Accelerating Proof-of-Concept
Clinical Success Driven by Science & Strategy
OCTOBER 3-5, 2011
Crowne Plaza Hotel Philadelphia Downtown, Philadelphia, PA

SESSION TOPICS:
Accelerating Proof-of-Concept Strategies: Proof-of-Concept
Data Strategy: Speeding Up Phase II to Slow Down Phase III?
Phase 0 and Early Development

KEYNOTES:
Antonio (Tito) Fojo, M.D., Ph.D., Head, Experimental Therapeutics Section, NCI, NIH
Neeta Amin, Pharm D., Director, CVMED Research Unit, Pfizer

PRE-CONFERENCE SHORT COURSE:
A Reasoned Approach to Proof-of-Concept Decision Making
John Arrowsmith, Ph.D., Science Director, Europe, Thomson Life Sciences Consulting
Richard K. Harrison, Ph.D., Scientific Director, North America, Thomson Life Sciences Consulting

FEATURED SPEAKERS:
Xiaoyin (Frank) Fan, Vertex Pharmaceuticals
Sean Zhang, Bristol-Myers Squibb
Chan Beals, Merck & Co.
Lloyd Dethloff, Pfizer, Inc.
Samuel Blackman, GlaxoSmithKline
Robert Sims, Dendreon Corporation

SCIENCE. STRATEGY. SUCCESS.
The Pharmaceutical Industry is currently faced with major issues due to decreased revenue generation and low productivity. Consequently, it has been actively adopting a variety of strategies, aimed at managing costs and increasing the flow of novel compounds into their pipelines. Strategies aimed at R&D productivity include downsizing and outsourcing, increasing access to new drugs and technologies through partnering, acquisitions and mergers, and realignments with a more narrowly focused portfolio. New revenue generating strategies include repurposing old drugs, expanding into emerging markets, greater reliance on biologics, and expansion into vaccines, consumer health, animal health and diagnostics.

These strategies are being adopted as means to maintain revenue streams and to mitigate some risk, but fundamentally they are being driven by the low output of new medicines from the R&D divisions of Pharma.

How did we get here? Despite the huge increases in the investments made in Pharma R&D over the last few decades productivity, as measured by the NDA approval of new molecular entities, has remained fairly constant. The 20 NMEs produced yearly is not sufficient to sustain an R&D based pharmaceutical industry that relies heavily on NME’s to drive future revenue streams.

Analysis of benchmarking data reveals that Phase II survival is the Achilles Heel of R&D industry, as 1 in 5 drugs entered into a Phase II proof-of-concept study (PoC) will successfully transition into Phase III. This is only marginally better than the 50% attrition from Phase III to submission. Clearly, such needs to be implemented in order to ensure survival of the industry. This interactive short course will discuss the key criteria that underpin quality PoC decision making in Phase II and will be used to highlight the impact on Phase III success.

Strategies: Proof-of-Concept

Chairperson: John Arrowsmith, Ph.D., Scientific Director, Thomson Reuters Consulting

3:30-4:00 The Consequences of PoC Decision Making
John Arrowsmith, Ph.D., Scientific Director, Thomson Reuters Consulting
Clinical proof-of-concept is the single biggest point of failure in drug development continuum. Examination of actual project data shows that success is achieved by building a robust body of evidence to demonstrate that modulation of a target results in clear clinical benefit to the patient. Failure can occur because the body of evidence clearly shows there is no benefit to the patient or can result from the drug being inadequately tested in man. While the first reason for failure is acceptable the latter is not and all efforts need to be made to avoid such failures.

4:00-4:30 Innovative PoC Strategies: The VC Perspective and Approach
Peter Neubeck, M.D., Ph.D., M.B.A., Principal, TVM Capital GmbH
Life Science Venture Capital is in a state of dramatic transition:
• Biotech venture model is broken
• Very difficult fundraising environment
But there is hope:
• Medical innovation is in demand
• Big Pharma is struggling with innovation crunch and needs products
• Academia continues to produce highly innovative science

Key success factors going forward revolve around getting to PoC in a smart and fast way:
• Quality compound selection
• Development design with focus on smart translation from PC to PoC
• Execution of the development plan in a virtual setting

4:30-5:00 The Living Document: Developing an Accelerated Proof-of-Concept

Alan Copa, Pharm.D., President, Clinical Operations, Fargo, Cetero Research
This session focuses on how to's for developing a robust, yet flexible protocol to accommodate up to four different studies. Topics covered include: Regulatory and ethical concerns, Inclusion/exclusion criteria, Dose flexibility, Stopping points, Timing and logistics of overlapping cohorts, Safety reviews

