Next Generation Protein Therapeutics & Bioconjugates™ Summit

June 18-20, 2019
Park Central Hotel
San Francisco, CA

LOOKING BEYOND ANTIBODIES TO TRANSFORM PROMISING NEXT GENERATION PROTEINS INTO NEXT GENERATION MEDICINE

Employ the creativity behind protein engineering and design into innovative biologics. Maximize the therapeutic window with fresh perspectives and cutting-edge targets.

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LOOK BEYOND ANTIBODIES TO TRANSFORM PROMISING NEXT GENERATION PROTEINS INTO NEXT GENERATION MEDICINE

DAY 1: NEXT GENERATION BIOCONJUGATES: DESIGN & DEVELOPMENT

- **Learn about novel conjugation techniques** and technology to create a more cost effective, high efficacy, easier process.
- **Tackle bioconjugations beyond antibodies and cytotoxins: W**hat are the next generation delivery vehicles and modalities?
- **Overcome bioconjugate challenges** by maximizing your therapeutic window and maintaining stability.

DAY 2: NEXT GENERATION PROTEIN THERAPEUTICS: CREATIVE ENGINEERING & DESIGN APPROACHES

- **See the latest expansion of antibody mimetic molecules** and the future of these promising therapeutic proteins in a clinical setting.
- **Uncover creative engineering and design approaches** for next generation protein therapeutics: Bi and multi specifics, Bispecific T cell engagers, Non-Antibody Scaffolds, Checkpoint Inhibitors and Peptoids.
- **Are you up-to-date** on the use of novel protein therapeutics for diseases outside of oncology?

DAY 3: NEXT GENERATION PROTEIN THERAPEUTICS NEW PLATFORM DESIGN & PATIENT CARE

- **Discover how the use of systems and synthetic biology** can be used to identify novel targets.
- **Delve into Bispecific design and production to** achieve a product with maximum quality.
- **Achieve delivery into cells and across the blood-brain barrier.**
- **What do doctors look for** in new drugs and how can side effects be reduced?

NEXT GENERATION BIOCONJUGATES: DESIGN & DEVELOPMENT

7:00 *Breakfast and Registration*

The Latest Conjugation Methods & Technologies

8:15 **Combining Amunix XTEN® Polypeptides and THIOMAB™ antibodies to Enable Homogeneous High-DAR ADCs**

In this presentation, we will describe the development of a conjugate approach employing Cys-engineered antibodies and XTEN® polypeptides to enable the preparation of homogeneous ADCs with high drug load (>14), exceptional pharmacokinetics and anti-tumor efficacy. Considerations for the application to the delivery of non-conventional payloads will be discussed.

Jack Sadowsky, Scientist, **Genentech**

8:45 **Antibody Drug Conjugates for Immunology (iADC)**

Antibody Drug Conjugates (ADC) are a rapidly expanding area of pharma company pipelines. They combine the targeting of an antibody with the potency of a small molecule and were pioneered for oncology. There are now 4 marketed oncology antibody drug conjugates (oADC) and approaching 100 in clinical development. This talk will describe the technology behind oADCs and the challenges faced in modifying this technology for use with an immunology antibody drug conjugate (iADC).

Dr Adrian D Hobson, Research Fellow, **AbbVie Bioresearch Center,** *USA*

9:15 **Toward the Elucidation of Structure for Glycoconjugate Vaccines Using a Monosaccharide Peptide/Protein Model Conjugation Study**

Polysaccharide conjugated protein vaccines have benefited billions of people through the adaptive immune response against virulent bacterial infections. Reductive amination is one of the most widely used conjugation chemistries for generating such vaccines. However, due to the complex nature of polysaccharide conjugated proteins, a detailed structural characterization has been elusive. A recent study using model compounds, has brought new insights to the potential structure of these vaccines which can start to benefit vaccine design and inform on the mechanism of action of glyconjugate vaccines.

