

MAY 20 –MAY 21, 2010: BUFFALO, NEW YORK

# 2-DAY WORKSHOP ON MONOCLONAL ANTIBODY PHARMACOKINETICS & PHARMACODYNAMICS

## Concepts and Applications

### COURSE OUTLINE

This workshop has been designed to provide a detailed discussion of issues relevant to the pharmacokinetic / pharmacodynamic (PK/PD) modeling of antibody drugs. Lectures will address primary determinants of antibody pharmacokinetics (PK) and pharmacodynamics (PD), the design and implementation of pre-clinical investigations of antibody PK/PD, and state-of-the-art mathematical models to characterize and predict antibody PK and PD. Special emphasis is placed on discussion of the role of FcRn on the absorption, distribution, and elimination of antibodies, on the mathematical modeling of target-mediated antibody disposition, and on physiologically-based modeling of antibody pharmacokinetics. The workshop content is provided as a combination of formal lectures and informal review sessions.

Subjects that will be presented include:

**Determinants of antibody pharmacokinetics and pharmacodynamics:** mechanisms of antibody elimination, the role of convection in the kinetics of antibody distribution, the role of FcRn in antibody absorption, distribution, and elimination

**Common analytical assays for quantification of antibody in biological samples & implications for PK/PD investigations**  
**Immunogenicity and Antibody PK/PD**

**Evaluation of biosimilarity of antibody drugs:** Application of PK/PD for biosimilarity studies – opportunities and limitations

**Interspecies Scaling of Antibody PK**

**Target-Mediated Antibody Disposition:** modeling, implications for interspecies scaling, implications for First-in-Human studies

**Modeling of bimolecular antibody-ligand interaction**

**Physiologically-based pharmacokinetic modeling:** Incorporation of FcRn-mediated antibody transport in PBPK models, incorporation of target-mediated disposition, use of PBPK and preclinical data to predict antibody disposition in humans

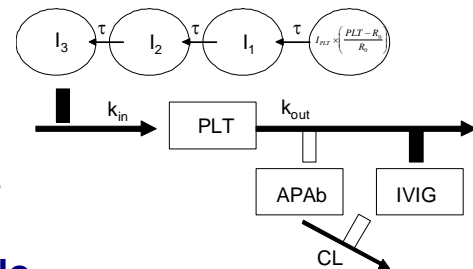
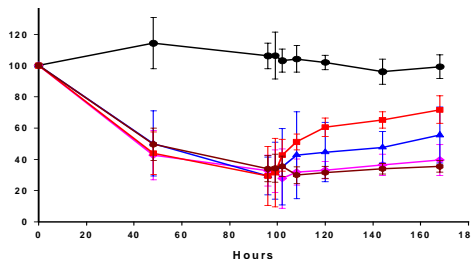
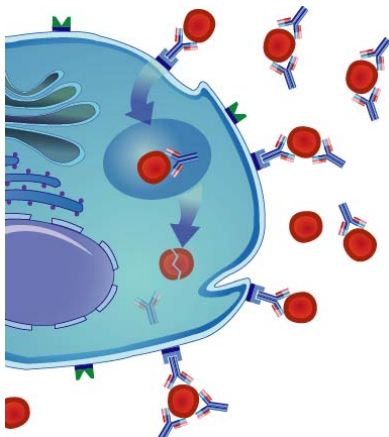
### COURSE DIRECTION

#### Joseph P. Balthasar, PhD

Dr. Balthasar is Professor of Pharmaceutical Sciences at the University at Buffalo, State University of New York and Director of the Center for Protein Therapeutics. His PK/PD modeling interests and capabilities include the development and preclinical evaluation of anti-toxin immunotherapies, the development and preclinical evaluation of anti-cancer immunotherapies (including immunoconjugate immunotherapies), and the development and preclinical evaluation of novel immunotherapies for humoral autoimmune conditions (immune thrombocytopenia, myasthenia gravis). He serves as a consultant to the NIH and pharmaceutical industry.



