Cambridge Healthtech Institute’s Inaugural

PK/PD of Novel Constructs
Bispecific Antibodies, Antibody Fragments, and ADCs

October 10-12, 2012
DoubleTree by Hilton Hotel
Bethesda, Maryland

Keynote Speakers:

Louis M. Weiner, M.D., Director, Lombardi Comprehensive Cancer Center; Professor and Francis L. and Charlotte G. Gragnani Chair, Department of Oncology, Georgetown University Medical Center

Joseph P. Balthasar, Ph.D., Professor, Pharmaceutical Sciences, School of Pharmacy and Pharmaceutical Sciences, SUNY Buffalo

Featured Presenter:

Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen

Register by July 20 and Save up to $350

healthtech.com/Novel-Constructs
Main Conference

WEDNESDAY, OCTOBER 10

7:30am Registration and Morning Coffee

UNIQUE CONSIDERATIONS FOR NOVEL CONSTRUCTS

8:30 am Chairperson’s Opening Remarks
Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen

8:35 KEYNOTE PRESENTATION
Antibody-Targeted Cancer Immunotherapy
Louis M. Weiner, M.D., Director, Oncology, Lombardi Comprehensive Cancer Center, Georgetown University
Antibodies have emerged as versatile and potent cancer therapy agents, exploiting properties such as signaling perturbation, delivery of toxic payloads and activation of anti-tumor immune responses. Work related to manipulation of immune responses will be discussed with a perspective on aligning antibody structural properties and effects on tumor cell signaling with clinically relevant mechanisms of action.

9:35 FEATURED PRESENTATION
Impact of Immunogenicity on PK Profiles of Novel Large Molecule Constructs
Vibha Jawa, Ph.D., Principal Scientist, Clinical Immunology, Amgen
An assessment of immunogenicity in single dose and multiple dose studies on clearance of novel drug constructs will be discussed and compared to fully human monoclonal antibodies.

10:05 Regulatory and Quality Considerations When Developing Novel Antibody-Related Constructs
Audrey Jia, M.D., Ph.D., M.S., Monoclonal Antibody Quality Reviewer, Division of Monoclonal Antibodies in the Office of Biotechnology Products, Center for Drug Evaluation and Research, U.S. Food and Drug Administration (FDA)
This talk discusses the unique features of novel antibody-related constructs, their regulatory challenges and quality considerations from a quality reviewer’s perspective.

10:35 Coffee Break in the Exhibit Hall with Poster Viewing (Sponsorship Opportunity Available)

SYSTEMS MODELING OF PK/PD

11:10 Chairperson’s Remarks
Birgit Schoeberl, Ph.D., Vice President, Discovery, Merrimack Pharmaceuticals

11:15 KEYNOTE PRESENTATION
Applications of Pharmacokinetic/Pharmacodynamic Modeling to Expedite Development of Novel Constructs
Joseph P. Balthasar, Ph.D., Professor, Pharmaceutical Sciences, School of Pharmacy and Pharmaceutical Sciences, SUNY Buffalo

12:15 pm Sponsored Presentation (Opportunity Available)

12:45 Luncheon Presentation (Sponsorship Opportunity Available) or Lunch on Your Own

SYSTEMS MODELING OF PK/PD CONTINUED

2:20 Bench to Bedside Translation of Antibody Drug Conjugates Using a Multiscale Mechanistic PK/PD Model:

A Case Study with SGN-35
Dhavalkumar K. Shah, Ph.D., Senior Scientist, Modeling & Simulation, Pfizer
The presentation will layout a 7 step procedure to build and validate a novel multiscale mechanism based PK/PD model for ADCs, using SGN-35 as an example. The model is designed to integrate pre-clinical biomasures and PK/PD data for pre-clinical to clinical translation of ADC efficacy. The presentation will highlight that it is essential to understand and characterize the disposition of ADC and payload, at cellular and physiological level, to better predict the clinical outcome of ADCs.

2:50 Talk Title to be Announced
Birgit Schoeberl, Ph.D., Vice President, Discovery, Merrimack Pharmaceuticals

3:20 Refreshment Break in Exhibit Hall with Poster Viewing (Sponsorship Opportunity Available)

4:00 A Generic Physiologically-Based Pharmacokinetic Model for Biologicals
Christoph Niederalt, Ph.D., Senior Scientist, Systems Pharmacology, Bayer Technology Services GmbH
A generic physiologically-based pharmacokinetic (PBPK) model for biologicals that can describe relevant distribution and clearance processes in different animal species and humans will be presented. The model will be illustrated by examples wherein non-standard processes such as target-mediated deposition and clearance are accounted for and discussed.

4:30 Combining Systems Biology and Pharmacokinetic Models to Translate in vitro Results into in vivo Efficacy
Ben-Filippo Krippendorff, Ph.D., Department of Oncology and Cancer Research UK, Cambridge Research Institute
In this talk we present a new modeling approach to combine in vitro derived knowledge about target dynamics into pharmacokinetic models. For the example of inhibiting growth factor signaling in cancer we advocate the potential of such systems pharmacology approaches to predict target dynamics in vivo from systems biology models derived in vitro.

