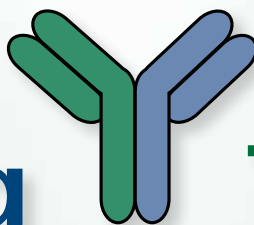


**Cutting-Edge Basic Science Combined with Updates of Clinical Progress**

IBC's 22nd Annual International Conference

# Antibody Engineering



IBC's 9th Annual International Conference

# Antibody Therapeutics

Annual Meeting of **The Antibody Society**

December 4-8, 2011 • Hilton San Diego Bayfront Hotel • San Diego, CA

**Invaluable Scientific Collaborations • New Approaches to Research Problems • Important Industry and Science Updates**

## Conference Sessions Include:

- Antibodies as Probes of Structure
- Antibodies as Signaling Modifiers
- Drug Conjugates and Bispecific Antibodies
- Model-Guided Generation of Binding Sites
- Next Generation Anti-Angiogenics
- Novel Selection Strategies
- Preclinical Development of Antibody Therapeutics
- Rational Vaccine Design
- Structure and Dynamics of Antibodies and their Membrane Receptor Targets
- Targeting Intracellular and Misfolded Proteins
- The Biology Behind Potential Blockbuster Antibodies
- Twenty-five years of Therapeutic Antibodies
- Updates of Clinical Stage Antibody Therapeutics
- Viral Retargeting with Engineered Binding Molecules

"The conference was a perfect mix of academic and industry participants and the topics covered ranged from new research to interesting clinical results."

*Sarah Batey, Ph.D., Research Scientist, Covagen AG, Switzerland*

## Keynote Presentations

### Structure/Function of HGF/SF and MET as a Basis for Therapeutic Targeting



**Ermanno Gherardi, M.D., Ph.D.**  
*Scientist, Medical Research Council Laboratory of Molecular Biology, United Kingdom*

### A New Mechanism for Allosteric Regulation of EGFR Family Members



**Mark A. Lemmon, Ph.D.**  
*Professor and Chair, Biochemistry and Biophysics, Perelman School of Medicine, University of Pennsylvania*

### Structures of GPCRs Interacting with Ligands, Drugs, and Antibody Fragments in Phospholipid Bilayers



**Stanley J. Opella, Ph.D.**  
*Professor, Chemistry and Biochemistry, University of California, San Diego*

### Broad Antibody Neutralization of Influenza Virus and HIV-1



**Ian Wilson, D.Phil.**  
*Hansen Professor of Structural Biology, The Scripps Research Institute*

# Antibody Engineering Antibody Therapeutics

Annual Meeting of The Antibody Society

## Pre-Conference Workshop: Antibodies as Probes of Structure (Page 3)

Cheryl Arrowsmith, Ph.D., Ontario Cancer Institute, *Canada*  
 Germaine Fuh, Ph.D., Genentech Inc.  
 James T. Koerber, Ph.D., University of California, San Francisco  
 Anthony Kossiakoff, Ph.D., University of Chicago  
 Erica Ollmann Saphire, Ph.D., The Scripps Research Institute  
 Sachdev Sidhu, Ph.D., University of Toronto, *Canada*

## Keynote Session: Structure and Dynamics of Antibodies and their Membrane Receptor Targets (Page 4)

Ermanno Gherardi, M.D., Ph.D., Medical Research Council, *United Kingdom*  
 Mark A. Lemmon, Ph.D., University of Pennsylvania  
 Stanley J. Opella, Ph.D., University of California, San Diego  
 Ian Wilson, D.Phil., The Scripps Research Institute

## Model-Guided Generation of Binding Sites (Page 4)

Roland L. Dunbrack, Jr., Ph.D., Fox Chase Cancer Center  
 Jeffrey J. Gray, Ph.D., Johns Hopkins University  
 Peter J. Hudson, FTSE, Ph.D., Avipep Pty Ltd., *Australia*  
 Matthew P. Jacobson, Ph.D., University of California, San Francisco  
 Brian Kuhlman, Ph.D., University of North Carolina  
 Andreas Plückthun, Ph.D., University of Zürich, *Switzerland*

## Novel Selection Strategies (Page 5)

Andrew Bradbury, M.D., Ph.D., Los Alamos National Laboratories  
 James D. Marks, M.D., Ph.D., San Francisco General Hospital  
 Franck Perez, Ph.D., Curie Institute, *France*  
 Klaus Schwamborn, Ph.D., Pepsan Therapeutics B.V., *The Netherlands*  
 Eric V. Shusta, Ph.D., University of Wisconsin-Madison  
 James A. Wells, Ph.D., University of California San Francisco

## Antibodies in a Complex Environment: Targeting Intracellular and Misfolded Proteins (Page 5)

Julian D. Gilmore, Ph.D., University College London Medical School, *United Kingdom*  
 Robert E. Hawkins, MB, BS, Ph.D., FRCP, University of Manchester, *United Kingdom*  
 Anne Messer, Ph.D., Wadsworth Center, New York State Department of Health  
 Rebecca Nisbet, Ph.D., CSIRO Materials Science and Engineering, *Australia*  
 Amber Southwell, Ph.D., University of British Columbia, *Canada*  
 Katherine Vallis, MBBS, Ph.D., University of Oxford, *United Kingdom*

## Rational Vaccine Design (Page 6)

Andrea Carfi, Ph.D., Novartis Vaccines & Diagnostics  
 Darrell J. Irvine, Ph.D., Massachusetts Institute of Technology  
 Philip R. Johnson, M.D., The Children's Hospital of Philadelphia  
 Bali Pulendran, Ph.D., Emory University  
 William Schief, Ph.D., The Scripps Research Institute

## Viral Retargeting with Engineered Binding Molecules (Page 6)

Christian Buchholz, Ph.D., Paul-Ehrlich Institute, *Germany*  
 Roberto Cattaneo, Ph.D., Mayo Clinic  
 Birgit Dreier, Ph.D., University of Zurich, *Switzerland*  
 Robin J. Parks, Ph.D., Ottawa Hospital Research Institute, *Canada*  
 Stephen J. Russell, M.D., Ph.D., Mayo Clinic

## The Biology Behind Potential Blockbuster Antibodies (Page 7)

Kim A Campbell, Ph.D., Centocor Research & Development  
 David Lacey, M.D., Amgen, Inc.  
 Thi-Sau Migone, Ph.D., Human Genome Sciences, Inc.  
 Stefan Rose-John, Ph.D., University of Kiel, *Germany*  
 Jochen G. Salfeld, Ph.D., Abbott Bioresearch Center  
 Gavin Thurston, Ph.D., Regeneron Pharmaceuticals

## Antibodies as Signaling Modifiers: Where Did We Go Right? And, Can We Learn from Success? (Page 7)

Mark S. Dennis, M.S., Genentech, Inc.  
 John McCafferty, Ph.D., Cambridge University, *United Kingdom*  
 Amita Patnaik, M.D., FRCP, START Center for Cancer Care  
 Louis M. Weiner, M.D., Georgetown University Medical Center  
 K. Dane Wittrup, Ph.D., Institute of Technology

## Twenty-Five Years of Therapeutic Antibodies: Lessons Learned and Future Challenges (Page 8)

Napoleone Ferrara, Ph.D., Genentech, Inc.  
 John Lambert, Ph.D., ImmunoGen, Inc.  
 Nils Lonberg, Ph.D., Bristol-Myers Squibb  
 Paul Parren, Ph.D., Genmab, *The Netherlands*  
 Janice Reichert, Ph.D., Tufts Center for the Study of Drug Development

## Preclinical and Early Stage Development of Antibody Therapeutics (Pages 8)

Ken Chang, Ph.D., Immunomedics, Inc.  
 John Corbin, Ph.D., XOMA (US) LLC  
 Henry Lowman, Ph.D., CytomX Therapeutics, Inc.  
 Bill Usinger, Ph.D., Trellis Bioscience, Inc.  
 Josh Xiao, Ph.D., Amgen, Inc.  
 Jin-San Yoo, Ph.D., PharmAbcine, Inc., *Korea*

## Next Generation Anti-Angiogenics (Page 9)

Rolf A. Brekken, Ph.D., University of Texas Southwestern Medical Center  
 Dario Neri, Ph.D., ETH Zurich, *Switzerland*  
 Joseph D. Rosenblatt, M.D., University of Miami School of Medicine  
 Jennifer Spratlin, Ph.D., Cross Cancer Institute, *Canada*  
 Philip E. Thorpe, Ph.D., University of Texas Southwestern  
 Maurice Zauderer, Ph.D., Vaccinex, Inc.

## Updates of Clinical Stage Antibody Therapeutics (Page 9)

Patrick A. Baeuerle, Ph.D., Micromet, Inc.  
 Naomi Hunder, M.D., Seattle Genetics  
 Vincent Ling, Ph.D., Neurotech  
 Roger Palframan Ph.D., UCB, *United Kingdom*  
 Mikkel Pedersen, Ph.D., Symphogen, *Denmark*  
 Petter Veiby, Ph.D., Millennium Pharmaceuticals

## Drug Conjugates and Bispecific Antibodies (Page 10)

Tom Davis, M.D., Celldex Therapeutics  
 Yajun Guo M.D., Ph.D., SMMU Cancer Institute, *China*  
 Bertolt Kreft, Ph.D., Bayer Schering Pharma AG, *Germany*  
 Susan Lacy, Ph.D., Abbott Bioresearch Center  
 Ulrik Nielsen, Ph.D., Merrimack Pharmaceuticals  
 William C. Olson, Ph.D., Progenics Pharmaceuticals, Inc.

## Two-Day Training Courses (Page 10)

### Introduction to Antibody Engineering

Instructor: David Bramhill, Ph.D., Director, Research Corporation Technologies

### Protein Characterization for Biotechnology Product Development

Instructor: Christine P. Chan, Ph.D., Senior Manager, Technology Development, Genzyme Corporation

## New! Antibody Platform Showcase

On Tuesday, December 6, a special exhibit hall lunchtime showcase session will present a set of significant antibody platform technologies before a three-judge response panel. These presentations will describe the background, use and benefits of the platform from a user's perspective and the panel will offer feedback on the technology and its use in the field of antibody engineering. For details on how your company can participate, please contact Sherry Johnson: (508) 614-1451; sjohnson@ibcusa.com.

Sponsor: 

For an updated list of participating companies, please visit: [www.ibclifesciences.com/antibodyeng](http://www.ibclifesciences.com/antibodyeng)

## Antibodies as Probes of Structure

12:00 *Registration Opens*

1:30 *Announcements*

### 1:35 **Co-Chairperson's Opening Remarks**

**Jamie K. Scott, M.D., Ph.D.**, *Professor, Dept. Molecular Biology, Biochemistry and Faculty of Health Sciences, Simon Fraser University, Canada*

**Sachdev Sidhu, Ph.D.**, *Professor, Department of Molecular Genetics, University of Toronto, Canada*

### 1:45 **Synthetic Antibodies: Structure and Function**

Phage displayed synthetic antibody libraries built on a single framework have simplified and expedited the discovery of highly stable antibodies for protein structural studies. Despite the simplicity of library design, synthetic antibodies have proven to be at least as versatile for generating high affinity antibodies against diverse protein antigens. Moreover, synthetic antibodies exhibit superior performance in crystallization studies due to their stable nature and predictable behavior.

