

Register Today to Hear New Data on Over 40  
Antibody Alternative and Protein Engineering Projects

IBC's 4th Annual

# Beyond Antibodies

*Novel Scaffolds, Clinical Progress  
and Manufacturing the  
Next Generation of Therapeutics*

# Protein Engineering & Design

*Enabling Technologies and Creative  
Engineering to Improve Drug-Like  
Properties of Proteins*

September 21-23, 2009 • Town and Country Hotel • San Diego, CA

*Accelerate your own projects by applying  
lessons you will learn from multiple scaffolds  
progressing to the clinic:*

- Clinical and preclinical results of non-antibody and antibody-like scaffolds
- FDA perspective on regulation of next generation antibodies and antibody alternatives
- Modified antibody formats: Bi-specifics and multi-specifics
- Novel and emerging scaffolds
- Downstream considerations to inform your discovery and design efforts

*Improve the functionality and biophysical  
properties of your molecules by applying  
novel approaches to engineering:*

- Engineering proteins for multifunctionality
- Improving half-life/PK, protein stability and delivery
- “Designer” protein engineering and computational modeling
- Engineering and designing peptides, chemokines, enzymes and other scaffolds
- Conjugation approaches and new frontiers in protein engineering

## Keynote Presentation



**Recombinant Immunotoxins:  
Building on Success in Hairy Cell Leukemia**  
**Ira Pastan, M.D., Chief, Laboratory of  
Molecular Biology, National Cancer Institute, NIH**

## Featured Presentations

**An FDA Perspective**  
Marjorie Shapiro, Ph.D., CDER/FDA

**Two-in-One Antibody**  
Germaine Fuh, Ph.D., Genentech

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**Register Early & Save**



# Engineering the Next Generation of Protein Therapeutics

This one-of-a-kind meeting features over 40 exclusive case studies giving you insights into novel strategies for accelerating antibody-like and non-antibody scaffolds to the clinic and emerging protein engineering and design strategies to improve properties of current platforms. Take advantage of this invaluable opportunity to make new contacts to help your company accelerate the next generation of products to the clinic – and move your career in the right direction. **Register early to maximize your savings – best rate ends June 26th.**

IBC's 4th **Beyond Antibodies** conference provides you with the latest preclinical and clinical results of novel scaffolds from all the key players/companies in this field. By attending, you will hear about the challenges, lessons learned and successes achieved to help you benchmark your own efforts against industry leaders.

IBC's **Protein Engineering & Design** conference explores the cutting-edge of practical protein engineering...where the field is heading and novel strategies being applied today...and provides you access to key thought leaders and strategies to help you improve protein properties and functionality.

## Scientific Advisory Board

**Jonathan Davis, Ph.D.**, *Principal Scientist, Protein Design, Adnexus, a Bristol-Myers Squibb R&D Company*

**David S. Wilson, Ph.D.**, *Vice President of R&D, Arana Therapeutics*

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**Bruce Dawson, Vice President, BAC bv, The Bio Affinity Company**

## Beyond Antibodies

Monday, September 21, 2009

7:30 *Registration and Coffee*

8:15 **Chairperson's Remarks**

**Paul Watt, Ph.D.**, *Chief Scientific Officer, Phylogica Ltd, Australia*

### Non-Antibody-Derived Scaffolds: Emerging Preclinical and Clinical Results

8:30 **Anticalins, A Novel Class of Binding Proteins and Their Use as Therapeutics**

Anticalins, which are derived from human lipocalins, are small 20kDa proteins with highly selective binding properties. The use of Anticalins has already been validated in vivo for e.g. oncology, ophthalmology and molecular imaging and the first clinical candidate PRS-050 (VEGF antagonist) will enter the clinic soon. Unique features such as hapten binding, dual targeting and pulmonary delivery will be presented along with data regarding the compact structure, intrinsic stability and broad formulation flexibility of Anticalins.

**Kristian Jensen, Ph.D.**, *Chief Operating Officer, Pieris AG, Germany*

9:00 **Centyrin Alternative Scaffolds: A New Biotherapeutic Platform for J&J**

While monoclonal antibodies have demonstrated good utility as therapeutics, they have some drawbacks related to their inherent complexity. Alternative scaffolds represent an emerging class of protein drugs that may combine the attractive specificity properties of mAbs with the simplicity, ease of manufacture and tissue penetration associated with small molecules. We aim to exploit the properties of alternative scaffolds to develop a series of protein platforms tailored towards the therapeutic application.