5:00 – 6:00 Breakout Sessions

6:00-7:00 Welcome Reception in the Exhibit Hall with Poster Viewing (Sponsorship Opportunity Available)

7:00 End of Day One

THURSDAY, OCTOBER 11

7:30 – 8:15am Breakfast Presentation (Sponsorship Opportunity Available)

IN VIVO DYNAMICS: Bispecific Antibodies, Dual Targeting Molecules and Pan-Specific Monoclonals

8:30 Chairperson’s Remarks

8:35 Targeted Potentiation of Endosomal Release of Macromolecular Payloads
K. Dane Wittrup, Ph.D., J.R. Mares Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology
Release of endocytosed payloads from endolysosomal
compartments is a typical rate limiting step for gene therapy, siRNA delivery, immunotoxins, nanoparticulate drugs, and antibody drug conjugates, striking a difficult balance to avoid general plasma membrane destabilization (toxicity), while maintaining efficient permeabilization within the endosomes of targeted cells (efficacy). Natural selection has crafted solutions to this problem used by pathogens such as viruses and intracellular bacteria. We describe here targeted cytolsins that greatly potentiate siRNA and immunotoxins.

9:05 Efficacy, Safety and PK/PD of Sym004 - From Bench to Bedside
Niels Jørgen Ø. Skartved, Ph.D., Principal Scientist, Symphogen A/S
Sym004 is a novel therapeutic antibody combination product consisting of two monoclonal antibodies targeting non-overlapping epitopes on the Epidermal Growth Factor Receptor (EGFR). In pre-clinical in vitro and in vivo tumor models, the antibody mixture displayed a potent and efficient anti-tumor activity, with a mode of action different from that of monoclonal antibody therapeutics. The unique mode of action translated into a distinct preclinical and clinical PK/PD relationship and an acceptable safety profile.

9:35 Pharmacokinetics of Dual Variable Domain Immunoglobulin (DVD-Ig™) Molecules
Edit Tarcsa, Associate Director, DMPK-BA Abbott Bioresarch Cener
Bispecific biologics are a novel class of therapeutics that are very promising but at the same time present new challenges to identifying the best candidates with good PK and drug-like properties. DVD-Ig™ molecules are versatile bispecifics that preserve many of the properties of their parental antibodies. Pre-clinical screening methods, including extensive physicochemical and PK characterization, were performed to select molecules. Discovery and development strategies for mAbs vs. DVD-Ig molecules will be compared and contrasted that lead to the identification of DVD-Ig clinical candidates.

10:05 Sponsored Presentation (Opportunity Available)

10:35 Coffee Break in the Exhibit Hall with Poster Viewing (Sponsorship Opportunity Available)

11:10 In vitro and in vivo stability of bispecific κλ-bodies
Krzysztof Masternak, Ph.D., Head of Biology, Novimmune SA
κλ-bodies are bispecific IgG consisting of a common heavy chain paired with two different light chains, one kappa and one lambda. The physicochemical and PK characterization of these molecules will be discussed.

11:40 Generation of Bispecific Antibodies with the Duobody Platform
Paul W.H.I. Parren, Ph.D., Senior Vice President & Scientific Director, Genmab
With the Duobody™ platform, which is based on the principle of controlled Fab-arm exchange, we have developed a novel, highly efficient, method to generate bispecific antibodies. Bispecific antibodies developed with this platform retain the biochemical structure of regular human IgGs, have Fc-mediated effector functions and regular IgG1 pharmacokinetics. Furthermore, the platform is compatible with standard unit operations for large scale IgG1 manufacturing. The technology, its scientific background and various proof-of-concept studies will be discussed.

12:10 pm Luncheon Presentation (Sponsorship Opportunity Available) or Lunch on Your Own

IN VIVO PHARMACOLOGY OF ANTIBODY-DRUG CONJUGATES

1:30 Chairperson’s Remarks

1:35 Application of PKPD Principles in Optimizing Antibody Drug Conjugates
Kedan Lin, Ph.D., Group Leader, Department of Pharmacokinetic and Pharmacodynamic Sciences, Genentech
Despite recent success of antibody drug conjugates in various stage of clinical development, there are significant challenges in optimizing and developing these complex molecules. This talk will discuss the emerging effort in integrating ADME, PK, efficacy and safety to establish meaningful PK/PD relationships and to support ADC optimization.

2:05 Extracellular Drug Conjugates – Targeting Small Molecule Drugs Right Where You Want Them
James R. Prudent, Ph.D., President and CEO, Centrose
Integral membrane protein activity is often dictated by accompanying peripheral proteins. These interactions as well as the composition, stoichiometry and environment of the complexes that form, characteristically regulate a wide range of cellular activities. In diseased cells, these multi-variant factors change and can lead to drastic changes in protein function. This talk will highlight a novel type of drug targeting system which uses proximity effects and cooperative specificity to direct small molecule drugs not only to a specified diseased cell, but specifically to the drugs active site.