Joseph P. Balthasar, PhD



# AGENDA

## Day 1

- 08:45-09:00 **Introductions**
- 09:00-10:30 **Introduction to Antibody PK and PD**
- Introduction to antibodies (isotypes, polyclonal vs. monoclonal, humanization, etc.)
  - Mechanistic determinants of antibody absorption, distribution, and elimination (contrasting with determinants of small-molecule ADME)
  - Comments on the mathematical modeling of antibody PK
  - Introduction to antibody pharmacodynamics
- 10:30-10:45 Break
- 10:45-11:45 **Analytical Assays for Antibodies: Implications for PK/PD Analyses**
- Discussion of major types of analytical assays for monoclonal antibodies (ELISA, RIA, LC MS/MS, SPR, "direct" labeling)
  - Characterization of antibody binding
  - Characterization of antibody concentrations in biological samples
  - What is measured? What are the concerns for assay interference?
  - Examples / case-studies
- 11:45-12:15 **Immunogenicity and Macromolecule PK/PD**
- Factors associated with immunogenicity
  - Identification of host "anti-drug" antibodies
  - Examples / case-studies
- 12:15-01:00 Lunch
- 01:00-01:30 **Use of PK/PD Studies to Support Comparability Assessments of Therapeutic Proteins: An Academic Perspective**
- 01:30-02:15 **Interspecies Scaling of Antibody PK & PD**
- General review of interspecies scaling
  - Considerations for scaling antibody pharmacokinetics
  - Considerations for scaling antibody pharmacodynamics
  - Examples / case-studies
- 02:15-03:30 **Mathematical Modeling of Target-Mediated Disposition of Monoclonal Antibodies**
- Introduction to TMD of Mab with examples
  - Review of mathematical models that have been applied to characterize Mab TMD
  - Comparison of model performance; discussion of implications for predicting Mab PK/PD

03:30-03:45

Break

03:45-05:00

**Review Module #1: Design & Analysis of a Preclinical Investigation of Antibody PK**

- Study objectives
- Consideration for study design
- Assay considerations
- Initial evaluation of data (Additional studies needed?)
- Initial characterization of ADME (NCA vs. modeling)
- Evaluation of NCA results

## Day 2

09:00-10:00

**Mathematical Modeling of Bimolecular Antibody-Antigen Interaction**

- Review of binding kinetics (Law of Mass Action, equilibrium vs. non-equilibrium binding)

- Mathematical modeling of antibody binding: Examples from antibodies used for immunotoxicotherapy

10:00-11:00

**Physiologically-Based PK Modeling of Mab**

- Review of PBPK models
- Application of PBPK models applied to Mab
- Discussion of major features of PBPK models for Mab & discussion of associated physiology (convection, restriction coefficients, sites of catabolism, "two-pore formalism", incorporation of specific binding, incorporation of FcRn)

11:00-11:15

Break

11:15-12:15

**Review Module #2: Design & Analysis of a Preclinical Investigation of Antibody PK (Part 2)**

- Development of mechanistic mathematical models

12:15-01:00

Lunch

01:00-02:00

**Application of PK/PD Theory to Guide the Discovery and Development of New Immunotherapies**

02:00-03:00

**Review Module #3: Prediction of the Influence of Shed Antigen on the Distribution of Mab in Solid Tumors**

- Study objectives
- Consideration for study design
- Model development
- Model simulations

03:00-03:15

Break

03:15-04:30

**Review Module #4**

- Review of exam questions from UBgraduate courses relating to Mab pharmacokinetics and pharmacodynamics

## REGISTRATION DETAILS

**Course location:** Course location: The course will be held at the Ramada Inn & Conference Center, 2401 N. Forest Road, Amherst, New York 14226-0823, U.S.A. Phone: (716) 636-7500. Fax: (716) 636-8296. The Conference Center is 15 min. from Buffalo International Airport.

**Fee:** The fee is \$1600. A US government employee rate of \$1200 and student rate of \$800 is available for up to 3 participants of each type. The registration fee includes course documentation and handouts. Lunches and break-time refreshments during the course are included.

**Accommodations:** Ramada Inn & Conference Center, 716-636-7500 or Marriott Hotel, 716-689-6900.

**Registration:** Given the special nature of the course, enrollment will be limited to 30 persons. Please register by filling out the form and returning to the address shown below. Confirmation of registration will be returned upon receipt, together with an invoice for the course fee. Registration will not be final until payment is received. Checks should be made out to the University at Buffalo Foundation Inc. Bank transfers and credit card payments are also accepted.

**Cancellations:** Cancellations with a full refund may be made until March 26, 2010. No refunds will be given for cancellations received after this date. Substitutions may be made at any time.

### REGISTRATION FORM: ANTIBODY WORKSHOP

Name: \_\_\_\_\_

Organization: \_\_\_\_\_

Address: \_\_\_\_\_

City: \_\_\_\_\_ State/Country: \_\_\_\_\_

Postal Code: \_\_\_\_\_

Telephone: \_\_\_\_\_ Fax: \_\_\_\_\_ E-mail: \_\_\_\_\_

For credit card payment:

Credit card number: \_\_\_\_\_

Signature: \_\_\_\_\_ Expiration Date: \_\_\_\_\_

**Kindly return to:** ANTIBODY PK/PD MODELING Workshop, Dept. of Pharmaceutics, School of Pharmacy, University at Buffalo, 519 Hochstetter Hall, Buffalo, NY 14260; phone: 716 645 4834; fax: 716 645 3693; e-mail Rita Urben at rrunben@buffalo.edu.