**Karyn T. O'Neil, Ph.D.**, *Chief Scientific Officer, Centyrex, Johnson & Johnson Ventures*

9:30 **Powerful and Fast: DARPIn Therapeutics**

DARPins are a novel class of high-affinity, low-immunogenicity protein drugs that combine the advantages of antibodies and small molecule drugs. The favorable properties of DARPins enable the fast generation and production of a variety of drug candidates for different indications. We have validated several DARPIn drug candidates in a variety of disease models. DARPins can be tailored to the format of choice allowing the generation of ideal drugs. A best-in-class therapeutic program illustrating the potency of the DARPIn therapeutic platform will be presented.

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

10:00 **Ecallantide: Discovery and Development of an Engineered Human Protease Inhibitor Scaffold**

Dyax has engineered potent and selective serine protease inhibitors using a human Kunitz domain scaffold. Our most advanced drug candidate, ecallantide, was developed using this protein engineering platform. Examples of the discovery and development of ecallantide for the treatment of acute attacks of Hereditary Angioedema (HAE) will be presented.

**Christopher TenHoor, Ph.D.**, *Senior Vice President, Pharmacology and Preclinical Development, Dyax Corp.*

10:30 *Networking Refreshment Break*

11:00 **Hitting Intracellular as well as Extracellular Targets by Phenotypic Screening of Phylomer Libraries**

Phylomers are a new class of peptide derived from genomic fragments of biodiverse archaeal and bacterial species. Phylomer peptides can exhibit superior functional hit-rates, when compared to randomly derived peptides, possibly due to an evolutionary selection for structure and stability. We have exploited these high hit rates to allow direct screening for particular phenotypes. The Cambridge Centre for Molecular Therapeutics has demonstrated an unprecedented hit rate of approximately 0.1% of unselected Phylomers, for specific blockade of AP1 dependent signaling pathways. Phylomer peptides were also identified via a direct Phenotypic screen for binding to live bacteria, which demonstrated potent antimicrobial activity against clinical isolates of multi-drug resistant microorganisms. We have recently obtained in vivo data from a pneumonia model, showing that these Phylomers can block lung colonization upon injection.

**Paul Watt, Ph.D.**, *Chief Scientific Officer, Phylogica Ltd, Australia*

"In one conference you can see and meet people involved in the emerging science of novel protein therapeutics"

**Leslie Hickie, VP Business Development, Bioatla**

**11:30 Case Study: The Molecular Basis for Avimer™ Protein Recognition**  
 Avimer proteins are a class of multi-domain proteins designed and selected for specific binding and/or inhibitory properties. They are based on so-called "A domains" found in a number of human extracellular receptors. Linking multiple independent binding domains increases avidity and results in improved affinity and specificity compared with conventional single-epitope binding proteins. We have determined complex crystal structures of neutralizing anti-IL-6 Avimers bound to the pro-inflammatory cytokine IL-6 which demonstrate the molecular basis for Avimer recognition in this system.  
**Zhulun Wang, Ph.D.**, *Scientific Director, Molecular Structure, Amgen, Inc.*

**12:00 Ubiquitin: An Ideal Scaffold**  
 The Ubiquitin-based Affilin® platform is a novel approach in the field of alternative scaffold development, which has been validated in efficacy, safety and immunogenicity studies in animals. Ubiquitin-based binding Affilin® molecules offer the advantage of using standard animal models even for chronic treatments and predicting the immunogenicity of candidates using animals. A flexible multimerisation strategy creates binding molecules ranging from 8 kDa to more than 60 kDa supporting the modulation of pharmacokinetic parameters. In addition, Affilin® multimerisation dramatically affects affinity and specificity of binding molecules and is a powerful tool to develop novel biopharmaceuticals.  
**Arnd Steuernagel, Ph.D.**, *Chief Scientific Officer, Scil Proteins, Germany*

**12:30 Lunch on Your Own**

**1:45 Working at the DNA Level: Development of a Novel Class of Human Therapeutics**  
 Sangamo BioSciences, Inc. is focused on the research and development of a novel technology platform employing zinc finger DNA-binding proteins (ZFPs) for therapeutic regulation and modification of any disease-related gene. The most advanced ZFP Therapeutic™ development program is currently in Phase 2 clinical trials for the treatment of diabetic neuropathy and ALS. Sangamo also has a Phase 1 clinical trial underway for the treatment of HIV/AIDS. Other therapeutic development programs are focused on cancer, neuropathic pain, nerve regeneration, Parkinson's disease and monogenic diseases.  
**Edward Lanphier, President and CEO, Sangamo Biosciences, Inc.**

