Next Generation Protein Therapeutics & Bioconjugates Summit

June 12-14, 2018
Park Central Hotel
San Francisco, CA

DRIVING CREATIVE PROTEIN ENGINEERING & DESIGN TO SUCCESSFULLY TRANSFORM PROMISING NEW MOLECULES INTO DIFFERENTIATED PRODUCTS

Get unparalleled coverage of the discovery, engineering, and development of novel protein therapeutics and bioconjugates

Learn from Industry Visionaries

Christopher Sheth
Supervisory Pharmacologist,
Division of Hematology Oncology Toxicology
FDA

Sachdev Sidhu
Professor,
Donnelly Centre
University of Toronto

Rakesh Dixit
Vice President R&D,
Global Head,
Biologics Safety Assessment
MedImmune Inc.,
USA

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NEXT GENERATION BIOCONJUGATES DESIGN AND DEVELOPMENT

7:00 *Breakfast & Registration*

8:00 **Chairman's Remarks**

Beyond ADC's - Advances in New Linkers and Higher Drug Payloads

8:15 **Adnectin Conjugates for Cancer Therapy and Imaging**
Adnectins are a family of engineered target-binding proteins based on the 10th human fibronectin type III domain. We will describe the properties of Adnectin-drug conjugates and Adnectin-based PET imaging agents, both of which rely on a combination of high affinity for a therapeutically relevant target and fast clearance from tissues free of the target.
Dasa Lipovsek, Senior Principal Scientist, **Bristol-Myers Squibb,** *USA*

8:45 **Abdurin-Drug Conjugates: Small Size and Long Half-Life Delivers More Payload to Tumors than Antibodies**
Abdurins are an antibody-like scaffold platform derived from the CH2 domain of Fc, retain FcRn-binding, leading to a prolonged circulating half-life. The small size coupled with long half-life facilitates better tissue/tumor penetration and higher target drug concentrations. Recent studies demonstrate that Abdurin-drug conjugates can increased the Therapeutic Index and safely and more effectively deliver toxic payloads in a xenograft model.
Kurt Gehlsen, Vice President and Chief Scientific Officer, **Research Corporation Technologies, Inc.**

9:15 **Conjugation and Targeting Ligand Design Strategies for Targeted Polymeric Nanoparticles**
Manoj Charati, Senior Principal Scientist, **Pfizer**

9:45 *Exhibit Hall Opens for Networking Refreshment Break*

10:30 **Expanding Linkers Beyond Cytotoxins And Higher Drug Payloads: Innovative Linker And Payload Technologies**
If you are interested in presenting on this topic please contact catherine.marshall@knect365.com

11:00 **Preclinical Validation Of Site-Specifically Conjugated Adcs With Potent Anthracycline Payloads In Solid & Hematologic Tumors**
We present a novel ADC format based on the site-specific conjugation of a derivative of the anthracycline PNU-159682 using the transpeptidase Sortase A. The use of a non-cleavable peptide linker provides exquisite stability in vivo, whereas the anthracycline payload endows the ADC with superior potency combined with attractive immune-oncology properties intrinsic to this class of payloads. Validating data obtained in numerous PDX models, as well as in immunocompetent syngeneic models, will be presented.
Roger Beerli, CSO, **NBE-Therapeutics Ltd,** *Switzerland*

11:30 **Thought Leaders Discussion: Future Visions - What are the Next Conjugates and How to Overcome Development Challenges?**
- Where does the future lie for bioconjugates – What other conjugates are out there?
- What kind of linker is required?
- Cleavage sites
- Safety profile and ensuring long term efficacy
- Challenges of conjugations and delivering other potent non-antibody molecules e.g. RNAi, modRNA?
- Cost considerations for complex bioconjugates
- What disruptive technologies are being developed and applied to overcome development challenges

Panellists made up of speakers from the event

12:00 **Spotlight Presentation**

Presented by: MabPlex

12:30 *Luncheon in the Exhibit Hall*

Novel Conjugation Techniques to Improve Selectivity, Yield and Stability

1:45 **Developing A Conjugation-Based Multivalent Ab Format**
We describe a novel multivalent format based on protein conjugation (TRACS). The building blocks are mAbs and Fabs with good expression yields and stability. A conjugation site that supports high conjugation rates and an efficient process was identified. The spatial arrangement of all the Fabs allows their simultaneous binding with reduced steric hindrance. We provide examples of different TRACS that require concurrent binding of all Fabs for their biological activity.
Diego Ellerman, Principal Scientific Researcher, **Genentech**

