entities have the potential to enable increased drug-loading (drug-antibody ratios at or above 8) while improving PK profiles, efficacy and tolerability of the conjugates. Our efforts in developing a hydrophilic monodisperse polysarcosine-based ADC platform will be presented. Impact of polysarcosine on physicochemical and pharmacological properties of conjugates bearing different payloads will be discussed.

Warren Viricel, Chief Scientific Officer, **Mablink Bioscience**

Site Specific Lysine and Cysteine based conjugation

- The traditional methods used to prepare ADCs and the issues associated with these strategies;
- How to create homogeneous ADCs using Cysteine and Lysine targeting reagents;
- Achieving regioselectivity: how to modify a particular amino acid side-chain at one site when multiple copies of the same side chain are also available to react at other protein sites;
- Examples of proteins/antibodies that can be modified with these reagents;
- How to evaluate the activity of these conjugates.

Barbara Bernardim, Professor, **Cambridge University**

TMAC: a novel drug conjugate platform for the treatment of cancer

The Affimer-TMAC (tumour microenvironment activated conjugate) is a novel antibody mimetic drug conjugate platform that allows the release of toxic chemotherapeutics preferentially in the tumour microenvironment (TME).

The Affimer platform is a fully human scaffold based on the protease inhibitor Stefin and high affinity protein antagonist can be generated using phage display. The Affimer scaffold can be used to either target the chemotherapeutic to the TME or extend the serum half life to improve the therapeutic index.

The release of the toxic payload occurs within the TME by the specific cleavage of a novel linker that is only cleavable by the enzyme FAP-alpha. Increase levels of expression of FAP-alpha are associated with a number of solid tumours compared to normal tissue.

We have shown in PoC studies that Affimer-TMACs can be generated, cleaved to release the active warhead in the TME.

Amrik Basran, Chief Scientific Officer, **Avacta Life Sciences**

Glycoengineering next generation bioconjugate vaccines using E. coli as a platform

- Quick summary of conjugate vaccines targeting bacterial pathogens
- Introduce microbial glycoengineering for the production of a new class of conjugate vaccines termed bioconjugate vaccines
- Highlight the advantages of developing and manufacturing bioconjugate vaccines compared to conventionally produced conjugate vaccines
- Case examples of VaxNewMo bioconjugate vaccines preventing Streptococcus pneumoniae, Klebsiella pneumoniae and Group B Streptococcus disease.

Christian Harding, Co-Founder & CEO, **VaxNewMo**

CM-09, a Novel Antibody-Drug-Conjugate to TRA-1-60, a Cellular Reprogrammed Target in Metastatic Gastric and Pancreatic Cancers

- Cellular Reprogramming is an emerging theory on the origin, development and progression of cancer
- Cellular Reprogramming results in malignant cells with stemness properties and clinically untested new therapeutic cancer targets
- CM-09 is an ADC to a reprogrammed target, TRA-1-60, in metastatic and aggressive cancers

Michael Schopperle, CEO**, CureMeta**

Peptide Drug Conjugates for Targeted Therapy

Peptides represent an indispensable class of medicines that have unique virtues when compared to conventional small molecule and antibody-based drugs. Peptide Drug Conjugates represent an emerging trend that aim to achieve superior therapeutic outcomes with diminished adverse effects. This talk provides an overview of the recent advances in synthetic methods and biological performance of peptide conjugates in treatment of multiple major diseases.

Rongjun He, Research Scientist**, Novo Nordisk**