**Sachdev Sidhu, Ph.D.**, *Professor, Department of Molecular Genetics, University of Toronto, Canada*

### 2:15 **The Chaperone-Enabled Biology-Structure (CEBS) Technology Platform**

The CEBS technology generates and utilizes customized "Synthetic Affinity Binders" (sABs) as crystallization chaperones for recalcitrant protein systems. Highly controlled phage display selection strategies allow for targeting sABs that can: bind to a predetermined region on a protein's surface, trap a desired conformational state and capture and stabilize a transient protein-protein complex. By studying both structure and function using the same identical set of sABs, we can determine the functional importance of a specific region/conformation/complex that will provide a direct link between structure and function.

**Anthony Kossiakoff, Ph.D.**, *Otho S. A. Sprague Professor and Chair, Department of Biochemistry and Molecular Biology, University of Chicago*

### 2:45 **Application of Antibodies in Structural Genomics**

Structural Genomics (high throughput structural biology) initiatives have generated large repertoires of recombinant proteins that make excellent antigens for the generation of recombinant antibodies and related affinity reagents. We are generating large numbers of such reagents to human proteins involved in epigenetic and ubiquitin signaling pathways. I will discuss the application of these reagents for understanding protein structure, function and their cellular biology.

**Cheryl Arrowsmith, Ph.D.**, *Chief Scientist, SGC-Toronto, Senior Scientist, Ontario Cancer Institute, Professor, Medical Biophysics, University of Toronto, Canada*

### 3:15 *Networking Refreshment Break*

### 3:45 **Structure-Based Engineering of Anti-Peptide Antibodies**

Currently, detection of biologically relevant peptides and defined peptide epitopes (e.g. phosphopeptides) relies upon the generation of monoclonal antibodies through hybridoma technology, which is costly and low throughput. Our work aims to apply a mixture of structure-based and combinatorial methods to construct both large ( $>10^{10}$ ), diverse antibody libraries as well as small, focused libraries that efficiently target peptide epitopes. We will discuss the ongoing development of antibodies targeted to specific peptides involved in apoptotic signaling.

**James T. Koerber, Ph.D.**, *Life Sciences Research Fellow, University of California, San Francisco*

### 4:15 **Dual Action Hot Spot: How does Monospecific Antibody Evolve Dual Binding Specificity?**

We have demonstrated that a monospecific antibody may recruit a secondary specificity through mutation at the antigen binding site and evolve high affinity dual specificity toward two very different antigens. I will discuss the structure/function studies of two such two-in-one antibodies against HER2/VEGF and EGFR/HER3, and the molecular basis of the evolution of the second binding specificity while retaining its first binding specificity.

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

### 4:45 **Antibodies Against the Ebola Virus**

Understanding the components of an effective immune response against the ebolaviruses is a major goal of biodefense. We will present X-ray structures of four unique mAbs against ebolaviruses in complex with their glycoprotein epitopes. Two, human kZ52 and murine 16F6, bind the base of the trimeric envelope glycoprotein and appear to function by blocking conformational changes required for membrane fusion. Two others, 14G7 and 13F6, recognize the unusual, heavily glycosylated mucin-like domains of the viral glycoprotein.

**Erica Ollmann Saphire, Ph.D.**, *Associate Professor, Immunology and Microbial Science, The Scripps Research Institute*

5:15 *Workshop Ends*

"Overall the breadth covered was very nice.  
There was also a nice balance between industry and academia."

**Kevin Schutz, Ph.D.**, *Postdoctoral Fellow, Adimab*

## The Antibody Society

The Antibody Society continues its tradition of stimulating our field with its 2011 Annual Meeting.

The Society was formed to broadly further the interests of the antibody, related binder, and associated therapeutics community. The Guidelines and Information About Therapy Experiments (GIATE) initiative has begun to stimulate community involvement in development of guidelines for the safe and thorough development of antibody and related therapeutic agents. The official journal of the Society is PEDS (Protein Engineering, Design and Selection), its therapeutic journal is mAbs, and members receive substantial discounts for journal subscriptions and for registration to our Annual Meeting.

The Society represents this increasingly diverse field by supporting the resources that promote successful engineering of recombinant antibodies, single scaffold binders, related immunobiology, informatics, and therapeutic development. The Society seeks to provide a forum and voice for all aspects of this global field.

*By joining The Antibody Society, members will help to support the Society and its goals:*

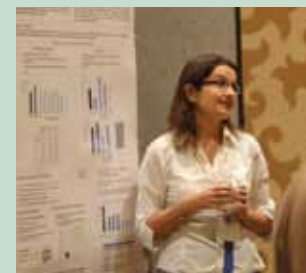
- Reinforce the contribution of meetings in our field, starting with our Annual Meeting
- Establish committees that will assess topics of urgency, such as formulating guidelines for information about antibody therapy experiments (GIATE) that help to ensure the safety of antibody or related therapeutics, from the research lab through preclinical and clinical testing
- Work for development and acceptance of formats for the interoperability of data, databases, informatics and computational resources underpinning this field
- Work for the support, maintenance, and improvement of other critical resources in this field
- Encourage the attraction, training, and funding of students, postdocs, and others in this field, for which we are developing The Antibody Society Research and Education Foundation
- Cooperate with our Board of Distinguished Advisors to broaden our role and impact in the development of this field

For further information on how you and your organization can join The Antibody Society, please visit [www.AntibodySociety.org](http://www.AntibodySociety.org). Graduate students may join at no charge.

## Student Poster Scholarship Program

To support the education and professional development of students working toward careers in antibody engineering-related disciplines, IBC Life Sciences and The Antibody Society will offer ten complimentary registrations and posterboard spaces for this year's Antibody Engineering conference. The recipients will be selected by the Society's board of directors, and each student chosen will present his/her poster in the Antibody Engineering poster hall and receive complimentary registration for the full five-day conference. Eligibility requirements and instructions on how to participate are shown below:

- Student must be a full-time graduate student at a university or academic research institute
- Post-doctoral researchers are not eligible
- Poster abstracts must be submitted no later than Friday, October 21, 2011 at: [www.IBCLifeSciences.com/antibodyeng](http://www.IBCLifeSciences.com/antibodyeng)
- Winners will be notified by Friday, November 11, 2011 – and those not awarded a complimentary registration will receive a discount to attend the meeting
- The award includes a complimentary full registration to the conference and pre-conference workshop. Travel and lodging expenses are the responsibility of the recipient



*See page 6 for non-student poster information and deadlines.*

7:15 Registration, Networking Coffee

7:45 Announcements

## Session I: Structure and Dynamics of Antibodies and their Membrane Receptor Targets

### 8:00 Chairperson's Opening Remarks and Keynote Introduction

**Andreas Plückthun, Ph.D.**, Professor of Biochemistry, Department of Biochemistry, University of Zürich, Switzerland

### Keynote Presentations

#### 8:15 Broad Antibody Neutralization of Influenza Virus and HIV-1

Influenza and HIV-1 continue to constitute significant threats to global health. We have determined structures of several potent, broadly neutralizing antibodies against a variety of different and novel epitopes on the HIV-1 and flu surface glycoproteins that include the highly conserved stem fusion region, receptor binding site and the glycans themselves. The structural and functional information can be used to aid in structure-assisted vaccine designs for HIV-1 and for a universal flu vaccine.

**Ian Wilson, D.Phil.**, Hansen Professor of Structural Biology, The Scripps Research Institute



#### 9:00 Structures of GPCRs Interacting with Ligands, Drugs, and Antibody Fragments in Phospholipid Bilayers

GPCRs remain a largely untapped resource as pharmaceutical targets. There are estimates that approximately equal numbers of GPCRs are susceptible to intervention by small molecules and antibody fragments. The role of structural biology in drug screening and optimization is well established. Therefore, our first priority has been to develop a general NMR method for determining the structures of membrane proteins, like GPCRs, in their native bilayer environment. This will enable the local and conformation effects of drugs and antibody fragments to be described at atomic resolution, accelerating the process of developing therapeutics.

**Stanley J. Opella, Ph.D.**, Professor, Chemistry and Biochemistry, University of California, San Diego



9:45 Networking Refreshment Break

#### 10:15 Structure/Function of HGF/SF and MET as a Basis for Therapeutic Targeting

The polypeptide growth factor HGF/SF and its receptor MET, the product of the proto-oncogene c-MET, have essential roles in embryogenesis and tissue regeneration but also play a major way in human cancer and, specifically, in the early stages of metastasis. This talk will discuss the available data on the structure of HGF/SF and MET as a basis for the development of small molecule inhibitors of the MET kinase and anti-HGF/SF and anti-MET antibodies for cancer therapy.

**Ermanno Gherardi, M.D., Ph.D.**, Scientist, Medical Research Council Laboratory of Molecular Biology, United Kingdom



#### 11:00 A New Mechanism for Allosteric Regulation of EGFR Family Members

The epidermal growth factor receptor (EGFR) is generally viewed as a "prototypic" receptor tyrosine kinase (RTK), and it is the target of several important cancer therapeutics. However, as mechanistic studies advance it becomes increasingly clear that EGFR and other ErbB family members have unique properties that are not shared by other RTKs. Outlining our structural and biochemical studies, I will describe a new mechanism for allosteric regulation of EGFR focusing on the extracellular and juxtamembrane regions - which has significant implications for function and therapeutic targeting.

**Mark A. Lemmon, Ph.D.**, Professor and Chair, Biochemistry and Biophysics, Perelman School of Medicine, University of Pennsylvania



11:45 Lunch on Your Own

### 1:15 Scientific Briefing

#### Discovery & Optimization of XB 2202, a Potent, Stable, Soluble Anti-RTK VH Domain Implicated in Angiogenesis, by dsDNA Display and Deep Sequencing



We describe a platform for generating and optimizing hMABs under mammalian folding conditions by dsDNA display of fully human libraries. Sequencing of thousands of hits provides an early read on the function, affinity and specificity of lead candidates. We have affinity matured these VH domains using a rapid framework optimization that maintains their fully human character. A novel VL pairing method has been used to construct fully human scFv and IgG with the biological functional activity that was predicted by deep sequencing.

