'There is no doubt that a more efficient dissemination of scientific knowledge and the removal of drug discovery silos will aid the deepening productivity crisis.'

editorial

Charlotte Carey
Content Manager, PharmaDiscovery
Elsevier

PharmaDiscovery: closing the productivity gap

There is a well-documented crisis occurring in the pharmaceutical industry. We regularly hear about rising R&D costs, decreasing productivity and the widening productivity gap. But on a scientific level what does that mean for the individual molecular biologist, medicinal chemist, HTS scientist, or toxicologist? What part should they be playing in closing the productivity gap and how does that relate to the overall drug discovery landscape?

A significant issue is that every pharmaceutical industry leader is talking about the need for integration of scientific effort, data sharing and communication. There is no doubt that a more efficient dissemination of scientific knowledge and the removal of drug discovery silos will aid the deepening productivity crisis. But how can this be realistically achieved?

PharmaDiscovery: a new type of meeting

This year will see the birth of a new type of conference – an event for scientists by scientists, focused on addressing, and attempting to solve existing productivity issues within drug discovery. PharmaDiscovery is produced by Elsevier's *Drug Discovery Today* magazine and an exceptional Scientific Leadership Committee. This unique approach has combined the global reach of Elsevier in a new knowledge-based forum, and over 1000 drug discovery scientists are expected to descend on Washington D.C., on 10–12th May 2005, to take part in what will be the first conference of its kind – a highly interactive and integrated forum for information exchange, discussion and debate on the vital issues affecting drug discovery performance.

More than just a conference

PharmaDiscovery has been organized to offer more than a standard conference of conventional talks on new technologies and long-term visions of the industry. Leading pharmaceutical, biotech, and academic figureheads felt that there was a need for a new type of interactive conference for the drug discovery sector, and have volunteered to act as session chairs. Chairs have been responsible for defining key objectives for each session, as well as inviting an eminent panel of speakers to tackle the issues raised. Audience participation will be encouraged during facilitated discussion times, when the chairs will lead and force debate on emerging themes within each session.

Daily sum-up sessions led by the session chairs will serve to fully integrate the program by relaying the key points and conclusions from each session back to the entire audience for further discussion.

1359-6446/04/$ – see front matter PII: S1359-6446(04)03372-6

This should facilitate the exchange of information between chemists and biologists and early- and late-stage drug discovery scientists, thereby moving some way towards removing, or at least connecting, existing silos in drug discovery.

How is it structured?

PharmaDiscovery's Keynote speakers Dr Bob Ruffalo, President, R&D, Wyeth, and Dr Janet Woodcock, Acting Deputy Commissioner, FDA, will provide an overview of drug discovery and early development productivity issues, and will set the scene and key objectives for each day. Sessions will be chaired by pharmaceutical industry leaders who will encourage data sharing and communication, with a common aim of integrating scientific knowledge, and forcing debate within vital areas of drug discovery. Critical issues will be debated within each session, moving from target discovery through to early clinical development.

A perceived aftermath of the genomic revolution was that the pharmaceutical industry was 'awash with targets'. Unfortunately, even with all these new targets, the number of NCEs filed on an annual basis both in the US and Europe continues to decline. The **Target Assessment** session will address the reasons why this is happening, with particular reference to determining the biological relevance of a target in a specific disease indication. The session will also assess the role of systems biology in target discovery, and ask whether our ability to define disease-related pathways and networks can really help the drug discovery process.

Molecular modelling has the potential to impact all stages of the drug discovery process. Whereas early efforts in the field focused on lead optimization, more recently, applications to lead finding and ADME property prediction have emerged. The ***In Silico* Drug Discovery** session will be to review the performance of current *in silico* methods at different stages of the drug discovery process, focussing on three areas: lead finding, lead optimization, and ADME prediction.

Solving some biological problems are well suited to parallel computation in large clusters, while others perform best in large multiprocessing environments. Computer platforms for drug discovery must comprehend both types of problem and provide a mechanism for distribution in clustered, heterogeneous, and large multiprocessing environments. The **IT Infrastructure as a Source of Value Creation**, and **Data Integration** sessions, will tackle issues relating to the design of informatics platforms in drug discovery, and strategies to deal with multiple data types and volumes, as well as how to interface systems across multi-disciplinary teams.

Chemistry-driven drug discovery will be covered in two sessions. The **Proof-of-Concept Ligands** session will address how chemical diversity should be integrated into both lead generation and optimization, and how both therapeutic target structure- and mechanism-guided drug design technologies should be optimally integrated in chemistry-driven drug discovery strategies. Small-molecule drug discovery is driven by chemistry with respect to molecular diversity, structural novelty (patentability), therapeutic target structure/mechanism-guided drug design, and drug-like properties (*in vitro* and *in vivo* 'proof-of-concepts'). Relative to the theme of 'novel ligand to breakthrough medicine', the **Breakthrough Medicines** session will review progress in chemistry-driven drug discovery technologies using case studies relative to the development of clinical candidates and knowledge gained from human testing.