Wei Huang, Senior Scientist, **Pfizer**

9:45 *Networking Refreshment Break*

The Future of Novel Conjugates & Delivery Molecules

10:30 **Structural Characterization of Antibody-Drug Conjugates**

During clinical development of ADCs, it is critical to understand the impact of product quality attributes and variants on safety and efficacy. This presentation focuses on applying novel analytical techniques to characterize ADCs produced with different linker-drug and conjugation chemistries. Case studies include analyzing rare product variant and drug degradation pathways. Unique mass spectrometry methods that provide automatic and comprehensive characterization will be highlighted.

Zhiqi Hao, Scientist, Analytical Development & Quality Control, **Genentech**

11:00 **Amanitin-Based Antibody-Drug-Conjugates as New Therapeutic Modalities for Cancer Therapy**

Antigen-Targeted Amanitin-Conjugates (ATACs) represent a new class of ADCs using the payload Amanitin. This payload introduces a novel mode of action into oncology therapy, the inhibition of RNA polymerase II. The technology platform includes Amanitin supply, site-specific conjugation, demonstrated safety profile and biomarker. HDP-101 is the first ATAC directed against BCMA entering Phase I trials by the end of 2019.

George Badescu, Vice President Scientific Affairs, **Heidelberg Pharma AG**

11:30 **Improved Tumor Growth Inhibition of Diabody-Drug Conjugates Achieved by Half-Life Extension**

Half-life extension technologies such as PEGylation and albumin-binding domains (ABDs) have been widely used to improve the pharmacokinetics of many different types of biologics. In this study, we used an anti-5T4 diabody conjugated with a highly potent cytotoxic pyrrolobenzodiazepine (PBD) warhead to assess and compare the effects of PEGylation and albumin binding on the in vivo efficacy of antibody fragment drug conjugates.

Qi Ling, Scientist, **MedImmune/AstraZeneca**

12:00 **WuXiBody™, an Innovative and Versatile Bispecific Antibody Format Opens a New Era for Therapeutic Antibody Development**

Abstract: Bispecific antibodies are a 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.

George Wang, Vice President of Biologics Discovery, **WuXi Biologics**

12:30 *Luncheon*

1:45 **TBC**

Design Strategies To Overcome Common Bioconjugate Challenges

2:15 **Modulating Therapeutic Window of Antibody Drug Conjugates by Protein Engineering: An Industry Prospective**

This presentation will focus on engineering multiple properties of monoclonal antibodies to maximize the therapeutic window. Properties such as conjugation location, antibody internalization, antibody affinity, drug and linker type, and use of dual payloads will be discussed.

Pavel Strop, Senior Director, **Bristol-Myers Squibb**

2:45 **Development of Antibody-Drug-Conjugates to Novel Embryonic Targets in Cancer**

Cellular reprogramming or de-differentiation is an emerging concept for the origin and development of aggressive and metastatic cancers. Reprogramming leads to malignant cells with primitive characteristics and embryonic gene signatures. We have developed therapeutic antibody-drug-conjugates specific to embryonic targets not expressed in normal tissues and re-expressed in cancer.

Michael Schopperle, CEO, **CureMeta**

3:15 *Networking Break*

4:00 **Daiichi Sankyo (DS) ADC Technology: The Features as Next Generation ADC Technology**

We have been developing several ADCs, such as DS-8201a and U3-1402a, which showed a potent and broad spectrum of anti-tumor activity both in preclinical and clinical. Our ADC technology has unique features; stable linker, high clearance of the payload, high DAR, and bystander effect. I will review our 'smart chemo' ADC technology and discuss the features as next generation ADC technology.