**Rick Wagner, Ph.D.**, Co-Founder and Chief Scientific Officer, X-Body BioSciences

### 1:45 Scientific Briefings

#### Evaluating Diabodies and Multimerization Domains to Enhance Binding Avidity



Recombinantly expressed antibody variable domains can provide valuable recognition elements for the rapid detection of biologicals. The functional affinity of these reagents can be enhanced by expression as multimers. A simple method to dimerize an scFv is to shorten its linker, which results in diabody formation. We evaluated the monomer and dimer forms of an scFv. Multimerization domains such as alkaline phosphatase or streptavidin core create high affinity homodimers or tetramers that can provide the enhanced affinity required for the detection of threat agents.

**George Anderson, Ph.D.**, Research Chemist, Naval Research Laboratory

#### Ylanthia: A New Antibody Library Concept for Improved Developability and Manufacturability



To overcome limitations in antibody stability and other physicochemical properties we have generated a new, fully human antibody platform. All H/L pairs which pose the frameworks for this library were preselected with respect to expression levels, thermostability and aggregation propensity and great care was invested into the CDR design. In combination with the highly flexible arYla optimization technology this library constitutes an outstanding antibody platform to generate drug candidates with significantly improved developability and manufacturability.

**Stefanie Urlinger, Ph.D.**, Director, MorphoSys AG, Germany

2:15 Announcements

## Session II: Model-Guided Generation of Binding Sites

### 2:20 Chairperson's Opening Remarks

**James S. Huston, Ph.D.**, Chairman, The Antibody Society; Adjunct Scientist, Boston Biomedical Research Institute; Managing Member, Huston BioConsulting, LLC;  
**Anthony Rees, MA DPhil DSc**, Chief Scientific Officer, Biotage AB, Sweden

### 2:30 Towards a Modular Protein-Sequence Specific Binding Code

Up to now, all recombinant and immunization strategies alike have required that binder selection for every single target is an independent "project". To work towards overcoming this limitation, we are developing a strategy towards a modular peptide-sequence recognition code. It is based on a combination of structure-guided, computational and evolutionary engineering of Armadillo Repeat Proteins. The development of this scaffold through several generations will be discussed.

**Andreas Plückthun, Ph.D.**, Professor of Biochemistry, University of Zürich, Switzerland

### 3:00 Antibody Fragments Designed with Efficient Payloads for Cancer Diagnosis and Therapy

Antibody fragments (murine and human scFv and diabodies) were designed with unique surface disulphides for precise loading of either therapeutic-drug or radio-imaging payloads. With single-compound PEGylation, Tag72-targeting diabodies demonstrated remarkable xenograft-tumour uptake (>70% ID/gm at 24hrs with fast blood clearance and low kidney (<10% ID/gm). Examples include PET-imaging with AVP04 diabody (an Avibody™ product) and an ADC (drug-loaded) therapeutic formulation. GMP-manufacture has exceeded 1gm/litre in bacterial fermentation and a Phase I biodistribution (radioimaging) trial is imminent for prostate and ovarian cancer.

**Peter J. Hudson, FTSE, Ph.D.**, Director, Victorian Cancer Biologics; Chief Scientific Officer, Avipep Pty Ltd., Australia

### 3:30 Structure Prediction of Fv and VHH Domains and Docking to their Antigens

We have developed high-resolution methods to predict the structure of antibodies and antibody-antigen complexes. The RosettaAntibody approach uses a database of antibody templates; ab initio construction of the CDR H3 loop; and simultaneous refinement of side chains, CDR loops, and relative V<sub>H</sub>-V<sub>L</sub> orientations. The SnugDock method for docking exploits the known antibody model uncertainties to enable successful docking of homology models. Recently we have extended the work to single-chain VHH domains utilizing conserved cysteine and loop distances to constrain the unusually long H3 loops.

**Jeffrey J. Gray, Ph.D.**, Associate Professor, F. Stuart Hodgson Faculty Scholar, Chemical & Biomolecular Engineering, Johns Hopkins University

4:00 Networking Refreshment Break

### 4:30 A New Clustering of Antibody CDR Loop Conformations for Structure Prediction and Design

Chothia's canonical clusters of antibody CDR structures are used extensively in antibody modeling and design. We have performed a new clustering with modern statistical methods, and developed an intuitive nomenclature for these clusters, e.g. L1-11-1 is CDR L1, length 11, and cluster 1. We analyzed 28 CDR-length combinations (e.g., L1-11), 15 of which had multiple conformational clusters. Approximately 85% of the non-H3 sequences can be assigned to a conformational cluster based on gene source and/or sequence. The analysis will be updated regularly as the structure database grows.

**Roland L. Dunbrack, Jr., Ph.D.**, Associate Professor, Institute for Cancer Research Program in Molecular and Translational Medicine, Fox Chase Cancer Center

### 5:00 Modeling the Complementarity Determining Regions in Antibodies: Structure and Dynamics

I will discuss our work on predicting antibody structure from sequence, focusing on the most challenging aspect, the H3 loop. In addition I will discuss related aspects of sequence-structure relationships in antibodies, including 1) the role of loop flexibility and its modulation by affinity maturation; 2) the energy landscape of the other 5 CDR loops; and 3) the relative orientations of the heavy and light chain variable domains.

**Matthew P. Jacobson, Ph.D.**, Professor and Vice Chair, Department of Pharmaceutical Chemistry, University of California, San Francisco

### 5:30 Computational Design of Protein-Protein Interactions

We have used iterative sequence optimization and docking with the molecular modeling program Rosetta to design a variety of protein-protein interactions. In each case, the designs are based on structural features found at naturally occurring interfaces, including beta-strand pairing, metal binding, and loop-mediated interactions. Sequence optimization simulations have also been used to design directed libraries that are enriched in sequences that bind a pre-specified target protein.

**Brian Kuhlman, Ph.D.**, Associate Professor, Biochemistry and Biophysics, University of North Carolina

6:00 Networking Cocktail Reception; Opening of Poster and Exhibit Hall

### Media Partners



Human Antibodies  
An International Journal



7:00 Registration, Networking Coffee

7:45 Announcements

## Session III: Novel Selection Strategies

7:50 Chairperson's Opening Remarks

**James D. Marks, M.D., Ph.D.**, Professor and Vice Chairman, Anesthesia and Perioperative Care, University of California, San Francisco; Chief of Anesthesia, San Francisco General Hospital

8:00 Selection of Internalizing Phage Antibodies Using Tumor Cells and Yeast Displayed Tumor Antigens

Antibodies that bind cancer cells and are internalized can be used for tumor targeted drug and nucleic acid delivery. We show that such antibodies to specific tumor antigens can be generated by first selecting phage antibody libraries on a tumor cell line expressing the target antigen followed by selection on yeast displaying the same antigen on their surface. Advantages of this approach and specific examples will be covered.

**James D. Marks, M.D., Ph.D.**, Professor and Vice Chairman, Anesthesia and Perioperative Care, University of California, San Francisco; Chief of Anesthesia, San Francisco General Hospital

8:30 Combining Phage and Yeast Display

Phage and yeast display have complementary capabilities. Phage antibody libraries have vast diversity, but selection is difficult to control. Selection on yeast, in contrast, is easy to control using flow cytometry, but large libraries are more difficult to manipulate. This talk will discuss the benefits of combining the two technologies.

**Andrew Bradbury, M.D., Ph.D.**, Research Scientist and Team Leader, Los Alamos National Laboratories

9:00 Selecting Antibodies and Enzymes for Unique Selectivities and Activities

Protein display technologies are extremely powerful approaches for selection of naïve or improved binders to other macromolecules. We are designing more subtle properties using protein display, namely conformationally selective binders and a peptide ligase with improved activity. We have used chemical inhibitors to lock different conformations of caspases and used these as antigens for isolating, by differential selections, antibodies that function to activate or inhibit the enzyme. We have also developed a selection for improving a peptide ligase called subtiligase either by display on phage or yeast.

**James A. Wells, Ph.D.**, Professor & Chair, Department of Pharmaceutical Chemistry, University of California San Francisco

9:30 Networking Refreshment Break, Exhibit and Poster Viewing

10:15 Yeast Display for Identification and Engineering of Antibodies Against Membrane Protein Targets

Membrane proteins are challenging to work with in terms of antibody selection, engineering, and antigen identification as a result of their insolubility in aqueous solutions. We have therefore developed a platform for antibody engineering using either whole cells or cell lysates as antigen sources. Such approaches are compatible with membrane protein targets, subcellular selections, and the rapid assessment of antibody specificity. Moreover, when combined with yeast display immunoprecipitation procedures, antigen analysis is facilitated.

**Eric V. Shusta, Ph.D.**, Associate Professor, Chemical and Biological Engineering, University of Wisconsin-Madison

10:45 CLIPS Technology Meets GPCR: A New Peptide Based Strategy for the Generation of Monoclonal Antibodies against GPCRs

CLIPS technology allows protein mimicry by design and synthesis of conformationally stabilized peptides with a well-defined 3D spatial structure, resembling the native functional protein surface. I will present data demonstrating the proof-of-principle that Pepsan's synthetic immunogens can induce antibodies against GPCR's and therefore are able to mimic the native receptor. Resulting antibodies do not bind only the native receptor, but also show functionality in different cell based *in vitro* assays.

**Klaus Schwamborn, Ph.D.**, Chief Development Officer, Pepsan Therapeutics B.V., The Netherlands

11:15 In Vitro Antibody Selection Against Native Protein Conformations

The antibody phage display is a powerful approach to select rapidly and at low cost monoclonal antibodies. In the past, we have shown that it allows the efficient selection of conformation-specific antibodies. We have also shown that these antibodies can frequently be used as intrabodies to track the dynamics of their endogenous target. We are now exploring several approaches to improve the selection of antibodies directed against native protein conformation. This will represent unique tools both for fundamental and applied research.

**Franck Perez, Ph.D.**, Group Leader and Research Director, Curie Institute, France

11:45 Scientific Briefings

### Generation of Therapeutic Antibodies against Inflammatory Disease and Cancer Targets with a Low Risk of Clinical Immunogenicity



Data from clinical studies show that one of the major issues with the use of therapeutic antibodies is the development of an anti-therapeutic antibody response. Such responses have been observed in many patients treated with anti-TNF $\alpha$  and  $\alpha$ 4 $\beta$ 7-integrin antibodies for RA and IBS, as well as with antibodies and conjugates for various cancers. Data will be presented providing evidence linking the presence of T cell epitopes in the sequences of therapeutic antibodies with immunogenicity observed in patients as well as how antibodies can be engineered to avoid T cell epitopes.

**Matthew Baker, Ph.D.**, Chief Scientific Officer, Co-Founder, Antitope Ltd

### Exploiting the Versatility of Fynomers for IL-17 Inhibition



Fynomers represent a new class of binding molecules based on the human Fyn SH3 domain. We will provide examples of the broad applicability of the Fynomer technology, show novel Fynomer formats and present *in vitro* and *in vivo* data from our IL-17 program.