2:15 **From Cells to ADCs: A Magnetic Bead-Based Conjugation And High-Throughput Analysis Of ADCs**
The use of automated high throughput screening in large molecule discovery research still lags behind that of small molecule discovery. Here, we developed a magnetic bead-based approach for antibody capture and conjugation, together with an automated platform to complete a bioconjugation optimization. Given LC-MS is a widespread analytical bottleneck, we also established a high-throughput MS platform to accurately detect and rapidly quantitate ADCs with acquisition time of 20 sec/sample, 10-50x improvement over traditional LC-MS methods.
Jelly Netirojjanakul, Scientist, **Amgen**

2:45 **Duorcarmycin Dimer-Based Antibody-Drug Conjugates**
To enable duocarmycin dimers as payloads for ADCs we investigated various locations on the drug for linker attachment. The use of structure-based drug design facilitated this process and led to highly efficacious conjugates. The impacts of these changes on both efficacy and toxicity will be discussed.
Thomas Pillow, Senior Scientist, **Genentech**

3:15 *Networking Refreshment Break in the Exhibit Hall*

4:00 **Novel Conjugation Techniques to Improve Selectivity, Yield and Stability**
Dante Romanini, Senior Scientist, **Amgen**

4:30 **ZymeLink™: A Novel Drug Conjugate Platform – Redefining the Therapeutic Window for ADCs**
ADCs have tremendous potential to provide meaningful outcomes in the clinic; however, dose-limiting toxicity remains the largest barrier to robust patient responses. Through the utilization of proprietary protease cleavable N-acyl sulfonamide (NAcS) linked hemiasterlin and auristatin payloads, termed ZymeLink™, we have generated highly efficacious ADCs with improved therapeutic indices.
Stuart Barnscher, Senior Scientist and ADC Biology Group Leader, **Zymeworks Inc.**

5:30-7:00 *Cocktail Reception in the Exhibit Hall*

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NEXT GENERATION PROTEIN THERAPEUTICS: CREATIVE ENGINEERING, DISCOVERY TECHNOLOGIES AND DESIGN APPROACHES

7:00 *Breakfast & Registration*

8:00 **Opening Remarks**

Next Generation Protein Therapeutics – Latest Developments

8:15 **KEYNOTE PRESENTATION:**
From Antibodies to Synthetic Proteins

Synthetic antibodies enable applications beyond the reach of natural antibodies. Moreover, alternative scaffolds such as ubiquitin can be used to modulate proteins in live cells. In addition, small scaffolds that function like antibodies but are amenable to full chemical synthesis enable D-protein engineering. In sum, these advances greatly extend the applications of protein engineering in biological research and therapeutic development.

Sachdev Sidhu, Professor, Department of Molecular Genetics, **University of Toronto**

8:45 **Next Generation Protein Therapeutics for Treating Cancer**

We use natural ligands and receptors as scaffolds for protein engineering to leverage their inherent biophysical and biochemical properties. I will present our recent data on new therapeutic candidates engineered to possess high affinity and unique specificity for applications in oncology.

Jennifer Cochran, Shriram Chair of Bioengineering, **Stanford University**

New Technologies for Design and Discovery of Next Generation Protein Therapeutics

9:15 **Optimization of Biologics using mRNA Display and NGS**

Julie Su, Research Investigator II, Molecular Discovery Technologies, **Bristol-Myers Squibb**

9:45 *Networking Refreshment Break in the Exhibit Hall*

10:30 **New Technologies for Design and Discovery of Next Generation Protein Therapeutics**

Medha Tomlinson, Principal Research Scientist, **Abbvie,** *USA*

11:00 **Protein Selections in the Absence of a Physical Genotype-Phenotype Linkage**

NestLink is a novel method that combines the benefits of selections and screens. Binder candidates are nested into a peptide library designed for optimal detection and a virtual genotype-phenotype linkage is established by combining mass spectrometry and deep sequencing. This enables the biophysical characterization of several thousand individual proteins in one single experiment. The technology offers unprecedented selection pressures and deep mining of diverse binder pools and it paves the way for a paradigm shift in biopharmaceutical drug delivery testing.

