Tuesday 14 March 2006

K1 - Keynote Presentations

08.30 

Chairman's Opening Remarks
Dr Phil McHale, Vice President, Corporate Communications and Scientific Affairs, Elsevier MDL, USA

08.40 

AstraZeneca R&D Strategy and Portfolio for a Changing World
The decline in R&D productivity, despite increasing investment, is a major challenge for the Pharmaceutical industry. At AZ we have tackled this systematically by introducing a strategy designed to address the major problem areas. The presentation will cover the key elements of our approach, chart the productivity improvement that has occurred since its introduction and show how we intend to grow and shape the pipeline of drug projects.
Dr Jan Lundberg, Head of Global Discovery Research, AstraZeneca, Sweden

09.20 

Going All the Way: A Scientific, Technical and Organisational Challenge
Taking a compound from an early idea stage to market entry is a formidable challenge. It requires an end-to-end alignment between all major disciplines involved in the process, build up of specific scientific insights and targeted technological development. While major advances have been made in all aspects of the drug discovery process, organisational models which allow all of these to optimally integrate in an end-to-end vision are extremely hard to implement. The need for entrepreneurial approaches, and the role of project champions will be highlighted during the presentation.
Dr Jan Hoflack, Vice President of Medicinal Chemistry and ADME-Tox, Johnson & Johnson Pharmaceutical Research and Development, Belgium

10.00 **Discussion with the Keynote Plennary**

10.10 Exhibition Opening and Networking Break

B1 - Biological Pathways - Establishing Cellular Systems to Accurately Validate Drug Targets

Biological pathways are predicted to be relevant to drug discovery through a knowledge of the biological roles of active metabolites, the function of related pathways in model organisms or analysis of phenotypic impact of mutations in pathway members.

10.50 **Chairman's Opening Remarks**

10.55 **Predictive Integrative Biology and Downstream Experimental Testing**
Two examples will be described in this synergistic paradigm that significantly improves the entire drug development process. The first example addresses the as yet poorly understood pathological mechanisms leading to vacuolation and neuronal death in Creutzfeld-Jakob Disease. Here, the synergistic interplay between predictive modeling and in vivo experimentation revealed mechanisms hitherto unsuspected such as regional differentiation in the molecular details of the pathological processes. The second example addresses the mode of action of a peptide observed to induce, by unknown means, dormancy in aggressively malignant epithelial cells both in vivo and in vitro. Here, the synergistic interplay between predictive modeling and experimentation revealed the mechanisms used by this peptide to achieve the observed effects together with the reasons why it induces dormancy in malignant cells.
Dr François Iris, CSO, Bio-Modeling Systems, France

11.20 **Genome-Scale Functional Screening as an Enabling Technology in Drug Discovery**
Craig S. Mickanin, Research Investigator II, Novartis Institutes for Biomedical Research, USA

11.45 **Systems Biology in Drug Discovery and Development**
We have assembled a multidisciplinary capability, combining experimental and theoretical techniques, as a first step towards applying Systems Biology to projects both in discovery and development. This platform has already demonstrated its potential to have a broad impact on projects at all stages of the pipeline. This talk will use examples to illustrate our approach to Systems Biology and consider its potential in supporting the discovery and development of new medicines.
Dr Adriano M. Henney, Director, Pathways Capability, Global Discovery Enabling Sciences & Capabilities, AstraZeneca, UK

12.10 **Technology Tutorial**
If you have a technology, product or resource that would be of interest to this audience, please contact sanjay.singh@informa.com for further information.

12.40 Lunch and Exhibition Viewing

B2 - Biomarkers - One of the Most Promising Avenues to Predictive Medicine

Consideration of proof of mechanism versus proof of principle versus proof of concept biomarkers and the reliance people place on each and the types of markers that are used.

14.10 **Chairman's Opening Remarks**

14.15 **Combining HT-Biology and Computational Biology to Identify Pharmacodynamic Biomarkers**

We present a computational approach to rationally identifying pharmacodynamic biomarkers that are the most sensitive indicators of IGF1-R antagonism at the molecular level. A detailed mathematical model of the IGF signaling pathway was developed, trained with experimental data, and validated by comparing the predicted activity of a novel IGF1-R antagonist on downstream ERK and AKT phosphorylation to in vitro experimental results. Using the validated model, a portfolio of sensitivity analyses and simulations was generated that highlighted the key proteins regulating the IGF pathway and identified the biomarkers that characterized the efficacy of the antagonist.