**2:15 Clinical Validation of Adnectins: Latest Data on CT-322**  
 Adnectins offer various potential advantages compared to traditional biologics, including speed of discovery, ease of manufacturing, and the ability to create multi-functional targeted products. Our first Adnectin to enter clinical studies, CT-322, has demonstrated potent VEGFR-2 blocking activity in a Phase I study. With over 70 patients treated across multiple studies, CT-322 establishes significant clinical validation of the Adnectin class.  
**Eric Furfine Ph.D.**, *Senior Vice President, Research and Preclinical Development, Adnexus, A Bristol-Myers Squibb R&D Company*

**2:45 Designed 3-helical Proteins for Molecular Imaging and Therapy**  
 Clinical imaging and biodistribution data on Affibody molecules support further development. The second generation Affibody molecules display improved biophysical and biodistribution properties. They have also been combined with a novel albumin-binding domain to obtain a long in vivo half-life suitable for therapeutic application. A high affinity albumin-binding domain has been shown to be superior.  
**Lars Abrahmsen, Ph.D.**, *Chief Scientific Officer, Affibody AB, Sweden*

**3:15 Networking Refreshment Break**

### Antibody-Derived Scaffolds: Emerging Preclinical Results

**3:45 The Development of Shark-Derived, Single-Domain Binding Molecules as Human Therapeutics**  
 Wyeth is working on the novel antigen-binding molecules found associated with immunoglobulin and some TCRs in sharks. These molecules bind antigen as small (~12 kDa), soluble, single-domains with high affinity, specificity and stability. This presentation will detail our progress in developing this platform for the generation of new human therapeutics.  
**Helen Dooley, Ph.D.**, *Senior Research Scientist, Wyeth Research, United Kingdom*

**4:15 Shark Antibodies and Their Human Analogues as Potential Therapeutics**  
 Shark antibodies (IgNARs) have been shown to possess an elongated CDR3 loop that is considered to be ideal for targeting cleft-type epitopes such as enzyme active sites and surface receptors which are otherwise inaccessible to conventional antibodies. Elucidation of the IgNAR structure revealed a striking similarity with the I-set class of molecules which includes cell adhesion molecules such as N-CAM. Based on the principles that have been identified in the shark antibody binders a humanized version of our shark antibody library has been constructed. This library of "i-bodies" will provide humanized binders with the features of the shark antibodies.  
**Mick Foley, Ph.D.**, *Associate Professor, Department of Biochemistry, La Trobe University, Chief Scientific Officer, AdAlta, Australia*

**4:45 Accelerating scFv Antibody Fragments for Topical Applications into the Clinic**  
 Due to their low molecular weight (26 kDa) and the resulting pharmacokinetic properties, single-chain antibody fragments qualify for local therapies and delivery routes that have not yet been explored for full-size antibodies and larger fragments thereof. Stable naturally occurring variable domain scaffolds allow to engineer scFvs with drug-like properties. ESBA105 is a humanized anti-TNF scFv, developed for the treatment of inflammatory ocular diseases as well as for osteoarthritis. This antibody fragment, upon administration to the ocular surface by eye drops, penetrates into all ocular compartments and reaches therapeutic concentrations in the aqueous and the retina. Preclinical efficacy with topical application of eye drops containing ESBA105 is shown in the monkey laser-injury model for choroid revascularization.  
**David Urech, Ph.D.**, *Head of R&D, ESBATech, Switzerland*

**5:15 Panel Discussion**  
**Accessing Target Diversity of Novel Scaffolds**

- Which scaffolds are biased to which target classes?
- Targets inside cells
- Expanding target class accessibility of a given scaffold

**5:45 Close of Day One**

"Excellent overview of the latest developments in the 'Beyond Antibodies' field"  
**Dragan Grabulovski, Chief Scientific Officer, Covagen**