The **Pharmacological Models for Human Diseases** session will tackle how to use biochemical measurements, for example, genes, proteins and metabolites to understand the predictive value of models. Imaging technologies will be assessed to compare drug response in models and patients, as well as metabolism of specific drugs in animals and man. Preclinical *in vivo* testing of drug candidates for Central Nervous System (CNS) diseases is a key step to assess potential efficay in human clinical trials. However, the predictability is highly variable from one model to another, and in vivo activity is required from several models within a given disease to gain confidence that the candidate drug might work in human patients. The **Pharmacological Models for CNS Diseases** session will provide specific views (pros and cons, limitations) of major CNS models such as depression, Alzheimer's, schizophrenia and stroke. More generic models of cognitive deficits, memory losses, neurodegeneration and brain injury will also be critically reviewed.

The ***In Vivo* Models for Drug Development** session will focus on the use of intact *in vivo* surrogate models in drug development. The value of existing manipulated rodent models will be emphasized, as will the use of emerging in vivo models that can be adapted to a holistic approach to measuring biological endpoints relating to toxicity and drug safety. Opportunities for exploiting new models in drug development will be outlined and the current status of preclinical models in drug development will be highlighted.

The **Evaluating Success in Drug Discovery** session will outline the case for the drug discovery productivity dilemma through retrospective analysis and metrics that have been collected across the industry. This will be followed by an analysis of the impact of investments in technological solutions and where future opportunities could exist that have the potential to reverse this trend. The session will ask what lessons have been learned from failed drug discovery and development projects, and what the potential technological solutions are that will drive success forward in the future.

In most analyses, safety remains the single most important cause of drug development attrition and drives the need for extended clinical trials and an ever increasing number of patients required to assess the expectations of

a negative experiment. Safety is perhaps the most important challenge to the productivity of the pharmaceutical industry. Not only has our industry recognized these challenges, but regulatory agencies have declared their role in spawning improvements as articulated in the recent FDA Critical Path Document. The **Pre-Clinical Safety and Drug Development** session will highlight the emerging opportunities in the safety sciences to optimize the chemistry and safety attributes of compounds early in the discovery process.

Finally, the **Efficacy Biomarkers in Early Clinical Development** session will discuss the value and limitations of efficacy biomarkers for decision making in early clinical development and address issues related to biomarker discovery, validation and application. Specific challenges and issues that hamper clinical development and decision making for new disease areas and/or paradigm shift therapies will be also discussed.

To complement the main conference programme, one-day symposiums on Tuesday 10th May will focus on strategies for improving the quality of new leads through a better understanding of the target classes including protein kinases, G-protein coupled receptors, ion channels and proteases. In addition the biomarker technologies symposium will address vital issues relating to biomarker discovery, validation and application in discovery and early clinical development.

So join us in Washington D.C. this May and make sure you have your say in the discussions of the key issues in the industry in this exciting new conference format from Elsevier. Visit www.pharmadiscovery2005.com to read the full conference programme and register your place today.

PharmaDiscovery – An Elsevier Event
10–12th May 2005, Washington D.C. Convention Centre
www.pharmadiscovery2005.com

Editorial

PharmaDiscovery Session Chairs

Pharmacological models for CNS diseases
Professor Patrick Nef CEO, Faust Pharmaceuticals, and former Global Business Development Director, F. Hoffmann-La Roche, Ltd

Pharmacological models for human diseases
Professor Jan Tornell Global Director Transgenics and Comparative Genomics, AstraZeneca R&D Molndal
Dr Richard Woychik Director, The Jackson Laboratory

Target assessment
Professor Bernhard Palsson Dept of Bioengineering, University of California, San Diego
Professor Steve Naylor Computational Systems Biology Initiative, Massachusetts Institute of Technology

IT infrastrucure as a source of value creation
Dr Dimitris Agrafiotis Senior Research Fellow and Team Leader, Molecular Design and Informatics, Johnson & Johnson
Dr Jeff Augen President and CEO, TurboWorx

***In silico* drug discovery**
Dr Mark Murcko Chief Technology Officer, Vertex Pharmaceuticals
Dr Wendy Cornell Director of Molecular Systems, Merck

Chemistry-driven drug discovery: proof-of-concept ligands
Dr Tomi Sawyer Senior Vice-President Drug Discovery, ARIAD Pharmaceuticals
Dr Zhong-Yin Zhang Department of Molecular Pharmacology, Albert Einstein College of Medicine

Evaluating success in drug discovery
Dr Martyn Banks Director of Drug Discovery, Bristol Myers Squibb
Dr James Summers Divisional Vice President, Advanced Technology, Abbott Laboratories

***In vivo* models for drug development**
Dr James Stevens Research Fellow, Toxicology and Drug Disposition, Lilly Research Laboratories
Dr Peter Lord Director of Mechanistic Toxicology, Johnson & Johnson

Pre-clinical safety and drug development
Dr Jack Reynolds Global Head of Safety Sciences, Pfizer Research and Development
Professor Ian Wilson Principal, Dept of Drug Metabolism and Pharmacokinetics, AstraZeneca

Efficacy biomarkers in early clinical development
Dr Hans Winkler Senior Director of Functional Genomics, Johnson & Johnson
Dr Anthony G Quinn Vice President Discovery Medicine, Roche Palo Alto

Data integration strategies
Dr Eric Neumann Global Head of Knowledge Management, Aventis Drug Innovation and Approval
Dr Phil McHale VP Corporate Communications and Scientific Affairs, MDL Information Systems

Chemistry-driven drug discovery: breakthrough medicines
Dr Ronald J. Doll Director, Chemical Research, Infectious Diseases and Tumor Biology, Schering-Plough
Dr Tomi Sawyer Senior Vice-President Discovery, ARIAD Pharmaceuticals