2:35 Sponsored Presentation (Opportunity Available)

3:05 Refreshment Break in the Exhibit Hall with Poster Viewing (Sponsorship Opportunity Available)

3:30 Pre-Clinical Development of IMGN853, an Antibody-Maytansinoid Conjugate Targeting FOLR1 for the Treatment of Solid Tumors
Jan Pinkas, Ph.D., Director, Pharmacology, ImmunoGen, Inc.

4:00 Panel Discussion with Speakers

4:30 Breakout Sessions

5:30 End of Day Two

FRIDAY, OCTOBER 12

PHARMACOKINETICS OF ANTIBODY FRAGMENTS

8:30 am Chairperson’s Remarks
Dimiter S. Dimitrov, Head, Protein Interaction Group & Senior Investigator, Membrane Structure & Function, NIH NCI

8:35 Strategies to Extend the Half-Life of Small Recombinant Antibody Therapeutics
Roland E. Kontermann, Ph.D., Professor, Biomedical Engineering, Institute of Cell Biology & Immunology, University of Stuttgart
With a growing number of small antibody therapeutics being developed, there is an increasing need to extend their half-life to improve efficacy and safety profiles. This talk will review recent advances in ADC optimization.
developed, including bispecific and bifunctional antibodies, half-life extension strategies have become increasingly important to improve their pharmacokinetic and pharmacodynamic properties. An overview of the various strategies to extend the half-life of recombinant antibodies as well as results from a comparative study including novel strategies utilizing binding to serum albumin and serum immunoglobulins are presented and discussed.

9:05 Pharmacokinetics of Engineered Antibody Domains
Dimiter S. Dimitrov, Head, Protein Interaction Group & Senior Investigator, Membrane Structure & Function, NIH NCI

Antibody fragments and antibody-like scaffolds have improved penetration into tissues due to their small size but exhibit relatively short serum half-life. We measured the pharmacokinetics of wild-type monomeric CH2D, a short stabilized CH2D variant and a dimeric CH2D in normal B6 mice, human FcRn transgenic mice and cynomolgus macaques. The data demonstrate that engineered CH2D-based variants have relatively long serum half-lives (on the order of 10 hours), making them a unique scaffold suitable for development of targeted therapeutics.

9:35 The Unique PK/PD Characteristics of Antibody Fragments
Lu Xu, Ph.D., Pharmacokinetics and Pharmacometrics, OncoMed Pharmaceutical

Antibody fragments such as Fab (fragment antigen-binding) and (Fab’)2 (Fab with hinge region, both arms) have been developed into therapeutic agents, taking advantage of their unique pharmacokinetic (PK) and pharmacodynamic (PD) characteristics. The mechanism and implications of the unique PK and PD characteristics of antibody fragments are reviewed in this presentation, with a case study of the preclinical and clinical development of ranibizumab.

10:05 Sponsored Presentation (Opportunity Available)

10:35 Coffee Break in the Exhibit Hall with Poster Viewing (Sponsorship Opportunity Available)

TOOLS FOR PHARMACOKINETIC PROFILING

11:10 Selected Poster Presentations
12:10 End of Conference
Sponsorship, Exhibit and Lead Generation Opportunities

CHI offers comprehensive sponsorship packages which include presentation opportunities, exhibit space and branding, as well as the use of the pre- and post-show delegate lists. Customizable sponsorship packages allow you to achieve your objectives before, during, and long after the event. Signing on early will allow you to maximize exposure to hard-to-reach decision makers!

**Agenda Presentations**
Showcase your solutions to a guaranteed, highly-targeted audience. Package includes a 15 or 30-minute podium presentation within the scientific agenda, exhibit space, on-site branding and access to cooperative marketing efforts by CHI.

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Opportunity includes a 30-minute podium presentation. Boxed lunches are delivered into the main session room, which guarantees audience attendance and participation. A limited number of presentations are available for sponsorship and they will sell out quickly. Sign on early to secure your talk!

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- Your campaign will receive targeted promotion to Cambridge Healthtech Institute’s unparalleled database of over 800,000 individuals, representing all sectors of the life sciences – lists can be segmented based on geography, research area, title and industry.
- All custom lead generation programs are promoted through our experienced marketing team that will develop and drive targeted campaigns to drive awareness and leads to your lead generation program.
- For our webinar programs, we offer assistance in procuring speakers for your web symposia through our extensive roster of industry recognized speakers across multiple disciplines within life sciences, as well as provide an experienced moderator and dedicated operations team to coordinate all efforts.
- If choosing a whitepaper program, we can offer editorial experience and provide an industry recognized author to write your whitepaper.

To customize your participation at this event, please contact:

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Pricing and Registration Information

**POST-CONFERENCE SHORT COURSE***

*Separate registration is required

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Poster abstracts are due by September 12, 2012. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact jring@healthtech.com. *CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

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Additional discounts are available for multiple attendees from the same organization. For more information on group rates contact David Cunningham at +1-781-972-5472

If you are unable to attend but would like to purchase the PK/PD of Novel Constructs CD for $350 (plus shipping), please visit healthtech.com/novel-constructs Massachusetts delivery will include sales tax.

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