### New Research to Share? Present a Poster

The organizers of **Beyond Antibodies** and **Protein Engineering & Design** recognize the significant educational value in poster presentations. Any registered conference attendee may sign up to present a poster. The deadline to submit your abstract online, at the address below, is **September 4, 2009** to be included in the conference materials. Poster abstracts and registrations received after **September 4, 2009** will be subject to availability for an onsite poster board and will not be included in the conference materials. Full payment of conference registration and poster fees must also be received by **September 4, 2009** for the abstract to be included in the conference materials and poster board assignment to be made (see the registration page for details on the poster fee). The size of the conference poster board is 4'h x 8'w. Please note: Poster presentations may not be used as exhibit displays or for marketing purposes. All posters are subject to approval by conference organizers. Poster abstracts must be submitted online at [www.IBCLifeSciences.com/Beyond](http://www.IBCLifeSciences.com/Beyond). Only one poster presentation will be allowed per registered attendee/author.

7:45 *Morning Coffee*8:15 **Chairperson's Remarks****Keynote Presentation**8:30 **Recombinant Immunotoxins: Building on Success in Hairy Cell Leukemia**

Recombinant immunotoxins are hybrid proteins composed of an Fv reacting with a tumor antigen and a portion of Pseudomonas exotoxin A. One of these, BL22, binds to CD22 and has produced many complete remissions in drug resistant Hairy Cell Leukemia. Another, SS1P, is directed at the mesothelin antigen on mesothelioma and lung cancers. We have used protein engineering to produce immunotoxins that have a higher affinity and activity, protease resistance and decreased immunogenicity that should allow more treatment cycles to be given to patients and an increase in efficacy.

**Ira Pastan, M.D.**, Chief, Laboratory of Molecular Biology, National Cancer Institute, NIH

**Engineering Functionality**9:15 **Immunoglobulin Fc as a Scaffold for Antigen Binding (Fcabs): Long Half Life and Effector Functions**

f-star's Modular Antibody Technology can be used to engineer additional binding sites into antibody constant domains. We have developed large yeast surface display libraries of correctly folded IgG1 Fc randomized in non-CDR-loops (Fcabs). These libraries were used to select specific, low nM binders against a number of protein antigens. Fcabs are shown to induce ADCC with antigen-positive cells and show half life comparable to antibodies. Fcabs can also be used to engineer multivalent or multispecific antibodies (mAb2) by replacing the Fc fragment with an Fcab. New data (animal and in vitro) validating this approach will be presented.

**Gottfried Himmler, Ph.D.**, CEO, f-star, Austria

9:40 **Enabling the Power of Peptides**

Peptides have promise as potent and selective drug candidates but have not succeeded primarily because of poor pharmacokinetics. The fusion of these peptides to our scaffold antibody has produced molecules that have the advantage of the peptide activity but with pharmacokinetics determined by the scaffold. Examples will be discussed that have enabled rapid SAR to be carried out producing pre-clinical and clinical candidates with optimized activity and pharmacokinetics.

**Gary Woodnutt, Ph.D.**, Vice President of Biology, CovX Research LLC

10:05 **Unibody<sup>®</sup>, A Novel Nonactivating Antibody Format**

Nonactivating antibody formats are needed for certain clinical applications where target binding and inhibition is sufficient. Engagement of the immune system or bivalent binding may even be undesired and cause unwanted side effects or restrict therapeutic efficacy. Unibody<sup>®</sup>, represents a novel antibody format which provides a tailored solution for applications where a true antagonist is required and immune activation or target cross-linking may be detrimental.

**Paul W.H.I. Parren, Ph.D.**, Senior Vice President Research and Pre-Clinical Development, Genmab, The Netherlands

10:30 *Networking Refreshment Break and Exhibit/Poster Viewing*11:00 **Scorpions<sup>™</sup>: Multi-Specific Binding Proteins with Effector Function**

Scorpions are multi-specific binding proteins which contain two binding moieties separated by an immunoglobulin Fc domain. Scorpions can be generated to both soluble and cell surface targets. We will present pre-clinical data demonstrating unique biologic consequences of engaging two targets and manufacturability data demonstrating feasibility for clinical and commercial production.

**Kendall M. Mohler, Ph.D.**, Senior Vice President, R&D, Trubion Pharmaceuticals

11:30 **The AlbuAb<sup>™</sup> Platform Delivers Highly Potent Long Acting Biologics**

Our proprietary AlbuAb<sup>™</sup> platform is based on 12kD human domain antibodies which bind to serum albumins of various species. Using IFN as a showcase we will demonstrate that fusion of a short-lived biologic with an AlbuAb<sup>™</sup> delivers at a low cost, highly potent biologics with class-leading PK/PD profiles.