**Speaker TBA**, Covagen AG, Switzerland

### OMT Antibody Platform: Fully Human Antibodies From Transgenic Rats



Open Monoclonal Technology, Inc. ("OMT") is a private, California-based biotechnology company, that developed a fully human monoclonal antibody (mAb) platform based on transgenic rats. This new technology is the result of breakthroughs in the understanding of B-cell development and a novel approach to the inactivation of endogenous antibody expression. OMT's antibody platform has broad freedom to operate and uses technology protected by a new patent application.

**Roland Buelow, Ph.D.**, Chief Executive Officer, Open Monoclonal Technology, Inc.

12:15 Networking Luncheon, Exhibit and Poster Viewing and NEW Antibody Platform Showcase

1:45 Scientific Briefings

### A Phage Display Approach for Anti-Inflammatory Therapeutic Antibody Discovery



The ability to identify high affinity antibodies from Dyax's antibody phage display libraries has been demonstrated in over 70 selection campaigns, including dozens of therapeutic programs. The selection and screening of the library can be completed in days and the output of binders characterized in weeks. Here we will present a case study from Dyax's internal discovery pipeline that illustrates selection strategies and potency of the identified antibodies.

**Andrew E. Nixon, Ph.D.**, Vice President, Lead Discovery & Biochemistry, Dyax

### Screening and Characterization of Fully Human Antibodies from Velocimmune® Mice using Real-Time Label-Free Interaction Analysis



During antibody development, generation of high quality binding interaction data is essential for identifying antibodies with potential therapeutic use. However, many challenges can occur throughout the screening and characterization phase of development. Such challenges include the analyses of target antigen proteins with a propensity for nonspecific binding and the analyses of large numbers of unpurified antibody supernatant samples. Here, we will discuss how different label-free interaction analysis platforms are used to overcome these various challenges and how they can facilitate the identification and characterization of potential therapeutic antibodies.

**Matthew C. Blome, Ph.D.**, Scientist, Therapeutic Proteins, Regeneron Pharmaceuticals, Inc.

### $\kappa\lambda$ -Body: A Platform Approach to Produce Fully Human Bispecific IgGs



$\kappa\lambda$ -Bodies are unmodified fully human bispecific IgGs. In contrast to existing engineered formats,  $\kappa\lambda$ -Bodies are unique in offering the typical functional and biochemical characteristics of a human antibody. A streamlined platform approach for the identification, production and characterization of  $\kappa\lambda$ -Bodies will be demonstrated.

**Greg Elson**, Head of Manufacturing, NovImmune SA, Switzerland

## Session IV: Antibodies in a Complex Environment: Targeting Intracellular and Misfolded Proteins

2:15 Chairperson's Opening Remarks

**Richard H.J. Begent, M.D.**, Emeritus Professor of Oncology, UCL Cancer Institute, University College London, United Kingdom

## Session Keynote Presentation

2:30 Gene and Antibody Therapies for Neurodegenerative Diseases Caused by Abnormal Protein Accumulation

Abnormal intracellular protein accumulations and interactions are critical mediators of a wide range of diseases. Neurons are especially vulnerable, given high metabolic demands and extreme longevity. Intrabodies offer a targeted proteomic approach to manipulating the conformations and intracellular localization of abnormal species for validation, direct therapeutics, and rational drug design. We have used a combination of antibody engineering and gene delivery to counteract pathogenic neurodegenerative phenotypes in culture and animal models.

**Anne Messer, Ph.D.**, Professor and Senior Research Scientist, Molecular Genetics, Wadsworth Center, New York State Department of Health

3:15 Huntington's Disease – Developments in Intrabody Therapy

Huntington's disease is an autosomal dominant, neurodegenerative disease caused by the expansion of a polyglutamine repeat in the protein huntingtin (HTT). Gain of toxic function as a result of the mutation is thought to contribute to the complex disease process. The use of anti-HTT intrabodies that interfere with aberrant protein interactions, alter localization, or increase clearance of this toxic protein as a therapeutic strategy will be discussed.

**Amber L. Southwell, Ph.D.**, Postdoctoral Researcher, University of British Columbia, Canada

3:45 Immunity Proteins as Scaffolds for Stabilization of the Amyloid  $\beta$  Peptide

Alzheimer's Disease (AD) is a neurodegenerative disease thought to be caused by soluble, neurotoxic oligomers of the amyloid  $\beta$  peptide (A $\beta$ ). To overcome its aggregation we have trapped A $\beta$  within protein scaffolds that exhibit high conformational tolerance, to stabilize the A $\beta$  monomer and soluble oligomers. Using this technology we have successfully solved the crystal structure of the A $\beta$  p3 fragment, which forms a novel dimeric structure. We are now utilizing the A $\beta$ -scaffold proteins to develop conformational and region specific antibodies targeting A $\beta$ .

**Rebecca Nisbet, Ph.D.**, OCE Postdoctoral Fellow, CSIRO Materials Science and Engineering, Australia

4:00 Networking Refreshment Break, Exhibit and Poster Viewing

4:45 Treatment of Amyloidosis with Antibodies to Human Serum Amyloid P Component

Accumulation of amyloid fibrils in the viscera causes systemic amyloidosis. Amyloid deposits consist of the respective amyloid fibril protein and also contain serum amyloid P component (SAP). Current treatments, which can arrest amyloid accumulation, focus on substantially reducing the abundance of the amyloid fibril precursor protein, but this is not always possible. No therapy exists that enhances clearance of amyloid deposits. Administration of anti-human-SAP antibodies to amyloidotic mice swiftly removed massive visceral amyloid, and should be applicable to human amyloidosis.

**Julian D. Gilmore, Ph.D.**, Senior Lecturer, National Amyloidosis Center, University College London Medical School, United Kingdom

5:15 Engineering T cells with Antibody Based Chimeric Receptors: Preclinical and Early Clinical Results

Engineering T cells with antibody based chimeric receptors to target tumor associated antigens is a potentially general approach to treating malignant disease – these have been extensively optimized to produce efficient expression of functional, folded protein as an active receptor. Preclinical models suggest that the adoptive transfer of such engineered T cells is most effective when it follows chemotherapy as this greatly facilitates expansion and survival of the gene-modified cells. Based on preclinical models, trials targeting CD19 and CEA have been undertaken.

**Robert E. Hawkins, Ph.D.**, Cancer Research UK Professor of Medical Oncology, University of Manchester, United Kingdom

5:45 Intracellular Delivery of Radioimmunoconjugates that Target the DNA Repair Signaling Protein,  $\gamma$ H2AX, for Imaging and Therapy of Cancer

DNA damage responses are induced by many anticancer drugs and by radiotherapy. A real-time method to image DNA damage *in vivo* would be useful to monitor treatment. Radiopharmaceuticals that target DNA damage signaling proteins could be used for treatment themselves, through amplification of pre-existing DNA damage. I will describe our work to develop fluorophore- and radioisotope-labeled immunoconjugates that target the DNA damage signaling protein,  $\gamma$ H2AX, which forms foci at sites of DNA double-strand breaks.

**Katherine Vallis, MBBS, Ph.D.**, Professor, Department of Oncology, University of Oxford, United Kingdom

6:15 Networking Cocktail Reception, Exhibit and Poster Viewing

7:30 Registration, Networking Coffee

8:00 Announcements

## Session V: Rational Vaccine Design

### 8:05 Chairperson's Opening Remarks

**Dennis R. Burton, Ph.D.**, Professor, Department of Immunology and Microbial Science, The Scripps Research Institute

### 8:15 Engineering Effective Vaccine Antigens

Most current vaccines are based on antigens that are essentially the native macromolecules of pathogens. Using structural information, we can engineer antigens that are more stable, homogeneous, and efficiently produced, making immunization more practical and affordable. Understanding the structural basis for immunogenicity and immunodominance will allow us to improve vaccine efficacy and broaden the range of vaccine-preventable diseases. Examples that apply structural biology for the rational design of novel antigens will be presented.

**Andrea Carfi, Ph.D.**, Head, Protein Biochemistry, USA, Novartis Vaccines & Diagnostics

### 8:45 Scaffolding Epitopes to Provide Directed Antibody Responses

Structure-guided approaches to vaccine design for a variety of pathogens have been enabled by structural information on epitopes targeted by neutralizing antibodies and by advances in computational design methods. In one approach – epitope scaffolding – epitopes are transplanted to scaffold proteins for conformational stabilization and exposure to the immune system. Biophysical, crystallographic, and immunologic results will be presented on scaffolds for selected epitopes from HIV and RSV.

**William Schief, Ph.D.**, Principal Scientist, International AIDS Vaccine Initiative and Associate Professor of Immunology, The Scripps Research Institute

### 9:15 Learning Immunology from Successful Vaccines: Innate Immunity to Systems Vaccinology

Despite their great success, we understand little about how effective vaccines stimulate protective immune responses. Two recent developments promise to yield such understanding: the appreciation of the crucial role of the innate immune system in sensing microorganisms and tuning immune responses, and advances in systems biology. In this presentation, I will discuss how these developments are yielding insights into the mechanism of some of the most successful vaccines ever developed, and the broader implications for vaccinology.

**Bali Pulendran, Ph.D.**, Professor Pathology & Laboratory Medicine, Emory University

### 9:45 Networking Refreshment Break, Exhibit and Poster Viewing

### 10:30 Antibody Gene Delivery – A New Approach to Vaccines

The discovery of new and potent human monoclonal antibodies against a wide array of human pathogens has opened the door to a new form of immunoprophylaxis. Genes representing a given antibody (or combinations thereof) can be transferred to a naïve human subject wherein the gene directs production of the antibody *in vivo*. Thus, the gene recipient is endowed with the antibody specificity of the pre-selected molecule. The use of this approach for an HIV vaccine will be highlighted.

**Philip R. Johnson, M.D.**, Chief Scientific Officer, The Children's Hospital of Philadelphia

### 11:00 Engineering Nanomaterials as Vaccine Adjuvants to Shape Humoral and Cellular Immunity

New nanomaterials for vaccine delivery will be described, based on classical liposome structures as well as a new class of lipid nanoparticles, interbilayer-crosslinked multilamellar vesicles (ICMVs). ICMVs are composed of multilamellar liposomes, stabilized by covalent crosslinks across bilayers within the vesicle walls. Using both model and disease (HIV and malaria) antigens, we demonstrate how the structure of these nanomaterials impacts the induction of follicular helper T-cell responses and subsequent humoral responses, leading to enhanced breadth of the antibody response against subunit antigens.

**Darrell J. Irvine, Ph.D.**, Associate Professor, Biological Engineering, Materials Science & Engineering, Massachusetts Institute of Technology

## Special Presentation

### 11:30 The Antibody Society

The Antibody Society (TABs) was formed in 2007 to further the broad interests of the antibody engineering and antibody therapeutics community. This presentation will describe recent progress and initiatives for the coming year.