Prof. Dr. Markus Seeger, Research Group Leader, **University of Zurich**

Creative Engineering and Design Approaches for Next Generation Protein Therapeutics

11:30 **From Format to Function – Engineering Transformative Antibody Therapeutics**

Bi- and multispecific antibodies enable the exploration of new biological concepts and treatment strategies. Within Roche such next generation biologics have found broad application prospects in onco-immunological and anti-inflammatory approaches. But their use goes far beyond these established applications to convey unique mode of actions.

- We have generated a portfolio of T cell bispecific antibodies and novel, engineered targeted checkpoint modulators that show promising pre-clinical and clinical activity as single agent or in combination with other cancer immunotherapy agents.
- The CrossMAb technology has proven to be very versatile, allowing the generation of various bispecific antibody formats providing great opportunity to tackle novel biology and to convey superior efficacy.
- The DutaFab technology platform brings forward a novel class of fully human Fab molecules that bind any two antigens with high affinity and specificity. This format of bispecific molecules is uniquely suited to be used for Ophthalmology indications.
- Examples will be given how antibody format fundamentally influences the mode of action and activity of these next generation antibody drugs.

Martin Steegmaier, Head of Discovery, Large Molecule Research, **Roche Diagnostics GmbH,** *Germany*

12:00 **SPOTLIGHT PRESENTATION:**
An Integrated Approach To Managing Immunogenicity Risk And Optimum Protein Design

PROIMMUNE www.proimmune.com

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 Inc.**

12:30 *Luncheon in the Exhibit Hall*

1:45 **ProTIA – Bispecific T Cell Engagers Designed for Local Activation in the Tumor Environment**

- ProTIAs are highly potent bispecific T cell engagers
- ProTIAs are administered to patients as inactive long half-life prodrugs
- Activation by tumor-associated proteases occurs within tumor tissue
- The released active form has a short circulation half-life to minimize the risk of systemic exposure
- Amunix' proprietary XTEN™ protein polymer provides half-life modulation, masking of binding sites, and facilitates manufacturing of ProTIA prodrugs

Volker Schellenberger, CEO and President, **Amunix**

2:15 **A Novel T-Cell Engaging Bispecific Antibody Platform: In Vivo Tumor Clearance with Minimal Cytokine Release**

Using transgenic rats and a unique discovery approach, we have created a large collection of fully human anti-CD3 antibodies with diverse T-cell agonist activities. Our novel discovery platform combines antibody repertoire deep sequencing, high-throughput gene assembly, and recombinant expression and allows us to identify antibodies with finely tuned functional activities. The collection of CD3 antibodies identified by our platform show diverse in vitro T-cell activation profiles measured by CD69 upregulation, IL2, and IFNg production. Using our discovery platform, we have also generated human domain antibodies targeting tumor antigens that may be combined with our unique CD3 antibodies to create multi-specific molecules that mediate redirected T-cell killing of tumor cells. As one example, we have created a CD3xBCMA bispecific antibody (TNB-383B) for the treatment of multiple myeloma. TNB-383B kills multiple myeloma cells in vitro and in vivo in a BCMA-dependent manner, and kills primary patient myeloma cells ex vivo. Futhermore, TNB-383B induces significantly reduced cytokine secretion by T-cells without reduction of efficacy in vivo or ex vivo. In summary, we have created a novel T-cell engaging bispecific antibody platform with tunable T-cell agonism that can be used to optimize the therapeutic index for a variety of tumor antigens.

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

DAY TWO • Wednesday June 13th 2018 (continued)

2:45 **A MET x MET Bispecific Antibody That Induces Receptor Degradation Potently Inhibits The Growth of MET-Addicted Tumor Xenografts**

We have developed a novel bispecific antibody that binds to two distinct epitopes on MET. The METxMET bispecific antibody blocks HGF binding and exhibits very low agonist activity Furthermore, the METxMET bispecific antibody effectively promotes MET degradation, thereby inhibiting ligand-independent signaling in MET-amplified tumor cells. The METxMET bispecific antibody exhibits strong anti-tumor efficacy in xenograft models harboring MET genetic alterations.