**Bruce Hamilton, Ph.D.**, Principal Scientist, Domantis Limited a GSK Company, United Kingdom

12:00 *Networking Luncheon and Exhibit/Poster Viewing***Antibody-Derived Scaffolds: Emerging Clinical Results and Downstream Considerations**1:10 **Nanobody<sup>®</sup> Development from Bench to Bedside**

This presentation will illustrate the utilities of the Nanobody<sup>®</sup> platform to rapidly generate clinical drug candidates. Translational research from discovery to drug development and the use of biomarkers will be discussed in 2 case studies of Ablynx's clinical candidates targeting platelet aggregation and bone resorption.

**Josefin-Beate (Josi) Holz, M.D.**, Chief Medical Officer, Ablynx, Belgium

1:40 **Domain Antibody (dAb) Targeting TNF-alpha - From Concept to Clinic**

Combinatorial methods were used to produce a domain antibody (dAb) with fully human frameworks that neutralizes TNF-alpha. The dAb was then fused to an Fc domain to improve its pharmacokinetic profile. The resulting molecule, ART621, weighs in at only half the size of a full-length antibody but has an IgG-like circulating half-life in humans. ART621 is effective in animal model studies of rheumatoid arthritis (RA) and was shown to be well-tolerated in healthy volunteers. An update on the development of ART621, which has completed a phase II clinical trial in psoriasis and is currently undergoing phase II trials in RA, will be presented.

**David S. Wilson, Ph.D.**, Vice President of R&D, USA, Arana Therapeutics Ltd.

2:10 **Antibody Engineering Novel Molecules for Clinical Applications**

Molecular imaging is playing an increasingly important role in the detection, disease staging and response to treatment of cancer. The radiolabeled anti-CEA recombinant antibody fragments, T84.66 minibody and diabody, have entered pilot clinical imaging trials. Data will be presented on the design, small scale manufacture, preclinical and clinical results.

**Paul J. Yazaki, Ph.D.**, Research Professor, Department of Cancer Immunotherapy & Tumor Immunology, Beckman Research Institute, City of Hope Medical Center

**2:35 Purification Strategies for Diabodies and Minibodies**

This case study will compare chromatographic retention behavior of diabodies and minibodies with intact IgG, Fab and Fc fragments on anion exchangers, cation exchangers, and hydroxyapatite. Data from an integrated 3-step purification process for preparation of clinical material will be presented.

**Pete Gagnon, CSO, Downstream Process Development, Validated Biosystems**

**3:00 Networking Refreshment Break and Exhibit/Poster Viewing****Regulatory Perspectives on Antibody Alternatives and Next Generation Antibodies****3:30 Featured Presentation****Therapeutic Monoclonal Antibodies, Next Generation Antibodies, and Antibody Alternatives: An FDA Perspective**

The clinical success of therapeutic monoclonal antibodies in the 1990's spurred an increase in the number of these products in the development pipeline. Currently there are over 200 monoclonal antibodies in clinical development including 2nd generation products and novel antibody constructs. The FDA perspective on the regulation of monoclonal antibodies, related products novel antibody constructs and antibody alternatives will be discussed.

**Marjorie A. Shapiro, Ph.D., Chief, Laboratory of Molecular and Developmental Immunology, Division of Monoclonal Antibodies, CDER/FDA**

**Bi-Specifics and Multi-Specifics I****4:00 DART: A Robust Fv-Based Dual Affinity Therapeutic Platform**

One of the unmet challenges of antibody engineering has been the development of a robust and stable bispecific format. To address this problem, we developed a novel Fv-based platform termed DART (Dual Affinity Re-Targeting). In vitro and in vivo studies show that their properties compare favorably with those of other bispecific formats and demonstrate remarkable robustness in terms of stability, potency and manufacturability.

**Syd Johnson, Ph.D., Vice President, Antibody Engineering, MacroGenics, Inc.**

**Exhibit and Sponsorship Opportunities****at The Beyond Antibodies and Protein Engineering & Design Conferences**

IBC's sponsorships ensure you the proper balance between attendees and exhibitors so you can spend more time developing your deals and less time searching for potential partners. IBC will assist you in meeting all of your company objectives pre-event, onsite and post-event.