**Jamie K. Scott, M.D., Ph.D.**, Professor, Dept. Molecular Biology, Biochemistry and Faculty of Health Sciences, Simon Fraser University, Canada

### 12:00 Scientific Briefing

#### Presentation Title to be Announced

This abstract was not available at the time of printing the brochure. For up to date program information, please visit [www.IBCLifeSciences.com/Antibodyeng](http://www.IBCLifeSciences.com/Antibodyeng)

Speaker TBA



### 12:30 Networking Luncheon, Last Chance for Exhibit and Poster Viewing

## Session VI: Viral Retargeting with Engineered Binding Molecules, Especially for Oncolytic Viruses

### 2:00 Chairperson's Opening Remarks

**Andrew Bradbury, M.D., Ph.D.**, Research Scientist and Team Leader, Los Alamos National Laboratories

### 2:15 Specific Gene Delivery to Cell Types of Choice by Cell Entry Targeted Lentiviral Vectors

Lentiviral vectors mediate stable and long-term transgene expression making them ideal gene delivery vehicles for research and therapy. Here we present a technology that enables cell type specific gene delivery by displaying single-chain antibodies on the vector envelope thereby restricting cell entry to antigen positive cells. Gene transfer with an unprecedented degree of specificity to endothelial cells, lymphocytes, neurons and tumor cells is demonstrated, not only *ex vivo* but also *in vivo* upon local or systemic application.

**Christian Buchholz, Ph.D.**, Section Head, Professor of Biochemistry, Division of Medical Biotechnology, Paul-Ehrlich Institute, Germany

### 2:45 Retargeting of Adenovirus Vectors through Genetic Fusion of a Single-chain or Single-domain Antibody to Capsid Protein IX

Adenovirus (Ad)-based vectors are widely used to deliver therapeutic genes to a variety of cell types and tissues. To target viral infection specifically to cancer cells, we investigated the Ad capsid protein IX (pIX) as a platform for addition of single-chain and single-domain antibodies directed towards cell surface antigens. We show that fusion of such molecules to pIX can enhance Ad infection of cancer cells, which should improve Ad safety and efficacy for cancer gene therapy.

**Robin J. Parks, Ph.D.**, Senior Scientist, Regenerative Medicine Program, Ottawa Hospital Research Institute, Canada

### 3:15 Antibody-Targeting with Added Value: Measles Virus

Measles is a simple (six genes) enveloped RNA virus that can be re-targeted by adding single-chain antibodies to its de-targeted attachment protein. Viral particles, lacking icosahedral symmetry, have variable cargo volume. Thus genes added for tracking or arming are well tolerated. Measles virus uses immune cells to move through the body, and hijacks a junction protein to transit through epithelial barriers. The use of armed, replicating measles viruses for targeted elimination of different tumors will be discussed.

**Roberto Cattaneo, Ph.D.**, Professor of Biochemistry and Molecular Biology, Department of Molecular Medicine, Mayo Clinic

### 3:45 Networking Refreshment Break

### 4:15 Antibody Display on Enveloped Viruses

The high structural fidelity of antibodies displayed on enveloped viruses may be of considerable value, both for the generation of viruses with unique tropisms, and to facilitate *in vivo* antibody selection and affinity optimization. While single chain antibodies have been successfully displayed on the envelope glycoproteins of several widely differing mammalian viruses, only in the case of the measles H glycoprotein have displayed antibodies been shown capable of redirecting membrane fusion through a broad range of surrogate cell surface receptors. Applications will be discussed.

**Stephen J. Russell, M.D., Ph.D.**, Professor of Medicine, Mayo Clinic

### 4:45 Generation of Bispecific DARPIn Adapters for Efficient Adenoviral Gene Transfer

We developed a bispecific adapter strategy based on the DARPIn scaffold that redirects Adenovirus serotype 5 (Ad5) to any target cell of choice. DARPins binding the Ad5 trimeric knob with nanomolar affinity were selected by ribosome display. Based on the crystal structure of the knob-DARPIn complex and computer modeling, trivalent knob binders were generated. When fused to a DARPIn recognizing HER2, the resulting trimeric, bispecific adapter enabled Ad5 virions deliver a luciferase reporter gene in a HER2-dependent manner.

**Birgit Dreier, Ph.D.**, Senior Scientist, Department of Biochemistry, University of Zurich, Switzerland

### 5:15 End of Antibody Engineering Sessions; Delegates May Attend Antibody Therapeutics 5:15 Presentation

## Take an Active Role in the Conference and Present a Poster

Did you know that 85% of our conference attendees say that reviewing posters is one of their favorite features of our events?

- **Justify Your Trip:** Presenting a poster at this conference helps justify the time and cost of your attendance at the conference. Not only are you learning new techniques and strategies, but you are also gaining well-deserved recognition for you and your organization for your innovative research findings, successful business models, unique service propositions, or creative business strategies.
- **Visibility:** Posters will be displayed for all attendees, exhibitors, and presenters to see in the exhibit hall during exhibit hall hours and networking functions.

The deadline to submit an abstract and be included in the conference documentation is Friday, October 28, 2011, and any registered and paid conference attendee may register to present a poster. Full payment of conference registration and poster fees must also be received by October 28, 2011 for the abstract to be included in the conference materials and a posterboard assignment to be made. Posters should be portrait orientation, with maximum dimensions of 36" wide (3 feet) x 48" high (4 feet). Please see the registration page for details on the poster fee.

Share your research with your peers and make your mark in this field – it could lead to exciting opportunities to advance your career. Complete details can be found at online at [www.IBCLifeSciences.com/Antibodyeng](http://www.IBCLifeSciences.com/Antibodyeng).

7:30 *Networking Coffee*

8:00 *Announcements*

## Session VII: The Biology Behind Potential Blockbuster Antibodies

### 8:05 Chairperson's Opening Remarks

**Ian M. Tomlinson, Ph.D.**, *Senior Vice President, Biopharmaceuticals R & D, GlaxoSmithKline, United Kingdom*

### 8:15 Who'd Have Gussed that Hitting TNF Would Create a \$10bn Market in Rheumatoid Arthritis

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**Jochen G. Salfeld, Ph.D.**, *Divisional Vice President Biologics, Distinguished Research Fellow, Abbott Bioresearch Center*

### 8:45 Is Anti-IL-12/23 the New Anti-TNF?

Ustekinumab is a human mAb that binds the shared p40 subunit of IL-12 and IL-23, resulting in the blockade of Th1 and Th17 inflammatory pathways. Ustekinumab is approved for the treatment of moderate-to-severe plaque psoriasis. Phase 2 studies demonstrated efficacy in Crohn's disease and psoriatic arthritis with no safety issues identified. Targeting both Th1 and Th17 cells via ustekinumab may provide new therapeutic options for patients with immune-mediated inflammatory diseases.

**Kim A Campbell, Ph.D.**, *Director, Immunology Product Support, Centocor Research & Development, a division of Johnson & Johnson Pharmaceutical Research & Development, L.L.C.*

### 9:15 IL-6 Signaling: Hit the Receptor, the Ligand or Both; The Pros and Cons

Treatment of autoimmune diseases with the anti-IL-6 receptor antibody Tocilizumab has underlined the importance of cytokines of the gp130 family. Disease progression by gp130 signaling and the special role of IL-6 with an emphasis on the role of the soluble IL-6 receptor in pro-inflammatory activities of this cytokine will be discussed. An overview will be given of preclinical and clinical blockade of IL-6 activity in autoimmunity, inflammation and cancer.

**Stefan Rose-John, Ph.D.**, *Professor of Biochemistry and Director, Department of Biochemistry, University of Kiel, Germany*

9:45 *Networking Refreshment Break*

### 10:15 Belimumab: A Human Monoclonal Antibody Against BLYS for the Treatment of SLE

For the first time in more than 50 years, a drug has been approved specifically for the treatment of systemic lupus erythematosus (SLE). This drug, belimumab (Benlysta<sup>®</sup>), is a monoclonal antibody that neutralizes the B cell survival factor, B lymphocyte stimulator (BLYS). The discovery of BLYS, its role in B cell biology and the effect of antagonizing BLYS in preclinical and clinical studies, with emphasis on B cells and biomarkers, will be discussed.

**Thi-Sau Migone, Ph.D.**, *Vice President, Research, Human Genome Sciences, Inc.*

### 10:45 What Does Anti-VEGF Therapy Actually do in the Tumor Vasculature?

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**Gavin Thurston, Ph.D.**, *Executive Director, Oncology and Angiogenesis Research, Regeneron Pharmaceuticals*

### 11:15 Dissecting the Biology of Bone to go Beyond Bisphosphonates; The Biology Behind Hitting the RANK Ligand

This abstract was not available at the time of printing the brochure. For up to date program information, please visit [www.IBCLifeSciences.com/Antibodyeng](http://www.IBCLifeSciences.com/Antibodyeng)

**David Lacey, M.D.**, *Senior Vice President, Head of Research, Amgen, Inc.*

11:45 *Lunch on Your Own*

1:15 *Announcements*

## Session VIII: Antibodies as Signaling Modifiers: Where Did We Go Right? And, Can We Learn from Success?

### 1:20 Chairperson's Opening Remarks

**Louis M. Weiner, M.D.**, *Director, Lombardi Comprehensive Cancer Center, Georgetown University Medical Center*

### 1:30 Antibody Therapy of Cancer: Where did we go Right, and Where Do We Go From Here?

Unconjugated antibody-targeted therapeutics have emerged as vital components of the therapeutic armamentarium for cancers. Anti-cancer antibodies may work through a variety of mechanisms, including direct signaling effects and immunological effects, but the relative contributions of these mechanisms remains uncertain. We have previously identified conditions for enhancing the anti-tumor effects of antibodies by modifying the molecular structures of human IgG proteins. We describe strategies and results employing functional genomics techniques to identify the tumor cell-based molecular determinants of responsiveness to either signaling perturbation or antibody-dependent cellular cytotoxicity.

**Louis M. Weiner, M.D.**, *Director, Lombardi Comprehensive Cancer Center, Georgetown University Medical Center*

### 2:00 Boosting the Delivery of Therapeutic Levels of Antibody to the Brain

Antibodies have a vast therapeutic potential for treatment of CNS diseases, but their passage into the brain is restricted by the blood-brain barrier (BBB). Here, we describe an approach to enhance receptor-mediated transcytosis pathways of brain endothelial cells to deliver therapeutically relevant dose levels of antibodies across the BBB.

**Mark S. Dennis, M.S.**, *Senior Scientist, Department of Antibody Engineering, Genentech, Inc.*

### 2:30 Strategies for the Generation of Receptor Blocking Antibodies

Recombinant antibodies provide a means to control receptor activation with potential utility in the treatment of cancer or the control of stem cell differentiation. Using phage display in conjunction with cell based screening assays we have generated and affinity matured human antibodies which affect cell signaling by a number of different modalities including ligand neutralization, receptor blocking, signal processing and stabilization of closed conformations. The different approaches used will be discussed.