John DaSilva, Senior Staff Scientist, **Regeneron Pharmaceuticals,** *USA*

3:15 *Networking Refreshment Break in the Exhibit Hall*

3:45 **The CTLA-4 x OX40 Bispecific Antibody ATOR-1015 Induces Anti-Tumor Effects Trough Tumor-Directed Immune Activation**

ATOR-1015 is a CTLA-4 x OX40 bispecific immune activating antibody developed for tumor-directed immunotherapy. ATOR-1015 binds both targets simultaneously, promoting cell-cell interactions expected to enhance the immuno-stimulating effect of the compound. The mode of action of ATOR-1015 is thought to be a combination of regulatory T cell (Treg) depletion and effector T cell activation. It can be seen as a next generation CTLA-4 antibody with tumor-directed activity and augmented Treg depletion. ATOR-1015 is currently in pre-clinical development and clinical trials will start in the second half of 2018.

Christina Furebring, SVP Research, **Alligator Bioscience,** *Sweden*

4:15 **Engineering and Biology of Our Multispecific Platforms (DART and TRIDENT Molecules)**

Annie K. Lam, Scientist II, **MacroGenics,** *USA*

4:45 **A Modular Single Domain Antibody Platform That Enables Generation of Optimized Biotherapeutics**

Inhibrx's modular single domain antibody platform enables crafting of differentiated biotherapeutics with functionalities beyond what is achievable with conventional antibodies. Therapeutic formats include multivalent and multispecific therapeutics to appropriately interface with the biology of each target antigen. These biotherapeutics can be designed for enhanced signaling, antigen-dependent agonism and specific immune cell recruitment and activation.

Katelyn McCabe Willis, Cell Biology Group Leader, **Inhibrx,** *USA*

5:15 **Next Generation Antibody Discovery**

Randall Brezski, Scientist, Antibody Engineering, **Genentech**

DAY THREE • Thursday June 14th 2018

7:00 *Breakfast & Registration*

8:00 **Opening Remarks**

Regulation Requirements

8:15 **KEYNOTE PRESENTATION: FDA Feedback: Regulatory Guidance and Expectations for Next Generation Protein Therapeutics and Bioconjugates**

Christopher Sheth, Supervisory Pharmacologist, Division of Hematology Oncology Toxicology, **FDA**

Next Generation Protein Therapeutics Translation from Discovery to the Clinic: Lessons Learnt from Preclinical and Clinical Studies

8:45 **KEYNOTE PRESENTATION: Lessons Learned from the Clinical Development of ADCs: Moving Forward**

The ADCs as cancer therapeutics have gained significant momentum in last few years with over 60 ADCs in clinical development. While this is highly encouraging development, it is also noted that nearly 90% of ADC molecules have failed in clinical trials either due to high toxicities or very poor clinical activity.
There is also high failure rate of ADCs in preclinical development as well. The presentation would review some common themes on failures and risk mitigation strategies to reduce the failure rate of ADCs and increase the clinical success.

Rakesh Dixit, Vice President R&D, Global Head, Biologics Safety Assessment, **MedImmune Inc.,** *USA*

9:15 **Next Generation Oncology Biologics**

The requirements of multi-functional oncology treatment match perfectly well with the strengths of the designed ankyrin repeat protein platform. With the successful first systemic validation of the platform by the oncology candidate MP0250, a dual VEGF/HGF inhibitor, we now are enabled to walk new avenues for cancer treatment. I will highlight these avenues in my presentation using preclinical and the most recent clinical data on novel therapeutic concepts for clinical oncology.

H Kaspar Binz, Vice President & Co Founder, **Molecular Partners AG,** *Switzerland*

9:45 *Networking Refreshment Break in Poster & Exhibit Hall*

10:30 **Daiichi Sankyo ADC Technology and Updates on Preclinical and Clinical Development of DS ADC Pipeline**

We developed a new ADC technology with the derivative of DX-8951 which is a novel DNA topoisomerase I inhibitor. Our ADC technology has seven unique features; novel payload, high potency, bystander effect, high clearance of the payload, stable linker, tumor selective cleavage, and high DAR. I will review this 'smart chemo' ADC technology and introduce some updates on ADC programs of Daiichi Sankyo.