Naoya Harada, PhD, Researcher, Biologics & Immuno-Oncology Laboratories, **Daiichi Sankyo Co., Ltd.**

4:30 **Characterizing the Stability of ADCs, and Bispecific Molecules Towards Improvingt the Therapeutic Index**

Julie Lade, Scientist**, Amgen**

5:00 *Networking Reception in Poster & Exhibit Hall*

NEXT GENERATION PROTEIN THERAPEUTICS CREATIVE ENGINEERING & DESIGN APPROACHES

7:00 *Breakfast and Registration*

Antibody Mimetics – An Overview

8:15 **KEYNOTE: Protein Engineering To Extend The Binding Protein Paradigms**

- Design strategies for creating binding protein scaffolds
- Beyond conventional applications
- A novel strategy to create modular binding proteins

Andreas Plückthun, PhD, Professor and Director, **University of Zurich**

8:45 **Stronger Than Ever – Past, Present, and Future of Novel Scaffold Drugs**

The 2018 chemistry Nobel laureates' work paved the way for the use of non-antibody binding proteins in drug development. It was while turning the academic ideas into businesses, when the differentiating strengths of novel scaffolds crystallized. With safety doubts dispelled with clinical data, we now start to see the technologies to unfold their key strengths.

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

9:15 **Multispecific DARPin® Therapeutics to Modulate the Tumor Microenvironment and Immune Cells Locally**

Molecular Partners is developing bi- and multi-specific therapeutic DARPin® molecules to address some of the limitations of current cancer treatments MP0250: a dual HGF and VEGF blocking molecule applicable in a wide range of cancer indications Improving the therapeutic index of immune agonists by localizing activity to tumor site: why & how? Further immune-oncology developments & potential for combination therapies

Laura Jeanbart, Scientist, **Molecular Partners**

9:45 *Networking Refreshment Break*

Novel Next Generation Protein Therapeutic Design Approaches

10:30 **Affimer Therapeutics: A Novel Human Scaffold for the Generation of Bi-specific Molecules**

Affimer therapeutics are based on the human protein Stefin A, a small (12kDa) intracellular protease inhibitor. We have built large phage display libraries (1x1010), generating Affimer binders to range of therapeutically relevant targets (e.g. PD-L1, LAG-3). We have shown that the Affimer scaffold can be formatted as in-line, Fc or antibody fusions to create bispecific molecules are able to engage both target antigens.

Amrik Basran, Ph.D.. Chief Scientific Officer, **Avacta Life Sciences**

11:00 **Functional Mimetic of the G-Protein Coupled Receptor CXCR4 on a Soluble Antibody Scaffold**

G-protein coupled receptors (GPCRs) constitute major drug targets however their characterization has been challenging due to the need for a lipid environment. We report an antibody scaffold mimetic (ASM) platform where we have recapitulated the extracellular functional domains of the GPCR CXCR4 on a soluble antibody framework. The engineered ASM molecule can be recognized by anti-CXCR4 antibodies, bind the HIV-1 glycoprotein ligand gp120, and the natural chemokine ligand SDF-1α. Further, it can competitively inhibit the SDF-1α signaling pathway and be used as an immunogen to generate CXCR4 specific antibodies. This platform will be useful in the study of GPCR biology in a soluble receptor context.

Adem Koksal, Scientist, Protein Engineer, **AstraZeneca**

11:30 **An Integrated Approach To Managing Immunogenicity Risk & Optimum Protein Design**

Integrated platforms can be used to mitigate immunogenicity risk and characterize immune responses during the drug design and development stages. ProImmune offers mutational activity mapping for optimal protein design, DC-T/T cell proliferation assays for biologic lead selection/ optimization, a Mass Spectrometry assay for characterization of antigen presentation; HLA-peptide binding assays to characterize individual epitopes & undiluted whole blood cytokine storm assays.