Dr Birgit Schoeberl, Associate Director of Computational Biology, Merrimack Pharmaceuticals, USA

14.40 **Discovery and Technical Validation of Candidate Pharmacodynamic Biomarkers for a Selective Kinase Inhibitor**

Pharmacodynamic (mechanism of action) biomarkers can be used to measure acute target inhibition in-vivo and potentially for interpreting dose response relationships. A preclinical case study will be presented on identifying candidate RNA transcripts and their qualification using quantitative PCR as potential pharmacodynamic markers for a selective inhibitor of T cell receptor signaling.

Dr Andrew Cherniack, Senior Scientist, Translational Medicine, Abbott Bioresearch Center, USA

15.05 **How Johnson & Johnson is Using Biomarkers in CNS Research: Case Examples**
Dr Wilhelmus Drinkenburg, Head Biomonitoring Research, Johnson & Johnson Pharma R&D, Belgium

15.30 **Technology Tutorial**
If you have a technology, product or resource that would be of interest to this audience, please contact sanjay.singh@informa.com for further information.

16.00 Afternoon Break and Exhibition Viewing

B3 - Pharmacogenomics - Effective Prediction of Safety and Efficacy

Where there is the possibility of shorter trials and more rapid updates, increased compliance and earlier treatments - how close are we to this situation?

16.40 **Chairman's Opening Remarks**

16.45 **Pharmacogenomics - Effective Prediction of Safety and Efficacy**

Adverse drug reactions (ADRs) are a major clinical problem accounting for 6.5% of hospital admissions. Clearly not all these ADRs are due to genetic predisposition, and many of these will be preventable through improved prescribing practices. Nevertheless, the occurrence of ADRs within families together with evidence suggesting that many of these ADRs may be due to metabolism by polymorphic enzymes, implies that pharmacogenetics may have an important role in improving drug safety. Genetic variation predisposing to ADRs may reside in the pharmacokinetic pathways (absorption, distribution, metabolism and excretion) or in the pharmacodynamic targets (receptors, ion channels, enzymes, etc.). For type A ADRs (predictable ADRs with a readily discernible dose-response relationship), it may be possible to use pharmacogenetics to guide drug dosage and choice, while for type B (idiosyncratic ADRs without a clear dose-response relationship), pharmacogenetics may guide drug choice. While individual SNPs that predispose to certain type A ADRs have been identified with a number of drugs, they have not been of sufficient predictive value to be incorporated into clinical practice. A typical example here is the variability in anticoagulation with warfarin - CYP2C9 polymorphisms are known to affect dose requirements, but have a low predictive value. Interestingly, even with type A reactions, variability in pharmacodynamic targets may have a greater quantitative effect on drug response, as has recently been shown with warfarin and VKORC1 polymorphisms. By contrast, with idiosyncratic ADRs, major gene effects have recently been identified for both abacavir hypersensitivity and carbamazepine-induced Stevens-Johnson syndrome. Importantly, these remarkable findings have been achieved with small numbers of patients, and with regard to abacavir, it may also be cost-effective to genotype patients prior to its use in HIV positive patients. There are likely to be many more advances in this area over the next few years, and pharmacogenetics thus may have huge potential in improving the safety of old drugs, as well as of new drugs currently in development.

Prof Munir Pirmohammed, Department of Pharmacology, University of Liverpool, UK

17.10 **Towards Targeted Therapy: Integrating Genetics into Clinical Trial Design**

The diseases we treat are complex genetic diseases and drug targets are polymorphic. Genetic knowledge is being leveraged to create opportunities to improve the quality of drugs in development. Examples will be given to illustrate how genetics is being applied in clinical trial design to maximise efficacy signal and

contribute to understanding variable response to therapy.
Dr Michelle Penny, Director, Molecular Profiling Group, Pfizer Global Research and Development, UK

17.35 **Pharmacogenetic Aspects in Early Drug Development**
Dr Georg Wensing, Head of Pharmacodynamics, Clinical Pharmacology, Bayer Healthcare AG, Germany

18.00 Close of Day One and Drinks Reception

Wednesday 15 March 2006

B4 - High Content Cellular Screening - What is the Real Role in Drug Discovery?

What is the real role of HCS in drug discovery and are there any projects in big pharma where HCS made a really critical contribution to the drug discovery process?