**John McCafferty, Ph.D.**, *Professor, Biochemistry, Cambridge University, United Kingdom*

3:00 *Networking Refreshment Break*

### 3:15 First-in-Class EGFR mAb Mixture, Sym004: Phase I Trial in Patients with Refractory Advanced Solid Tumors

Sym004 is a recombinant antibody 1:1 mixture of two chimeric anti-EGFR mAbs, targeting two non-overlapping epitopes, which elicits superior cancer cell growth inhibition in preclinical models. Uniquely, Sym004 mediates cell surface receptor removal by triggering EGFR internalization and degradation. Results from the first-in-human multicenter trial evaluating safety and tolerability of multiple doses of Sym004 are reported. Sym004 is well tolerated with no unexpected toxicities and shows preliminary signs of clinical activity.

**Amita Patnaik, M.D., FRCPC**, *Associate Director of Clinical Research, START Center for Cancer Care*

### 3:45 Next-Generation Tri-Epitopic Anti-EGFR Antibodies: Overcoming Resistance by Enhanced Clustering and Downregulation

A tri-epitopic anti-EGFR antibody containing binding sites against three epitopes is found to rapidly cluster EGFR and downregulate its surface levels. We have isolated Fn3-based binders against EGFR, and fusions of these Fn3 domains to cetuximab leads to a single agent that dramatically downregulates and inhibits EGFR in over 15 tumor lines tested. In particular, tumor lines that are KRAS mutant and/or BRAF mutant are found to be controlled by the tri-epitopic construct despite an absence of efficacy for cetuximab.

**K. Dane Wittrup, Ph.D.**, *C.P. Dubbs Professor of Chemical Engineering and Biological Engineering, Massachusetts Institute of Technology*

4:15 *Close of Meeting*

"The conference provides a nice balance between what's currently in the clinic and exciting new entities emerging. The two conferences sit nicely with each other and provide opportunity to move between the two."

**Anthony Shock, Ph.D.**, *Director, Immunology Project Management, UCB, United Kingdom*

## The 2011 Antibody Engineering Scientific Advisory Board

**Richard H.J. Begent, M.D.**, *Emeritus Professor of Oncology, UCL Cancer Institute, University College London, United Kingdom*

**Andrew Bradbury, M.D., Ph.D.**, *Research Scientist and Team Leader, Los Alamos National Laboratories*

**Dennis R. Burton, Ph.D.**, *Professor, Department of Immunology and Microbial Science, The Scripps Research Institute*

**James S. Huston, Ph.D.**, *Chairman, The Antibody Society; Adjunct Scientist, Boston Biomedical Research Institute; Managing Member, Huston BioConsulting, LLC*

**James D. Marks, M.D., Ph.D.**, *Professor and Vice Chairman, Anesthesia and Perioperative Care, University of California, San Francisco; Chief of Anesthesia, San Francisco General Hospital*

**Andreas Plückthun, Ph.D.**, *Professor of Biochemistry, University of Zürich, Switzerland*

**Jamie K. Scott, M.D., Ph.D.**, *Professor, Dept. Molecular Biology, Biochemistry and Faculty of Health Sciences, Simon Fraser University, Canada*

**Ian M. Tomlinson, Ph.D.**, *Senior Vice President, Biopharmaceuticals R & D, GlaxoSmithKline, United Kingdom*

**Louis M. Weiner, M.D.**, *Director, Lombardi Comprehensive Cancer Center, Georgetown University Medical Center*

7:00 Registration, Networking Coffee

7:45 Announcements

## Session I: Twenty-Five Years of Therapeutic Antibodies: Lessons Learned and Future Challenges

7:50 **Chairperson's Opening Remarks**

**Rathin C. Das, Ph.D.**, Chief Executive Officer, Synergys Biotherapeutics, Inc.

### Keynote Presentations

8:00 **Angiogenesis, Avastin and Beyond**

Vascular endothelial growth factor (VEGF)-A is a key regulator of angiogenesis. We developed a humanized anti-VEGF-A monoclonal antibody (bevacizumab), which has been approved by the FDA and worldwide for the treatment of several malignancies. Blocking VEGF-A had also a major impact on the progression of neovascular age-related macular degeneration. We have been investigating the mechanisms of refractoriness/resistance to anti-VEGF therapies in tumor models. Factors produced by tumor-infiltrating myeloid cells or by fibroblasts were identified as key mediators of VEGF-independent angiogenesis.

**Napoleone Ferrara, Ph.D.**, Genentech Fellow, Tumor Biology and Angiogenesis, Genentech, Inc.

8:45 **From Mouse Embryos to Antibody Therapies**

Human antibody expression from mice engineered with germline configuration human immunoglobulin transgenes was reported at the 1991 IBC Antibody Engineering conference. In the intervening 20 years, the FDA has approved seven therapeutic antibodies derived from transgenic mice. These approved drugs are indicated for a variety of disease areas including rheumatology, bone metabolism, and cancer. The history of this drug discovery platform will be reviewed, and new applications discussed.

**Nils Lonberg, Ph.D.**, Senior Vice President, Bristol-Myers Squibb

9:30 **Networking Refreshment Break, Exhibit and Poster Viewing**

10:15 **Maytansinoid Antibody Conjugates**

Conjugation of antibodies to highly potent cytotoxic payloads to create ADCs offers a strategy for developing anti-cancer drugs of great promise. Several antibody-maytansinoid conjugates have shown encouraging activity in clinical trials. The presentation will focus on considerations in designing highly effective, well-tolerated ADCs, from target selection to factors influencing the selection of each ADC component. Examples will be drawn from the newest AMCs in early development.

**John Lambert, Ph.D.**, Executive Vice President, and Chief Scientific Officer, ImmunoGen, Inc.

10:45 **CD20 Antibody Therapy: Learning from the Past for an Improved Future**

CD20 arguably represents the strongest validated target for immunotherapy. While standard rituximab immunotherapy continues to have a major impact on the lives of patients with B-cell malignancies and autoimmune disease, novel CD20 antibodies with enhanced or distinct mechanisms of action are being developed to achieve even higher and broader efficacy. Examples include ofatumumab, displaying improved CD20 binding, CDC and ADCC, and afutuzumab, which instead relies on ADCC and apoptosis induction. Novel developments drawing from past experience will be discussed.

**Paul Parren, Ph.D.**, Senior Vice President and Scientific Director, Genmab, The Netherlands

11:15 **The Antibody as a Therapeutic: Once and Future King?**

With global sales reaching \$50 billion, antibodies are clearly successful as therapeutics. Innovation in biological engineering in the 2000s led to the creation of a wide variety of antibody formats, but whether these new formats will be as successful as classical IgGs remains to be seen. Dr. Reichert will discuss lessons learned and the challenges ahead for generating clinically successful antibodies. The outlook and strategies for next-generation antibodies, including those for non-traditional indications such as CNS disorders, will be presented.

**Janice Reichert, Ph.D.**, Research Assistant Professor and Senior Research Fellow, Tufts Center for the Study of Drug Development

11:45 **Scientific Briefings**

### Generation of Therapeutic Antibodies against Inflammatory Disease and Cancer Targets with a Low Risk of Clinical Immunogenicity



Data from clinical studies show that one of the major issues with the use of therapeutic antibodies is the development of an anti-therapeutic antibody response. Such responses have been observed in many patients treated with anti-TNF $\alpha$  and  $\alpha 4\beta 7$ -integrin antibodies for RA and IBS, as well as with antibodies and conjugates for various cancers. Data will be presented providing evidence linking the presence of T cell epitopes in the sequences of therapeutic antibodies with immunogenicity observed in patients as well as how antibodies can be engineered to avoid T cell epitopes.

**Matthew Baker, Ph.D.**, Chief Scientific Officer, Co-Founder, Antitope Ltd

### Exploiting the Versatility of Fynomers for IL-17 Inhibition



Fynomers represent a new class of binding molecules based on the human Fyn SH3 domain. We will provide examples of the broad applicability of the Fynomer technology, show novel Fynomer formats and present in vitro and in vivo data from our IL-17 program.

**Speaker TBA, Covagen AG, Switzerland**

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**Roland Buelow, Ph.D.**, Chief Executive Officer, Open Monoclonal Technology, Inc.

12:15 **Networking Luncheon, Exhibit and Poster Viewing and NEW Antibody Platform Showcase**

1:45 **Scientific Briefings**

### A Phage Display Approach for Anti-Inflammatory Therapeutic Antibody Discovery



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**Andrew E. Nixon, Ph.D.**, Vice President, Lead Discovery & Biochemistry, Dyax

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During antibody development, generation of high quality binding interaction data is essential for identifying antibodies with potential therapeutic use. However, many challenges can occur throughout the screening and characterization phase of development. Such challenges include the analyses of target antigen proteins with a propensity for nonspecific binding and the analyses of large numbers of unpurified antibody supernatant samples. Here, we will discuss how different label-free interaction analysis platforms are used to overcome these various challenges and how they can facilitate the identification and characterization of potential therapeutic antibodies.

**Matthew C. Blome, Ph.D.**, Scientist, Therapeutic Proteins, Regeneron Pharmaceuticals, Inc.

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**Greg Elson, Head of Manufacturing, Novimmune SA, Switzerland**

2:15 **Announcements**

## Session II: Preclinical and Early Stage Development of Antibody Therapeutics

2:20 **Chairperson's Opening Remarks**

**Benjamin P. Chen, Ph.D.**, International Director, Burrill & Company

2:30 **Development of Tanibirumab™, Anti-KDR Neutralizing Fully Human Antibody and Next Generation DIG-bodies™ and PIG-bodies™**

I will present our preclinical data of anti-KDR neutralizing fully human IgG1, Tanibirumab, which has cross-species cross reactivity, and discuss our recent progress with dual target neutralizing multifunctional Ig like next generation protein therapeutics, DIG-KT (KDR & Tie2) from the DIG-bodies platform, and PIG-KM (KDR & cMET) from the PIG-bodies platform.

**Jin-San Yoo, Ph.D.**, Chief Executive Officer and President, PharmAbcine, Inc., Korea

3:00 **Leveraging the Human Immune System to Combat Infectious Diseases**

The human immune repertoire contains an immense untapped supply of therapeutically useful antibodies. Best in class antibodies are rare and hard to find. We have examined tens of millions of individual non-transformed B cells using a microscopic multiplexed assay and discovered picomolar affinity native mAbs with exquisite specificity and potency. Clinical lead antibodies for three infectious disease targets including RSV, CMV and Influenza will be highlighted in this talk.