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**4:30 Enhanced Cross-linking of Membrane CD23 with a Tetravalent Antibody Demonstrates the Importance of Receptor Cross-linking for Apoptotic Signaling via CD23 in B Lymphoma Cells**

A multivalent anti-CD23 antibody was generated using stability engineered scFvs to test the hypothesis that enhanced CD23 cross-linking drives stronger apoptotic signaling in CD23+ B cells. Data demonstrating the biological effects of increasing antibody valency when targeting CD23 will be presented.

**Ann MacLaren, Ph.D., Scientist II, Translational Oncobiology, Biogen Idec, Inc.**

**5:00 Molecular Design and Optimization of Anti-human IL-1 $\alpha$ / $\beta$  DVD-Ig Molecules for the Treatment of Inflammatory Diseases**

We have recently developed a novel dual variable domain immunoglobulin (or DVD-Ig) technology, which enables engineering distinct specificities of two mAbs into a single functional dual-specific, tetravalent IgG-like molecule. Based on this approach, we have developed anti-human IL-1 $\alpha$ / $\beta$  DVD-Ig molecules using several pairs of monoclonal antibodies with therapeutic potential. A case study will be presented addressing optimal design of a DVD-Ig therapeutic agent for this specific target pair combination.

**Chengbin Wu, Ph.D., Associate Research Fellow, Abbott Laboratories**

**5:30 Panel Discussion  
Managing Immunogenicity of Protein Therapeutics**

- Using design and modeling to de-immunize proteins
- Comparing alternative approaches to mitigate immunogenicity risk
- Is there any clinical validation linking engineering with reduced immunogenicity?

**6:00 Close of Day Two****6:30 Old Town San Diego Networking Dinner**

**Old Town San Diego, a state historic park, is considered the "birthplace" of California.**

The park includes a main plaza, exhibits, museums, living history demonstrations and "Bazaar del Mundo" known for its shopping. Dinner attendees will board the San Diego transit line ((\$5/person R/T, approx. at time of print) near the hotel for the short train ride to Old Town, and then enjoy a delicious meal at a local Mexican restaurant plus time to enjoy the colorful sights of Old Town. Space is limited and an additional fee applies. Check box on registration form to sign up.

"Beyond Antibodies is a comprehensive meeting that covers a wide range of issues related to the development of the next generation of biologics. tools, strategies, case studies and regulatory issues are all well represented"

**Mike Smith, Field Scientist, Sidec**

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7:45 *Morning Coffee*8:15 **Chairperson's Remarks**

**Jonathan Davis, Ph.D.**, *Principal Scientist, Protein Design, Adnexus, A Bristol-Myers Squibb R&D Company*

**Bi-Specifics and Multi-Specifics II**8:30 **Multi-Specific Adnectins: Realizing the Promise of a Novel Class of Targeted Biologics**

Adnectins offer numerous potential advantages compared to traditional targeted biologics, including speed of discovery, ease of manufacturing, and the ability to create multi-functional targeted products. We are currently advancing in our pipeline multi-specific Adnectin products where two different Adnectins are combined into a single molecule to specifically modulate two distinct targets. We will discuss methods to engineer and optimize multi-specific Adnectins, as well as present preclinical data demonstrating the clinical potential of these novel drugs.

**Jonathan Davis, Ph.D.**, *Principal Scientist, Protein Design, Adnexus, a Bristol-Myers Squibb R&D Company*

8:55 **Clinical Update on BiTE: A New Antibody Platform for Cancer Therapy**

We have developed bispecific T cell engager (BiTE) as a novel antibody platform for effective treatment of cancer. BiTE antibodies targeting CD19 for treatment of B cell malignancies (blinatumomab), and targeting EpCAM for treatment of adenocarcinoma (MT110) are in clinical development. New BiTE antibodies at preclinical stage target CEA (CD66e, CEACAM5), CD33, MCSP, EGFR and Her-2/neu. Clinical proof-of-concept will be presented for blinatumomab. We will also demonstrate elimination of cancer stem cells by MT110, and of KRAS- and BRAF-mutated colorectal cancer cells by a BiTE antibody based on anti-EGFR antibody cetuximab (Erbbitux).