5:00-6:00 Evening Reception with Exhibit and Poster Viewing

6:00pm End of Day One

TUESDAY, OCTOBER 4

7:30am-5:00pm Conference Registration

7:30 - 8:15 Breakfast Presentation (Sponsorship Opportunity Available) or Morning Coffee

8:15-9:30 Roundtable Discussions

Work with your colleagues in a dynamic discussion/working group to create the ideal definition of PoC for the pharmaceutical industry, while addressing the following in a resultant read-out for the group:
• How will this new definition impact future development?
• Is this definition applicable across all drug types (biologic vs. small molecule) and therapeutic areas?
• Will this new definition be inclusive of accelerated strategies?
9:30-9:35 Chairperson’s Opening Remarks  
Graham Anthony, M.B.A., CFO, Biovista

9:35-10:05 PoC: What Concepts? How Much Confidence?  
Oranee T. Daniels, Ph.D., Vice President, Clinical Pharmacology, Theravance, Inc.

One of the big debates in early clinical drug development is what the ‘proof-of-concept’ study should look like. What concepts do the study have to prove? Is demonstrating mechanism of action in humans sufficient? Do we need to differentiate our new chemical entity from standard of care or existing therapy? We’ve heard confusing terminology from PoC (proof-of-concept), PoM (proof of mechanism) to PoR (proof of relevance). Is there a one-size fits all answer for every program? The presenter will walk the audience through a proposed systematic approach that considers unique challenges of each program yet follows logical steps to identify potential pitfalls and desired confidence in decision making. Logistics and operational challenges will also be discussed briefly.

10:05-10:35 The Case for Early Failure Studies  
Doina Roman, M.D., Senior Medical Director, Translational Medicine Sciences, Takeda Global Research & Development Center, Inc.

Compound failure in Phase III is costly, but lessons can be learned from these studies and applied to the proof-of-concept phase. Identifying mistakes, patterns, and decision-making criteria can be a successful tool in both establishing PoC or assigning a go/no-go decision in earlier phases. Case studies will be presented and discussed.

10:35-11:00 Networking Coffee Break with Exhibit and Poster Viewing

DATA STRATEGY: SPEEDING UP PHASE II TO SLOW DOWN PHASE III?

11:00-11:30 Soluble Ligand PK/PD Modeling and Its Application to the Development of a Monoclonal Antibody  
Thomas A. Puchalski, Pharm.D., Director, Oncology PK/PD, Pharmacokinetic and Pharmacometrics Group, Bristol-Myers Squibb, Centocor R&D, a division of Johnson & Johnson Pharmaceutical Research & Development, LLC

Over the past decade, regulatory agencies have emphasized the importance of integrating pharmacokinetic and pharmacodynamic (PK/PD) data. The concept is also known as model-based drug development, involves building mathematical models to characterize the relationship between drug concentration (PK) and drug effect (PD). Recent literature has shown this can streamline drug development. I will describe the application of PK/PD modeling to an antibody targeting a soluble target. The mechanistic PK/PD model simultaneously described free target, total target and antibody serum concentration data. I will also discuss how the modeling and simulation results were used for dose selection.

11:30-12:00pm Acceleration in PoC, Speed or Confidence?  
Xiaoyin (Frank) Fan, M.S., Ph.D., Director, Biometrics, Vertex Pharmaceuticals

Proof-of-Concept (PoC) studies are often underpowered because of the lack of sufficient prior clinical efficacy information, limited trial size, and time pressure, unless the treatment effect is unexpectedly overwhelming. Thus the Go/No-Go decision based on PoC results often depends not just on a single hypothesis being tested but takes a more holistic assessment of the trial data. These include assessment of efficacy, safety, pharmacometrics, and biomarker data if available. It is important to recognize that the primary goal of a PoC study is to move the drug candidate into late phase development with both speed and reasonable confidence. Speeding up PoC only makes sense if it can accelerate the entire drug development program and improve the probability of success (PoS). We will use some real PoC examples as illustrations in this presentation.

12:00-12:30 Sponsored Presentation  
Graham Anthony, M.B.A., CFO, Biovista

12:30-2:00 Luncheon Presentation (Sponsorship Opportunity Available) or Lunch On Your Own

2:00-2:05 Chairperson’s Remarks  
Terri Roberson, Senior Director, Global External Research and Development, Lilly Research Laboratories

2:05-2:35 Pharmacometrics and PoC: Preventative Care for Drug Development  
Thaddeus Grasela, Pharm.D., Ph.D., Adjunct Professor, University at Buffalo

The synthesis of data and experience is a critical function of Pharma R&D teams. The synthesis process generally consists in the compilation of relevant study results by separate functional areas. Cross-functional, interdisciplinary analysis is often minimal or lacking. This lack of cross-functional synthesis has two important consequences: 1) unintended or unrecognized knowledge gaps and 2) research plans that rely on intuition rather than an explicit synthesis of knowledge. This presentation will describe a strategy for using pharmacometric methods to perform a comprehensive and interdisciplinary synthesis of available data that can play a central role in R&D planning and in the design, analysis, and interpretation of study results.