08.30 **Utilising Living Cells for High-Content Analysis**
Over the last few years, High-Content Analysis (HCA) has increasingly been finding its way into commercial and academic institutes. The analysis of target proteins in living cells during cell cycle progression opens up a new dimension in the field of HCA. This case study presents examples how living cells can be utilised for drug discovery.
Dr Stefan Prechtl, Group Leader, Subcellular Imaging, Schering AG, Germany

08.55 **Phosphoprotein Profiling, Multiplexed Technologies, and Drug Discovery**
Protein phosphorylation has a critical role in regulating all biological processes. We believe that it is possible to take a peek into 'cellular consciousness' by detecting the net change in the phosphorylation state of a relatively small number of cellular proteins. Thus, with all the challenges involved, bringing cell-based assays to the screening front-end is a prerequisite for identifying quality 'hits' with improved chances of becoming new therapeutic entities. The technologies that are developed in our group are meant to provide data-rich and biologically meaningful information that will aid in achieving this goal.
Dr Lekha Patel, Senior Scientist, Drug Discovery, Endocrine Therapeutics, Johnson and Johnson Pharmaceutical R&D, USAG

09.20 **Technology Tutorial**
If you have a technology, product or resource that would be of interest to this audience, please contact sanjay.singh@informa.com for further information.

09.50 Networking Break

K2 - Keynote Presentations

10.30 
Chairman's Opening Remarks
Dr Mikael Dolsten, Head of Corporate Division Pharma Research, Boehringer Ingelheim, USA

10.40 
Cardiovascular Diseases and Risk Management - A Patient Driven Research Strategy
Bayer HealthCare Pharma implemented a new research focus on cardiovascular diseases and risk management with the indications thrombosis, coronary heart disease, chronic heart failure, and diabetes. In addition to the standard monodimensional research process (single target for single indication), our revisited research strategy will particularly address common mechanisms in order to exploit scientific synergies across these areas.
Prof Dr Andreas Busch, Senior Vice President Discovery Europe, Pharma R&D, Bayer HealthCare AG

11.10 **Repositioning the Company: Challenges of Moving from Discovery to the Market**
Dr Anders Ullman, Senior Vice President, Head of R&D, Biovitrum, Sweden

RT1 - Round-Table Discussions

11.40 
Sponsored Round-Table Discussions
This session gives delegates the chance to informally quiz and probe the leader and contributor of each roundtable, who sets the agenda and mediates the discussion. At the same time you can brainstorm the topic with your fellow peers across the sector. Discussions will last for 20 minutes, with a bell sounding to indicate your move to another table, all attendees get the opportunity to sit in three discussions during these 60 minutes.

- **Toxicogenomic Profiling of Compounds at an Earlier Stage**

  Contributor: Dr Jeffrey F. Waring, Group Leader, Toxicogenomics, Abbott Laboratories, USA
  Leader: to lead this session please contact sanjay.singh@informa.com

- **Natural Products - An Increasingly Viable Option for Drug Targets**

  Contributor: Dr Thomas Henkel, Vice President Enabling Technologies, Bayer HealthCare Pharma R&D, Germany
  Leader: to lead this session please contact sanjay.singh@informa.com

- **Experimental Medicine - Developing a Product or Testing a Target?**

  Contributor: Dr Robert Holland, Vice President, AstraZeneca, UK
  Leader: to lead this session please contact sanjay.singh@informa.com

- **In-Vivo Models - Extrapolating Results for Prediction in Humans**

  Contributor: Dr Wilhelmus Drinkenburg, Head Biomonitoring Research, Johnson & Johnson Pharma R&D
  Leader: to lead this session please contact sanjay.singh@informa.com

- **Personalised Medicine - How it Compares with the 'Megabrand' Approach**

  Contributor: Dr Georg Wensing, Head of Pharmacodynamics, Clinical Pharmacology, Bayer Healthcare AG, Germany
  Leader: to lead this session please contact sanjay.singh@informa.com

- **Translational Medicine - Key Player in the Critical Path for Drug Discovery**

  Contributor: Dr Andrew Cherniack, Senior Scientist, Translational Medicine, Abbott Bioresearch Center, USA
  Leader: to lead this session please contact sanjay.singh@informa.com

- **New Concepts Established in Other Areas: Implications to Antibodies**

  Leader: Dr Jane Osbourn, VP of Biologics Discovery, Cambridge Antibody Technology, UK

- **The Future Generation of Biologicals: How will Medical Need, Technological Advances and Commercial Opportunities Converge?**

  Leader: Dr Mikael Dolsten, Head of Corporate Research/Discovery, Boehringer Ingelheim, USA

- **Immunogenicity of Antibodies: Prediction/Reduction**

Leader: Dr Mike Clark, Immunology Division, Department of Pathology, Cambridge University, UK

B6 - Biology and Chemistry - Linking the Systems and Blurring the Boundaries

The benefits of linking biology and chemistry are enormous where biology can be used to tell what chemistry will do and where the chemical structure is built on biology. It will shorten the process and help middle to senior management to decide which programmes to pursue.