**Bill Usinger, Ph.D.**, Vice President Research & Development, Trellis Bioscience, Inc.

3:30 **Sensitizing Insulin Receptor Antibody Potentiates Insulin Activity and Restores Glycemic Control in Murine Models of Diabetes**

This abstract was not available at the time of printing the brochure. For up to date program information, please visit [www.IBCLifeSciences.com/Antibodyeng](http://www.IBCLifeSciences.com/Antibodyeng)

**John Corbin, Ph.D.**, Associate Director, Preclinical Research, XOMA (US) LLC

4:00 **Networking Refreshment Break, Exhibit and Poster Viewing**

4:45 **Preclinical and Clinical Developments of Targeted Therapeutics in Malignant, Autoimmune, and Infectious Diseases**

The Dock-and-Lock (DNL) platform enables the design and generation of targetable therapeutics that are multivalent, multispecific and multifunctional. Since its invention in 2005, the versatility of the DNL approach has been validated in a variety of novel agents that include trivalent and hexavalent bispecific antibodies, PEGylated dimeric interferon- $\alpha 2b$ , immunocytokines, and immunoRNases, all of which display the properties desirable for pharmaceutical applications. The advances of select DNL products currently in development will be presented.

**Ken Chang, Ph.D.**, Vice President, Research & Development, Immunomedics, Inc.

5:15 **Characterizing the Activity and Safety of Probody™ Therapeutics in Animal Models of Disease**

CytomX Therapeutics has devised a novel approach to address the toxicity of antibodies that recognize target antigens in both diseased and normal tissues. The antigen-combining site of a conventional antibody is blocked with a masking peptide, which can be released by the action of endogenous proteases that are preferentially localized or overexpressed in diseased tissue. By virtue of their protease-regulated antigen binding, these molecules have the potential for reduced mechanism-based toxicities, improved pharmacokinetics and increased therapeutic indices.

**Henry Lowman, Ph.D.**, Vice President, Research, CytomX Therapeutics, Inc.

5:45 **Discovery by SLAM Technology and Characterization of XMAb55, a Fully Human mAb as a Potential Cancer Therapeutic**

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**Josh Xiao, Ph.D.**, Principal Scientist, Oncology Research, Amgen, Inc.

6:15 **Networking Cocktail Reception, Exhibit and Poster Viewing**

7:30 Registration, Networking Coffee

8:00 Announcements

## Session III: Next Generation Anti-Angiogenics

### 8:05 Chairperson's Opening Remarks

**Philip E. Thorpe, Ph.D.**, Professor of Pharmacology and The Serena S. Simmons Distinguished Chair, University of Texas Southwestern

### 8:15 Ramucirumab: The Next Avastin?

Attempts to inhibit angiogenesis have been a hallmark in the age of biologic anticancer therapies. Vascular endothelial growth factor receptor-2 (VEGFR-2) is the premier receptor responsible for many of the cancer-driven vascular endothelial growth factor induced modifications of blood vessel structure and function. Unlike all clinically approved angiogenesis inhibitors, ramucirumab specifically and potently inhibits VEGFR-2. Early clinical trials have shown safety across a range of ramucirumab doses with impressive anticancer activity. The clinical development of ramucirumab and ongoing trial data will be presented.

**Jennifer Spratlin, Ph.D.**, Assistant Professor, Medical Oncology, Cross Cancer Institute, Canada

### 8:45 Clinical Development of an Antibody to Sema4D, a Multifunctional Target in Cancer and Multiple Sclerosis

Semaphorin 4D (SEMA4D/CD100) regulates cell migration in multiple tissues including activation of endothelial cells for neo-vascularization and of epithelial cells to promote tumor invasion and metastasis. In neuronal tissues, SEMA4D negatively regulates the survival and migration of neuronal precursors and of pre-myelinating oligodendrocytes while promoting activation of neuroinflammatory microglia. Vaccinex initiated a Phase I clinical trial in patients with advanced solid tumors in February 2011 and plans to submit an IND for a second trial in MS patients in early 2012.

**Maurice Zauderer, Ph.D.**, President & Chief Executive Officer, Vaccinex, Inc

### 9:15 Targeting the Extracellular Matrix of Angiogenic Vasculature

Antibodies can be used to deliver bioactive molecules to the tumor environment, thus sparing normal tissues. The targeting of tumour neo-vasculature is particularly attractive, because of the dependence of cancer on new blood vessels and because of the accessibility of these structures from the bloodstream. In this lecture, I will present recent clinical results, obtained in collaboration with the Philogen group, using derivatives of three human monoclonal antibodies, specific to components of the sub-endothelial extracellular matrix of angiogenic vasculature in cancer and in arthritis.

**Dario Neri, Ph.D.**, Professor, Chemistry and Applied Biosciences, ETH Zurich, Switzerland

### 9:45 Networking Refreshment Break, Exhibit and Poster Viewing

### 10:30 Targeting Tumor Vasculature and Reactivating Tumor Immunity with Bavituximab: Preclinical and Clinical Studies

Bavituximab is a therapeutic monoclonal antibody that is in randomized clinical trials in lung cancer and pancreatic cancer patients. It targets the immunosuppressive lipid, phosphatidylserine, which becomes exposed on tumor blood vessels and tumor cells. Bavituximab causes MDSCs to differentiate into tumoricidal M1 macrophages that destroy the tumor vasculature and tumor cells by ADCC. It also causes immature dendritic cells in tumors to mature and present tumor antigens, resulting in the generation of tumor-specific cytotoxic T-cells.

**Philip E. Thorpe, Ph.D.**, Professor of Pharmacology and The Serena S. Simmons Distinguished Chair, University of Texas Southwestern

### 11:00 Identification of Pathways Involved in Resistance to Antibody Mediated Inhibition of VEGF in Murine Models of Cancer

Neutralizing antibodies to VEGF-A augment the activity of standard therapy in multiple tumor types. However, the variability in the response of different tumors to anti-VEGF therapy suggests that the mechanism of anti-VEGF action is complex and that resistance commonly develops. We have evaluated the response of 12 NSCLC xenografts to the anti-VEGF mAbs, bevacizumab and r84 (AT001), and have identified responder and non-responder cell lines. The biology has been interrogated through mRNA and protein profiling techniques linking particular genes/proteins to the resistance phenotype.

**Rolf A. Brekken, Ph.D.**, Associate Professor of Surgery & Pharmacology, University of Texas Southwestern Medical Center

### 11:30 Antibody-Endostatin Fusion Proteins for Treatment of Solid Tumors

We have developed anti-HER2 antibody-endostatin fusion proteins with greater anti-tumor activity due to longer half-life, endostatin presentation as a dimer and improved tumor targeting compared to anti-HER2 antibody or endostatin alone or in combination. We have generated two anti-HER2 human endostatin fusion proteins by fusing wild type or mutant human forms of endostatin with enhanced anti-angiogenic properties fused to a humanized anti-HER2 IgG3 antibody. We plan to initiate GMP production of a candidate fusion protein to permit toxicology testing and Phase I clinical trials in man.

**Joseph D. Rosenblatt, M.D.**, William Harrington Professor of Medicine, Microbiology and Immunology, University of Miami School of Medicine

### 12:00 Scientific Briefing

#### Presentation Title to be Announced

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Speaker TBA



### 12:30 Networking Luncheon, Last Chance for Exhibit and Poster Viewing

2:00 Announcements

## Session IV: Updates of Clinical Stage Antibody Therapeutics

### 2:05 Chairperson's Opening Remarks

**Mark R. Alfenito, Ph.D.**, President & CEO, EnGen Bio, Inc.

### 2:15 BiTE Antibody Blinatumomab for the Treatment of Acute Lymphocytic Leukemia

Blinatumomab is a CD19/CD3-bispecific BiTE antibody construct capable of engaging patients' T cells for lysis of CD19-expressing target cells. Exceptional response rates and encouraging response durations have been observed in patients with relapsed/refractory ALL and minimal residual ALL following single-agent treatment with the BiTE antibody. An update on the development of blinatumomab will be given.

**Patrick A. Baeuerle, Ph.D.**, Senior Vice President and Chief Scientific Officer, Micromet, Inc.

### 2:45 Encapsulated Cell Technology: A New Therapy for Biologics Delivery

Encapsulated Cell Technology (ECT) implants are miniature bioreactors that continuously secrete biologics into the patient. ECT implants can produce a variety of biologics such as Mab, Fab, ScFv, Fc-proteins and cytokines. When implanted into the eye, ECT biologics are secreted at therapeutic levels for up to two years. Phase 2 data will be presented summarizing clinical outcomes involving ECT treatment of patients with dry AMD and Retinitis Pigmentosa.

**Vincent Ling, Ph.D.**, Head of Biological Sciences, Neurotech

### 3:15 Olokizumab (CDP6038) – A Highly Potent Anti-IL-6 Inhibitor with a Novel Mechanism of Action

Olokizumab is an anti-IL-6 monoclonal antibody currently in Phase 2b clinical development in inflammatory arthritis. Olokizumab binds to IL-6 with high affinity and it is the first in a new class of IL-6 inhibitors that selectively blocks the final assembly of the IL-6 signaling complex. This talk will focus on the mode of action of olokizumab, with emphasis on the results of studies performed in whole blood assays in vitro, in pre-clinical models in vivo, and from Phase 1 clinical studies.

**Roger Palframan Ph.D.**, Global Project Leader, UCB, United Kingdom

### 3:45 Networking Refreshment Break

### 4:15 MLN0264, an Investigational Antibody Drug Conjugate (ADC) for the Treatment of Colorectal Cancer

MLN0264 is an investigational ADC targeting guanylyl cyclase C (GCC) a protein expressed on normal and malignant intestinal epithelial cells. The drug consists of a selective fully human mAb to GCC conjugated to the cytotoxic agent MMAE via a cleavable linker. MLN0264 targets malignant colon tumor cells but not normal GCC expressing tissues. MLN0264 is a promising new drug for the treatment of mCRC and other GCC expressing malignancies.

**Petter Veiby, Ph.D.**, Director, Molecular and Cellular Oncology, Millennium Pharmaceuticals

### 4:45 Exploiting the Mechanistic Advantages of Antibody Mixtures to Develop Novel Cancer Drugs

Mixtures of antibodies with non-overlapping epitopes offer a number of mechanistic advantages over mAbs including improved receptor downregulation, more efficient blocking of ligand-receptor interaction and increased activation of cdc. In addition, mAb mixtures have the ability to address multiple cell surface receptors and/or ligands. Historical evidence as well as results from Symphogen pre-clinical and clinical stage antibody mixtures will be highlighted in this talk to demonstrate mechanistic advantages of mAb mixtures. Discussed targets will include EGFR, HER2 and CD5.

**Mikkel Pedersen, Ph.D.**, Principal Scientist and Project Manager, Antibody Pharmacology, Symphogen, Denmark

### 5:15 Clinical Development of SGN-35

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**Naomi Hunder, M.D.**, Medical Director, Seattle Genetics

### 5:45 Close of Session

“One of those 'not to be missed' conferences on our annual calendar.”