2:35-3:05 The Utility of Decision Analysis in Early Clinical Development  
Eyas Abu-Raddad, Ph.D., Research Advisor, PK/PD Chorus, Eli Lilly & Co

3:05-3:35 Evaluating Clinical Research Sites, Let’s Get Scientific about Data Quality  
Neil K. Singla, M.D., CEO, Lotus Clinical Research, LLC

When speaking about data quality, most sponsors focus on data cleanliness and not data accuracy. Data cleanliness has to do with appropriate recording and transcription of data with the avoidance of queries. Data accuracy is much more important! Did the site reveal the treatment effect that the study was designed to show? By using a simple metric, the standardized effect size, the contribution of individual centers toward or away from the primary endpoint can be evaluated.

3:35-4:20 Networking Refreshment Break with Exhibit and Poster Viewing

Moderator: Terri Roberson, Senior Director, Global External Research and Development, Lilly Research Laboratories

5:20-6:20 Networking Happy Hour with Exhibit and Poster Viewing

6:20 End of Day Two

WEDNESDAY, OCTOBER 5

7:30-8:15am Breakfast Presentation (Sponsorship Opportunity Available) or Morning Coffee

PHASE 0 AND EARLY DEVELOPMENT

8:15-8:20 Chairperson’s Opening Remarks  
Terri Roberson, Senior Director, Global External Research and Development, Lilly Research Laboratories

8:20-8:50 Phase 0 Studies for Drug Development  
Sean Zhang, M.D., Medical Director, Discovery Medicine and Clinical Pharmacology, Bristol-Myers Squibb

Phase 0 studies are generally referred to human microdosing studies in accordance with the US FDA Guidance on exploratory Investigational New Drug (IND) Studies. However, the term of Phase 0 studies has been
sometimes extended beyond the concept of microdosing to include no-drug administration methodology and sub-therapeutic exploratory studies. Examples of human microdosing studies for drug R&D include PET imaging, biomarker or endpoint validation and absolute bioavailability studies. Sub-therapeutic exploratory study is increasingly being used for early candidate screening on human PK and PD. In this presentation, the basic concepts, regulatory guidance and IND enabling toxicology studies for Phase 0 studies will be reviewed. Case studies utilizing human Phase 0 studies for drug R&D will be elucidated. Finally, the challenges and limitations of Phase 0 studies will be discussed.

8:50-9:20 Short Stories of Early Development Decisions Using Fit-for-Purpose Biomarkers
Chan Beals, M.D., Ph.D., Executive Director, Head, Experimental Medicine, Merck & Co.

One proposed solution to high cost and low success in early development is to utilize biomarkers to confirm a pharmacodynamic effect in humans before further development. This talk will provide a high level overview of clinical biomarker qualification, and describe specific applications to effect early clinical decisions at Merck. While biomarkers may utilize many technologies for numerous uses, they will not realize their value without seamless integration into the discovery and development interface, focus on the pipeline, and excellent negotiation skills.

9:20-9:50 Building a Networked Pharmaceutical Enterprise
Kenneth A. Savin, Ph.D., Advisor to Special Projects, Global External Research and Development/Due Diligence, Eli Lilly and Company

The development of novel molecularly targeted cancer therapeutics remains slow and expensive with many late-stage failures. There is an urgent need to accelerate this process by improving early clinical anticancer drug evaluation through modern and rational trial designs that incorporate predictive, pharmacokinetic, pharmacodynamic, pharmacogenomic and intermediate end-point biomarkers. In this talk, I will discuss current approaches and propose strategies that will potentially maximize benefit to patients and expedite the regulatory approvals of new anticancer drugs.

10:25-10:55 envisioning the future of early phase Clinical trials
Timothy Yap, Ph.D., Senior Clinical Research Fellow, Royal Marsden Hospital and The Institute of Cancer Research, UK

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2:30-3:00 Accelerating Proof-of-Concept for Novel/Novel Drug Combinations in Oncology
Samuel C. Blackman, M.D., Ph.D., Director, Early Development Unit/Research and Development, GlaxoSmithKline

Successes and failures in monotherapy application of targeted therapeutics in oncology and expansion of pipelines have lead to a marked increase in novel/novel drug combination Phase I trials. The number of potential novel/novel combinations and the complexity of the development path for combinations has prompted the development of various strategies to address the “Combination Problem.” This talk will define the scope of this problem, strategies for prioritization, and methods for accelerating proof-of-concept using novel clinical trial designs.