Emilee Knowlton, Immunology Sales Specialist, **ProImmune**

12:00 *Luncheon*

1:15 **Modulating The Immune System With Multi-Specific Antibodies in Cancer**

Multi-specific antibodies have the unique ability to elicit an immune response at the site of a tumor. By minimizing the toxicities associated with a systemic immune response, tumor targeted multi-specific antibodies can increase the therapeutic index for new immune activating cancer therapies. Using a unique sequence-based discovery approach along with proprietary transgenic rats, we have created a large collection of fully human antibodies targeting a variety of tumor antigens and activating receptors on immune cells. Our novel discovery platform combines antibody repertoire deep sequencing, high-throughput gene assembly, and recombinant expression. Using machine learning tools, we are able to rapidly establish sequence-activity relationships and identify key residues and variable region positions in the antibody repertoire that had desired agonist behavior. As one example, we have created a panel of aCD3:aBCMA bispecific antibodies for the treatment of multiple myeloma that stimulate different levels of T-cell activity. These bispecific antibodies exhibit a spectrum of in vitro tumor cell killing activity with varied levels of cytokine release. In summary, we have created a platform for tunable immune activation at the site of the tumor that works with a variety of tumor antigens.

Nathan Trinklein, PhD, Vice President, **Teneobio, Inc.**

1:45 **Next Generation Cytokine-Fc Fusions Engineered for Superior Therapeutic Index**

Creating lymphocyte activating drugs from natural cytokines has proven challenging due to their high potency, low tolerability, and fast clearance, which limits therapeutic index. Xencor has developed several cytokine-Fc fusions using our engineered heterodimeric antibody Fc domain. Each molecule has been precisely tuned for potency and/or selectivity to allow higher dose levels and provide more sustained exposure.

Matthew Bernett, Associate Director, Protein Engineering, **Xencor**

2:15 **Avidity-based T-cell Engager Preferentially Kills Cells Overexpressing HER2**

T-cell engagers are potent molecules capable of killing cells expressing the target at low levels. HER2 is an important target overexpressed in many tumor but also expressed in normal tissue. We describe the development of T-cell engager based on a low affinity anti-Her2 antibody with a big avidity component that is more selective than a traditional IgG-like antibody format in killing tumor cells.

Diego Ellerman, Principal Scientific Researcher, **Genentech**

2:45 *Networking Refreshment Break*

3:15 **Screening, Optimization and Characterization of a Novel 4-1BB x 5T4 ADAPTIR™ Bispecific Antibody**

ALG.APV-527 is a novel 4-1BB x 5T4 targeting bispecific antibody that induces potent CD8 T cell activation only when engaged by 5T4, a tumor associated antigen. The binding domains of ALG.APV-527 were isolated from the ALLIGATOR-GOLD® human scFv library (Alligator Bioscience AB), then optimized and developed for use in the bispecific ADAPTIR Next Generation format (Aptevo Therapeutics Inc.).

David Bienvenue, Senior Director, Protein Sciences, **Aptevo Therapeutics**

3:45 **Discovering Peptoids- What are They and How Do They Work?**

- What are they?
- How do they work?
- Proof of concept data
- Clinical trial feasibility
- Next stages of therapeutic progression – where do we go from here?

Kent Kirschenbaum, Professor, **NYU**

4:15 **Therapeutic Antibody-based Strategies to Enhance Anti-Tumor Immunity: Concept To Clinic**

Application of the following antibody engineering approaches will be presented covering rationale, molecular design, preclinical validation and clinical experience

- Fc-engineering to optimize effector function of anti-HER2 mAb therapy
- Bispecific bivalent DART® molecules to direct T-cell lysis of tumor cells
- Bispecific tetravalent DART® molecules to simultaneously block two checkpoint pathways

Paul Moore, Ph.D., Vice President, Immunology & Cell Biology, **MacroGenics**

4:45 *Networking Reception*

NEXT GENERATION PROTEIN THERAPEUTICS CREATIVE ENGINEERING & DESIGN APPROACHES

7:00 *Breakfast and Registration*

Techniques & Technologies to Predict & Find New Targets

8:15 **KEYNOTE: Next Generation Methods For Protein Design**

Protein design has advanced significantly in recent years. However, the ability to capture the complexity found in native proteins is still lacking. We pioneer the use of generative machine learning (ML) models to build protein structures. While a protein design AI is still in its infancy, we have created a new de novo alpha/beta barrel with the help of powerful ML methods.