Takashi Kagari, Scientist; Biologics & Immuno-Oncology Laboratories, **Daiichi Sankyo Co.,Ltd.**

11:00 **A Novel Multi-Specific Antibody Targeting PD-L1-Overexpressing Cancers That Redirects and Stimulates Antigen-Committed CD8+ T Cells Through Concomitant Engagement Of A T Cell Costimulatory Receptor**

Targeting PD-L1-overexpressing cells with therapeutic antibodies is a clinically validated strategy for the treatment of multiple solid tumors. In order to increase efficacy, PD-1/PD-L1 blocking agents are currently being tested in combination with additional immune checkpoint modulators (ICMs). However, such combination therapies are associated with considerable treatment-related adverse events, resulting in a narrow therapeutic window and thereby limiting treatment efficacy. To maximize potency and improve the safety of ICM combination approaches, we designed a multi-specific molecule bearing two ICM domains that depletes PD-L1-overexpressing cancer cells via selective recruitment and stimulation of tumor-reactive effector T cells in the tumor microenvironment. The multi-specific antibody format potently blocks PD-L1/PD-1 signaling and elicits further T cell activation through its costimulatory domain solely in the presence of cells that overexpress PD-L1. In an HCC827 xenograft model in hPBMC-supplemented NOG mice, the tri-specific strongly slowed tumor growth and enhanced intratumoral CD8+ T cell activation to a greater extent than monospecific IgG variants of the anti-PD-L1 and anti-costimulatory receptor domains.

David Urech, Co-CEO; CSO, **Numab Therapeutics AG,** *Switzerland*

11:30 **SPOTLIGHT PRESENTATION: A Phase I Study of PF-06647020, an Antibody-Drug Conjugate Targeting Protein Tyrosine Kinase 7 (PTK7), in Patients with Advanced Solid Tumors**

Xiaohua (Robert) Xin, Executive Director, Global Clinical Lead Oncology Clinical Early Development, WRD, **Pfizer Inc**

12:00 *Luncheon in Poster & Exhibit Hall*

1:15 **Translation From Discovery To The Clinic Of Next Generation Protein Therapeutics And Bioconjugates**
Gregory Adams, Chief Scientific Officer, **Eleven Biotherapeutics**

1:45 **Affimer Therapeutics: A Novel Human Scaffold for the Generation of Bi-Specific Antibodies**
Affimer therapeutics are based on the human protein Stefin A, a small intracellular protease inhibitor. Using phage display we have generated highly selective Affimer binders to range of therapeutic targets. These molecules have then been fused to either the Fc domain or to a full antibody to create bispecific molecules that express and are able to engage both target antigens.
Amrik Basran, Chief Scientific Officer, **Avacta Life Sciences**

2:15 **Fully Human, Heavy-Chain Antibodies Facilitate Rapid Development Of Multi-Specific Antibodies**
Teneobio's discovery platform utilizes VH domains of fully human heavy chain antibodies (UniAbs) to develop bi-, tri-, and tetravalent antibodies. Binding domains of UniAbs are stable structures that can be easily put together into multi-specific antibodies. Clinical trials of Teneobio's first tri-valent antibody will be initiated in 2018.
Wim van Schooten, Chief Scientific Officer, **Teneobio, Inc.**

2:45 *Networking Refreshment Break*

Overcoming Delivery Challenges and the Blood Brain Barrier

3:15 **Engineering the Fc-Region of Antibodies to Improve Brain Exposure of Antibodies**
Adam Silverman, Group Leader Protein Engineering, **Denali Therapeutics**

Addressing Challenging Targets with Next Generation Protein Therapeutics

3:45 **Selecting Next Generation Protein Therapeutic Binders Against Difficult Targets**
Shohei Koide, Professor of Biologics Design,
NYU Langone Medical Center

4:15 *Conference Ends*

With Thanks to the Next Generation Protein Therapeutics & Bioconjugates 2018 Scientific Advisory Board

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