**Patrick Baeuerle, Ph.D.**, *CSO and SVP, R&D, Micromet AG, Germany*

9:20 **Protein Engineering for Bispecificity and Manufacturability**

This talk will cover protein engineering efforts focused on novel ways to produce bispecific protein therapeutics. Examples of proteins made using this molecular architecture will be discussed along with optimization of expression and stabilities.

**Michael Wittekind, Ph.D.**, *Executive Director, Protein Science - Amgen Washington, Amgen, Inc.*

9:45 **Featured Presentation****Two-in-One Antibody: The Story of Converting Herceptin to Also Bind VEGF with High Affinity**

A variant of Herceptin was selected on the basis of its ability to also interact with vascular endothelial growth factor (VEGF) at the antigen-binding site. Crystallographic and mutagenesis studies revealed that distinct amino acids of this antibody engage HER2 and VEGF energetically, but there is extensive overlap between the antibody surface areas contacting the two antigens. An affinity-improved version of this Two-in-One antibody inhibits HER2- and VEGF-mediated cell proliferation and tumor progression in mouse models.

**Germaine Fuh, Ph.D.**, *Scientist, Antibody and Protein Engineering, Genentech, Inc.*

10:10 *Networking Refreshment Break and Exhibit/Poster Viewing***Engineering for Improved Properties: Stability, Half-Life, Pharmacokinetics and Safety**10:40 **Half-life Extension and In Vivo Biological Activity of Peptide and Protein Therapeutics**

We have designed novel constructs containing long unstructured tails of hydrophilic amino acids (rPEG) that increase half-life. rPEG constructs of glucagon, exenatide, IL-1ra, and hGH had in vivo efficacy, prolonged half-life, and lack of immunogenicity in mice, rats, dogs, and monkeys. The technology allows control of peptide or protein half-life from a few hours to at least 100 hours without loss of biological effect in vivo. Case studies of these projects including preclinical data to support a regulatory submission will be presented.

**Jeffrey L. Cleland, Ph.D.**, *CEO, Versartis, Inc.*

11:05 **PASylation: A Novel Technology for Extending the Plasma Half-life of Therapeutic Proteins**

Chemical conjugation of small therapeutic proteins with poly-ethylene glycol (PEG) to extend their effective size beyond the threshold of kidney filtration is an established strategy to prolong their typically short circulation times to a clinically useful range. As an alternative we have developed sequences comprising the amino acids Pro, Ala, and Ser, which form a conformationally disordered biological polymer with large hydrodynamic volume and high solubility, are resistant against serum proteases, and permit efficient production of biochemically active fusion proteins without necessitating costly and laborious chemical modification steps.

**Arne Skerra, Ph.D.**, *Professor of Biological, Chemistry, Technische Universitaet Muenchen, Germany*

11:30 **Modulating the Pharmacokinetic Properties of Therapeutic Proteins via Fc Engineering**

Abstract not available at time of print.

Visit [www.ibclifesciences.com/beyond](http://www.ibclifesciences.com/beyond) for updates.

**William Dall'Acqua, Ph.D.**, *Director, R&D, MedImmune*

11:55 **Stability-Engineered IgG-like Bispecific Antibodies**

Stability engineering of scFvs has been used as an enabling technology at Biogen Idec to generate tetravalent and bispecific IgG-like molecules. Data on both the stability engineering and preclinical efficacy for several of these molecules will be presented.

**Brian R. Miller, Senior Scientist, Biogen Idec, Inc.**

12:20 *Networking Luncheon and Exhibit/Poster Viewing*1:30 **CB 813, an Improved Second Generation FVIIa Variant**

We have used structure-based rational design and molecular modeling to design an improved second generation variant of FVIIa (CB 813) that we are advancing towards clinical trials to manage acute bleeds in hemophilia patients that have developed anti-FVIII or anti-FIX antibodies (i.e., patients with inhibitors). CB 813 exhibits both improved binding to the co-factor Tissue Factor (TF) and enhanced catalytic efficiency for activation of the substrate, Factor X. Compared with recombinant, wild type human Factor VIIa (current therapy for patients with inhibitors), CB 813 displays 6-10 fold improved potency in three distinct models of acute bleeding.

**Edwin L. Madison, Ph.D.**, *Chief Scientific Officer, Catalist Biosciences, Inc.*

1:55 **Optimizing the Pharmacology of Protein Therapeutics with Improved Performance**

Ambrx is using its ReCode™ and EuCode™ technologies to site specifically attach effector molecules to Fabs and full length antibodies. The efficacy of tumor targeted antibodies is enhanced by site specific conjugation of toxic moieties to them in a way that does not interfere with their binding modality. Ambrx is also exploring using antibody backbones to improve the performance of peptide therapeutics. Various case studies will be presented.