**Philip Thorpe, Ph.D.**, Professor, University of Texas Southwestern Medical Center

## The 2011 Antibody Therapeutics Scientific Advisory Board

**Rathin C. Das, Ph.D.**, Chief Executive Officer, Synergys Biotherapeutics, Inc.

**Mark R. Alfenito, Ph.D.**, President & CEO, EnGen Bio, Inc.

**Benjamin P. Chen, Ph.D.**, International Director, Burrill & Company

**Philip E. Thorpe, Ph.D.**, Professor of Pharmacology and The Serena S. Simmons Distinguished Chair, University of Texas Southwestern

**Trudi Veldman, Ph.D.**, Director, Biologics Generation, Abbott Bioresearch Center

7:30 *Networking Coffee*

8:00 *Announcements*

## Session V: Drug Conjugates and Bispecific Antibodies

### 8:05 Chairperson's Opening Remarks

**Susan Lacy, Ph.D.**, Associate Director, Biologics, Abbott Bioresearch Center

### 8:15 Translational Studies of PSMA ADC, a Fully Human Anti-PSMA Monoclonal Antibody Linked to vcMMAE

Prostate-specific membrane antigen (PSMA) exhibits a unique pattern of expression that is dependent upon the cancer type. In prostate cancer, PSMA is expressed on neoplastic cells but not on the neovasculature, while in several non-prostatic cancers, PSMA is expressed on the neovasculature but not on neoplastic cells. Here we describe translational studies of PSMA ADC, including preclinical efficacy studies and preliminary tolerability and efficacy findings from an ongoing phase 1 dose-escalation study in advanced prostate cancer. **William C. Olson, Ph.D.**, Senior Vice President, Research & Development, Progenics Pharmaceuticals, Inc.

### 8:45 Clinical Development of CDX-011, an Antibody-Drug Conjugate Targeting Glycoprotein NMB (GPNMB) for the Treatment of Metastatic Breast Cancer and Advanced Melanoma

CDX-011 is an ADC comprised of a human IgG2 antibody conjugated to MMAE that targets a novel cell surface protein GPNMB. GPNMB is expressed on an assortment of malignancies including breast cancer, glioma, melanoma and hematologic malignancies. It is associated with invasion and immune evasion. Initial clinical studies have defined a tolerable phase 2 dose and shown significant disease control with tumor shrinkage in a majority of patients with heavily pretreated breast cancer and melanoma. Objective responses have been seen in GPNMB expressing disease including triple negative BRCA. A randomized phase 2 study in breast cancer is ongoing. **Tom Davis, M.D.**, Chief Medical Officer, Senior Vice President of Clinical Development, Celldex Therapeutics

### 9:15 Preclinical Updates for BAY 94-9343, a Mesothelin-Targeting ADC, and BAY 79-4620, a CA9-Targeted ADC

This presentation summarizes comprehensive preclinical data sets on two novel antibody drug conjugates both consisting of fully human monoclonal antibodies coupled to microtubule-targeting toxophores. BAY 79-4620, currently in Phase I clinical development, is directed against carbonic anhydrase IX (CA9), a hypoxia-inducible protein whose expression correlates with poor prognosis in multiple cancers. BAY 94-9343 is targeting Mesothelin, which is found overexpressed in all mesotheliomas as well as in ovarian and pancreatic cancers.

**Bertolt Kreft, Ph.D.**, Director, Targeted Biological Therapeutics, Oncology Research, Bayer Schering Pharma AG, Germany

### 9:45 Networking Refreshment Break

### 10:15 Rethinking Therapy of HER2-positive Cancers: MM-111 and MM-302

We have designed two novel experimental therapeutics for HER2-positive cancers to be effective also in patients refractory to current therapies. One is a bispecific antibody inhibitor of ErbB3 (MM-111); the other an ErbB2-directed nanotherapeutic (MM-302) that delivers doxorubicin directly into tumor cells. We will discuss our experience with these molecules from discovery through currently ongoing Phase 1/2 clinical trials.

**Ulrik Nielsen, Ph.D.**, Chief Scientific Officer, Merrimack Pharmaceuticals

### 10:45 A Bispecific Antibody Effectively Inhibits Tumor Growth and Metastasis by Simultaneous Blocking Vascular Endothelial Growth Factor A and Osteopontin

We engineered a bispecific antibody (VEGF/OPN-BsAb) using the humanized anti-VEGF antibody bevacizumab and the humanized anti-OPN antibody hu1A12. Compared with either hu1A12 or bevacizumab alone, VEGF/OPN-BsAb was significantly more effective in inhibiting tumor angiogenesis in a highly metastatic human hepatocellular carcinoma nude mouse model. Further study demonstrated that it could effectively suppress primary tumor growth and metastasis to lungs, suggesting that it might be a promising therapeutic agent for treatment of metastatic cancer.

**Yajun Guo M.D., Ph.D.**, Professor and Director, SMMU Cancer Institute, China

### 11:15 Modulation of the Interleukin-1 Axis for arthritis using DVD-Ig™ Technology

IL-1 $\alpha$  and IL-1 $\beta$  play a critical role in the pathogenesis of rheumatoid arthritis (RA) and osteoarthritis (OA). Neutralization of both IL-1 $\alpha$  and IL-1 $\beta$  either with a combination of IL-1 $\alpha$  and IL-1 $\beta$  mAbs or murine IL-1 $\alpha/\beta$  DVD-Ig™ is required for optimal efficacy in rodent models of arthritis. Based on preclinical studies, human IL-1 $\alpha/\beta$  DVD-Ig™ with drug-like properties were constructed and characterized in vitro and in vivo.

**Susan Lacy, Ph.D.**, Associate Director, Biologics, Abbott Bioresearch Center

### 11:45 Close of Antibody Therapeutics Meeting; Delegates are Invited to Attend the Afternoon Session of Antibody Engineering

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## Two-Day Professional Development Courses • December 4-5, 2011

Co-Located with the Antibody Engineering/Antibody Therapeutics Conferences. (See the registration form for a package that includes a two-day course plus three days of conference presentations)

## Introduction to Antibody Engineering

### Description

Today's wealth of knowledge of protein structures will be reviewed along with the genetics of diversity generation of antibodies, to give insights into the best strategies for improving protein function. There is particular emphasis on the choice of a functional assay to monitor effectively the changes in a desired property, and the use of functional enrichment steps where a library approach is employed. Not only is amino acid sequence amenable to engineering, but glycan structures and other modifications may also be engineered. The course will focus on the engineering and enhancement of antibodies and antibody-like scaffolds. Examples will include work on antibody fragment affinity improvement by 100-fold to low pM affinity. A background in biochemistry and molecular biology is useful, as the course is designed to progress rapidly from simple to advanced concepts.

### Instructor

**David Bramhill, Ph.D.**, Director, Research Corporation Technologies

### Course Agenda

- Functions amenable to engineering: affinity, specificity, stability, solubility, immunogenicity
- The measure of success: functional assays
- Engineering by design
- Engineering by random mutation
- Designed libraries
- Display technologies
- Improving manufacturing by protein engineering methods
- Glycosylation engineering – function and homogeneity
- Other protein modifications
- Immunogenicity engineering
- Bispecific antibodies
- Antibody-drug conjugates (ADCs)

## Protein Characterization for Biotechnology Product Development

### Description

This course covers the fundamentals of protein structural analysis using modern biochemical and biophysical technologies. We will review the post-translational modifications commonly observed on recombinant proteins produced from manufacturing cell lines and discuss the potential impact of the structural heterogeneities on biological activity. In addition, characterization of higher order structures, aggregates and particulates, binding and cell-based potency assays will be discussed. The impact of bioprocess parameters, including cell line selection, on product quality profile will be reviewed. Examples on characterization of different recombinant proteins including monoclonal antibodies using key orthogonal techniques will be highlighted. The objective is to provide participants with key technical information along with perspectives to enable them to apply the technologies to their own projects and evolve their own analytical strategies to support the various stages of product development.

### Instructor

**Christine P. Chan, Ph.D.**, Senior Manager, Technology Development, Genzyme Corporation

### Course Agenda

- Introduction to protein structure and post-translational modifications
- Protein Chemistry Techniques: capillary electrophoresis and HPLC, enzymatic methods and peptide mapping, mass spectrometry, amino acid analysis, top-down and bottom-up protein sequence analysis, sample treatment, preparation & work flow
- Biophysical Characterization: spectral methods including vibrational spectroscopy, fluorescence and circular dichroism. Light scattering, calorimetry, analytical ultracentrifugation, atomic force microscopy, and field flow fractionation techniques. Aggregation, subvisible and visible particles analysis.
- Quality control of biotechnology products: guidance documents
- Characterization of recombinant protein products: glycosylation analysis; monoclonal antibody structure and subclasses, additional recombinant proteins, product heterogeneity analysis
- Bioprocess impact on product quality: cell line selection, upstream process variables, downstream process impact, formulation/fill/finish and storage
- Quality by Design and process development, process transfer, comparability considerations
- Selecting characterization methods to support early vs. late stage product development

# Antibody Engineering Antibody Therapeutics

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## Feedback from the 2010 Attendees

- “A wonderful conference full of high-level presentations and big names in the field” – University of Chicago
- “One of those 'not to be missed' conferences” – University of Texas SW
- “Always a great conference to get a general update on progress in the antibody field” – Xencor, Inc.
- “A nice balance between industry and academia” – Adimab
- “The most informative antibody conference” – INSERM, France
- “There was always something new every day” – Agensys, Inc.
- “The ideal opportunity to share and discuss the latest developments in antibody technology” – Covagen AG, Switzerland

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# Antibody Engineering



# Antibody Therapeutics

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- Structure-Based Engineering
- Synthetic Antibodies
- GPCRs Interacting with Antibody Fragments
- Allosteric Regulation of EGFR Family Members
- Model-Guided Generation of Binding Sites
- Novel Selection Strategies
- Combining Antibody Engineering and Gene Delivery
- Rational Vaccine Design
- Viral Retargeting with Engineered Binding Molecules
- Strategies for IL-6 Signaling
- New Functional Genomics Techniques

## Clinical & Preclinical Updates of Therapeutic Antibodies in Development

- Maytansinoid Antibody Conjugates
- Human Monoclonal Antibody Against BlyS
- Novel CD20 Antibodies with Enhanced Mechanisms of Action
- Anti-KDR Neutralizing Fully Human Antibody
- VEGFR-2 Inhibitor
- Antibody-Endostatin Fusion Proteins for Treatment of Solid Tumors
- Lysis of CD19-Expressing Target Cells
- New Class of IL-6 Inhibitors
- Antibody-Drug Conjugate Targeting Glycoprotein NMB (GPNMB)
- Novel Experimental Bispecific Therapeutics for HER2-Positive Cancers

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