Possu Huang, Assistant Professor of Bioengineering, **Stanford University**

8:45 **Engineering Multi-Specific Antibodies Leveraging Patients' Active B Cell Responses**

Atreca discovers novel cancer-specific targets and native human antibodies to those targets, through examination of the active B cell responses of cancer patients. Antibodies that specifically bind non-autologous human tumor are advanced through our drug discovery pipeline, including standard IgG formats and next-generation multispecifics. I will discuss our selection of multispecific formats for cell engagement and the engineering of potent anti-tumor molecules.

Shaun Lippow, Ph.D., Director, Protein Engineering, **Atreca**

9:15 **Synthetic DNA Technologies Enable Antibody Discovery and Optimization**

- Antibody locating technology used in therapeutics
- Optimising these antibodies for therapeutics

9:45 *Networking Refreshments*

10:30 **Multi-Specific Antibody Development Using Sequence-Based Antibody Discovery**

We have developed a novel, sequenced-based approach for the rapid and high-throughput discovery of antibodies from our human transgenic rat (UniRat) platform. UniRats express fully human heavy chain only antibodies called UniAbs. UniAbs are ideal building blocks for antibody-based biologics because they can be genetically fused to other proteins and can be arranged to make multi-specific antibodies without the complication of heavy and light chain pairing. Our results show UniAbs have biochemical properties similar to conventional antibodies and have distinct advantages for developing next-generation multi-specific therapeutic antibodies.

Katherine Harris, Senior Director of Discovery, **TeneoBio Inc**

11:00 **PANEL DISCUSSION: Identifying New Targets**

- Methods & Technologies used to identify new targets within the body
- Finding good tumour antigens to target
- Non-tumour targeting
- FAP located in tumour microenvironment
- IL-10 and fibronectin
- Genome Sequencing
- GPCRs

Mike Schopperle, PhD, CEO, **CureMeta**
Katherine Harris, Senior Director of Discovery, **TeneoBio Inc**
David Bienvenue, Senior Director, Protein Sciences, **Aptevo Therapeutics**

Bi-Specifics in Production

11:30 **Bi-Specific Antibodies - Platform Approaches To Rapidly Generate Binder & Format Variability**

1. Effective and robust technology platform to generate large varieties of bsAbs in different formats
2. Automated production of bsAb binder-format combination matrices
3. Format defines function: screening of binder-format matrices identifies combinations with desired functionalities
4. Outlook - application examples and platform expansion

Stefan Dengl, Principal Scientist, **Roche**

12:00 *Luncheon*

1:30 **Immunoglobulin Domain Interface Exchange as a Platform Technology To Engineer and Manufacture Bispecific Antibodies**

Glenmark Pharmaceuticals' BEAT® platform is a robust and versatile bispecific antibody platform based on heavy chain heterodimerization. The technology relies on biomimicry wherein the protein-protein interfaces of two different immunoglobulin constant domain pairs are exchanged to design new heterodimeric CH3 domains. In transient transfections, at equimolar chain ratios, engineering allows for ≥ 95% heterodimerization in the bispecific Fab scFv and the Fab Fab common light chain antibody formats. Using our platform, we have engineered and in-house manufactured two clinical stage bispecific antibodies. Engineering concept, manufacturing, and latest improvements to the platform will be presented.

Stanislas Blein, Ph.D., Senior Director, Head Antibody Engineering, **Glenmark Biotherapeutics**

Delivery: What Happens After IV?