**Stuart Bussell, Ph.D.,** Director, Process Sciences, Ambrx

### New Frontiers in Protein Engineering

2:20 **Chemokine Structural Biology and Implications for Novel Therapeutics**

Antagonizing chemokine function has become a wide spread goal in the pharmaceutical industry. To aid such endeavors, we have been using structural and biochemical methods to understand the molecular details of chemokine-receptor interactions and function. In this presentation, structural details of how chemokines interact with chemokine receptors, glycosaminoglycans and viral chemokine binding proteins will be discussed. The results suggest several strategies for the development of novel therapies based on inhibition of chemokine function.

**Tracy M. Handel, Ph.D.,** Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, UCSD

2:45 **Products Derived from Non-human, 'Hypotopic' Proteins as A Safer Alternative to Human Proteins**

Human-derived proteins and even fully human proteins can be immunogenic in humans and raise an immune response that neutralizes the native protein. In order to avoid this fundamental safety problem, we propose to create products from non-human-derived sequences that will not cross-react and not pose a safety issue. We have designed two types of 'hypotopic' proteins, each depleted of MHC-epitopes and non-immunogenic across species: rigidly structured microproteins, 30-60AA long and containing a high density of disulfides, to create target binding sites, and unstructured linkers that provide flexibility and half-life.

**Willem 'Pim' Stemmer, Ph.D.,** CEO, Amunix, Inc.

3:10 *Networking Refreshment Break and Exhibit/Poster Viewing*3:40 **Engineering a Protein-Protein Interface Using a Computationally Designed Library**

We have taken advantage of both computational modeling and high-throughput screening of protein libraries to evolve a novel binding interface between E6AP and Ubc12. First, using computer simulations we have identified a library of mutations that should be introduced to E6AP. High-throughput screening of this designed library led to the selection of an E6AP mutant that bound to its target with a Kd of 36 nM (>3,000 fold higher affinity than parent E6AP).

**Gurkan Guntas, Ph.D.,** Postdoctoral Research Associate, Brian Kuhlman Lab, University of North Carolina at Chapel Hill

4:05 **Interfering Peptides Targeting Extended Protein Interaction Surfaces**

We use rational design in combination with in vivo and in vitro selection systems combining competitive and negative design aspects. Peptides specifically directed against the protein-protein interaction domain of transcription factors such as Jun, Fos, Myc and AF10 were generated and major energetic differences ( $\geq 5.6$  kcal/mol) are observed between desired and non-desired interaction stabilities.

In addition, we compiled a 'bZIP coiled-coil interaction prediction algorithm' (bCIPA) for the prediction of coiled coil-mediated protein-protein interaction of natural proteins as well as designed inhibitors. Cellular assays demonstrate inhibitory effects of our peptides. To improve serum half-life time, D-peptides have been exploited as well.

**Katja Arndt, Ph.D.,** Principal Investigator, Freiburg Institute for Advanced Studies, School of Life Sciences, University of Freiburg, Germany

4:30 **Computational Design of de novo Enzymes**

For many chemical transformations, no natural enzyme exists. Arzeda's technology bridges the gap by creating these synthetic enzymes. Our recently developed computational enzyme design methodology, licensed from the University of Washington, is applicable to any chemical reaction. Starting from a description of the ideal catalytic machinery, the enzyme design methodology generates novel enzymes predicted to catalyze the reaction.

**Eric Althoff, Ph.D.,** Post-Doctoral Fellow, David Baker Lab, University of Washington, Head of Chemistry, Arzeda

4:55 **Quantitative Modulation of Fusion Protein Components**

Evolution modulates the quantitative characteristics of protein interactions and often uses combinations of weak interactions to achieve specificity. We used quantitative optimization in designing fusion proteins that direct interferon-alpha or erythropoietin to a subset of receptor-bearing cells. The resulting proteins show enhanced cell-type specificity and thus should have reduced side effects.

**Jeffrey Way, Ph.D.,** Senior Staff Scientist, Wyss Institute for Biologically Inspired Engineering, Harvard Institutes of Medicine

5:20 *Close of Conference*

### Venue and Travel Information

#### Town and Country Hotel

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