3:30-4:00 Cancer Immunotherapy: Challenges in Clinical Development
Robert Sims, M.D., Senior Medical Director, Dendreon Corporation

Sipuleucel T is an autologous cellular immunotherapy for asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer. The IMPACT study demonstrated an improvement in overall survival (OS) for subjects treated with sipuleucel T compared with control (HR=0.78 [95% CI: 0.61, 0.98]; P=0.03), indicating a 22% reduction in the risk of death. No significant differences in time to objective disease progression were observed between groups. Immune responses to the immunizing antigen were observed, with correlations between these measures and OS. Challenges encountered in the development of sipuleucel-T will be discussed, along with the use of immunologic biomarkers and considerations for future development.

CASE STUDIES

3:30-4:00 Cancer Immunotherapy: Challenges in Clinical Development
Robert Sims, M.D., Senior Medical Director, Dendreon Corporation

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4:00-4:30 Learning From Failure: The COX-2 Saga
Tilo Grosser, M.D., Research Assistant Professor, Pharmacology, Institute for Translational Medicine and Therapeutics, University of Pennsylvania

Nonsteroidal antinflammatory drugs (NSAIDs) inhibit prostaglandin formation by cyclooxygenases (COX) -1 and -2. NSAIDs selective for inhibition of COX-2 are less likely than traditional drugs to cause serious gastrointestinal adverse effects, but predispose to adverse cardiovascular events, such as heart failure, myocardial infarction and stroke. Evidence from human pharmacology and genetics, genetically manipulated rodents and other animal models and randomized trials indicates that this is consequent to suppression of COX-2 dependent cardioprotective prostaglandins, particularly, prostacyclin. Lessons drawn from how this saga unfolded are relevant to how we integrate diversified forms of information, approach PoC efficacy and safety research and might pursue a more personalized approach efficacy and risk.

4:30pm End of Conference
SCIENTIFIC ADVISORS
John Arrowsmith, Ph.D., Science Director, Europe, Thomson Life Sciences Consulting
Day 1 Chairperson
Russell Linderman, Ph.D., Executive Director, Research Science & Technology PGRD, Pfizer Inc.
Day 2 Chairperson
Terri Roberson, MT (ASCP), M.B.A., Sr. Director, Operations, Global External Research and Development, Lilly Research Laboratories, Eli Lilly and Company Laboratories
Day 3 Chairperson

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Antonio Tito Fojo, M.D., Ph.D., Head, Experimental Therapeutics Section, NCI, NIH
Aris Persidis, Ph.D., President & Co-Founder, Biovista
Chan Beals, M.D., Ph.D., Executive Director, Head, Experimental Medicine, Merck & Co.
Neil K. Singla, M.D., CEO, Lotus Clinical Research, LLC
Peter Neubeck, M.D., Ph.D., M.B.A., Principal, TVM Capital GmbH
Robert Sims, M.D., Senior Medical Director, Dendreon Corporation
Samuel C. Blackman, M.D., Ph.D., Director, Early Development Unit/Oncology, GlaxoSmithKline
Sean Zhang, M.D., Medical Director, Discovery Medicine and Clinical Pharmacology, Bristol-Myers Squibb
Tilo Grasser, M.D., Research Assistant Professor, Pharmacology, Institute for Translational Medicine and Therapeutics, University of Pennsylvania
Xiaoyin (Frank) Fan, M.S., Ph.D., Director, Biometrics, Vertex Pharmaceuticals
Eyas Abu-Raddad, Ph.D., Research Advisor, PK/PD Chorus, Eli Lilly & Co
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Lloyd Dethloff, Ph.D., Vice President, Drug Safety R & D, Worldwide Research and Development, Pfizer, Inc.
Neeta Amin, Ph.D., Director, CVMED Research Unit, Pfizer
Oranee T. Daniels, Ph.D., Vice President, Clinical Pharmacology, Theravance, Inc.
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Thomas A. Puchalski, Pharm.D., Director, Oncology PK/PO, Pharmacokinetic and Pharmacometrics Group, Biologics Clinical Pharmacology, Centocor R&D, a division of Johnson & Johnson Pharmaceutical Research & Development, LLC

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For more information, please contact:
Carol Dinerstein
Director, Business Development
781-972-5471
dinerstein@healthtech.com

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CONFERENCE HOTEL:
Crowne Plaza Hotel Philadelphia Downtown
1800 Market Street, Philadelphia, PA 19103
Phone: 215-561-7500
Discounted Room Rate: $169 s/d
Discounted Room Rate Cut-off Date: September 10, 2011

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PRE-CONFERENCE SHORT COURSE: OCTOBER 3, 2011

A Reasoned Approach to Proof-of-Concept Decision Making

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