2:00 **Brain Drug Delivery of Therapeutic Antibodies with Blood-Brain Barrier Penetrating Bi-Specific Antibodies:**

Therapeutic antibodies can penetrate the blood-brain barrier (BBB) following the re-engineering of the antibody as a bi-specific antibody (BSA). The BSA is comprised of a therapeutic antibody domain and a BBB transporter antibody domain. The transporter antibody domain targets an endogenous BBB receptor such as the BBB insulin receptor or transferrin receptor, and acts as a molecular Trojan horse to ferry the fused therapeutic antibody across the BBB.

William Pardridge, M.D., Distinguished Professor Emeritus / Founder and CSO, **UCLA / ArmaGen**

2:30 **Generation of a Bi-specific ADAPTIR Molecule that Targets CD86 and Delivers IL-10 Inhibits Antigen Presenting Cells and Has Potential as a Therapeutic Treatment of Autoimmune Disease – An Example of Cytokine Delivery in Autoimmune Disease**

IL-10 is a key negative regulator of inflammation, however, development of IL-10 in the clinic for suppression of inflammation has been challenging. APVO210, an anti-CD86 scFv x monoIL10 fusion, offers key advantages over other IL-10 based drugs, due to its unique MOA: selective stimulation of the IL-10R on APC, without stimulating T and B cells. Potent biological activity has been demonstrated preclinically in vivo.

Gabriela Hoyos, Senior Director, immunobiology, **Aptevo Therapeutics**

3:00 *Networking Refreshment Break*

Patient Welfare in Drug Discovery

3:30 **Considerations For Immunogenicity Risk Assessment and Mitigation and Bioanalytical Strategies For the Next Generation of Biologics**

The multidomain biologics like bispecifics, trispecifics and nanobodies as well as transgenes being delivered by viral vectors as well as peptides that can activate immune system are being developed as next generation biologics. The intent of such novel modalities is to be able to engage multiple targets using a single molecule with a small size instead of developing co-formulation and combination strategies. The additional advantages are the ability to target solid tumors that might be inaccessible through systemic delivery. The immunogenicity risk assessment and bioanalytical considerations for the novel domains will have to consider the risks due to sequence and structure of each domain and the entire molecule, immune modulation due to target engagement and the design of bioanalytical assays to support immunogenicity assessments in clinic. For viral vector mediated therapies, an understanding of risk due to the virus specific proteins vs transgene and the design of bioanalytical assays that cover both cell and humoral immune responses would need to be developed.

Vibha Jawa, Director, **Merck**

4:00 **The Development of Innovative Therapeutics for Oncology**

BiXAb platform has a tetra-Fab IgG1 antibody structure and enables plug-and-play bispecific antibody formatting from any pair of monospecific mAbs. BiXAb antibodies possess excellent manufacturability in CHO cells and superior drug-like properties. We will illustrate the properties of this bispecific antibody platform by presenting two case studies, in which BiXAbs target solid tumors and hematological malignancies.

Eugene Zhukovsky, Ph.D., Chief Scientific Officer, Research, **Biomunex Pharmaceuticals**

4:30 **PANEL DISCUSSION: What is The Best Protein Therapeutic?**

- Comparison of mAbs, antibody fragments and alternative scaffolds at combating solid tumours.
- The perspective of a physician
- What does industry need to know to sell the drug?
- What do Doctors look for in Next Generation Therapeutics?

Nathan Trinklein, PhD, Vice President, **Teneobio, Inc.**

Paul Moore, Ph.D., Vice President, Immunology & Cell Biology, **MacroGenics**

Vibha Jawa, Director, **Merck**

5:00 *End of Next Generation Protein Therapeutics and Bioconjugates Summit 2019*

SPONSORSHIP OPPORTUNITIES

What can you expect?

- Connect one-on-one with the scientists who would be implementing your tools to generate interest and gain insight.
- Showcase your expertise and demonstrate thought leadership to industry leaders and decision makers.
- Learn about the latest developments in the industry so you can better anticipate future needs of the market.
- Uncover new potential clients and partnership opportunities to grow your business.
- Highlight your company as a member of the community in an intimate setting to grow relationships.

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