14.10 **Chairman's Opening Remarks**

14.15 **High-Throughput Affinity Selection of Compounds: The Missing Link between Biology and Chemistry**

The Novartis SpeedScreen technology uses high-throughput affinity selection (AS) which is based on fast size-exclusion chromatography (SEC) followed by microbore-liquid-chromatography/electrospray-ionization mass spectrometry (microLC/ESI-MS) for the identification of chemical binders to molecular targets. The approach is currently among the most straight-forward and powerful drug discovery techniques for both genomic targets with unknown biological function ("orphan targets"), as well as for conventional targets with known function but no feasible screening format ("non-tractable targets"). The presentation will describe the basic concept behind assay development, high-throughput screening and data analysis for this technology with case studies from the Novartis Lead Discovery Center (LDC), and will highlight the enormous potential of this technology for future low-cost and high-value lead discovery.

Dr Lorenz M. Mayr, Senior Unit Head/Executive Director, Head BioChemical Assay Development & Screening, Novartis Pharmaceuticals, Switzerland

14.40 **Discovery of New GPCR-Ligand Scaffolds via Navigating Through the Chemical Space**

We used the visualisation power of Kohonen Maps to find new GPCR-ligand scaffolds in HTS. We clustered large supplier compound libraries to find GPCR-ligand like molecules. For a scaffold independent description of the molecules, we developed topological pharmacophore histograms. The screening of the purchased compounds resulted in several new scaffolds for GPCR targets.

Dr Modest von Korff, Computational Chemist, Actelion, Switzerland

15.05 **The Challenge of Using Complex Biologic Models to Characterize Chemical Relationships and to Drive SAR**
Dr Lucienne Ronco, Associate Director, AstraZeneca R&D, USA

15.30 **Technology Tutorial**
If you have a technology, product or resource that would be of interest to this audience, please contact sanjay.singh@informa.com for further information.

16.00 Networking Break and Exhibition Viewing

B7 - Early ADME-Tox - Predicting the Value of Toxicity and Potential Adverse Events

What is the predictive value of the toxicology studies and also the predictive value of preclinical PK to clinical PK? This is an area which we still get wrong.

16.25 **Chairman's Opening Remarks**

16.30 **Establishment of Illumina Gene Expression Arrays for Hepatotoxicity Screening**

- In vivo-in vitro comparisons in gene deregulation
- Optimization of a primary hepatocyte sandwich culture system
- Rat vs. human in vitro hepatocyte differences
- Classification of hepatotoxic compounds using gene expression
- Use of pathway-analysis tools to aid interpretation of mechanism of toxicity

Dr Phil Hewitt, Head of Toxicogenomics, Institute of Toxicology, Merck KGaA, Germany

16.55 **Shifting Attrition in Drug Discovery Using Toxicogenomics**

Toxicity remains a major hurdle in drug development. We are using gene expression signatures to evaluate compounds in vitro for their toxic properties. These signatures were developed using microarrays, but have since been transferred to a higher throughput platform. Ultimately, this assay will result in drugs with better safety profiles.

Dr Jeffrey F. Waring, Group Leader, Toxicogenomics, Abbott Laboratories, USA

17.20 **High Content Screening in Drug Discovery for Assessing Human Toxicity Potential**

We evaluated a multi-parametric, live cell, pre-lethal cytotoxicity assay for assessing the potential of compounds for causing human toxicity. For 120 drugs with varying degrees of toxicity, the sensitivity of our in vitro assay was 85%. Specificity of these in vitro assays was >90%, thereby minimizing false

our in vitro assays was 85%. Specificity of these in vitro assays was >90%, thereby minimizing false positive results. However if the 10% results that were equivocal were excluded, the sensitivity would be 95% and the specificity 100%. Mitochondrial function, cell count and intracellular calcium concentration were the most predictive in vitro assays of drug toxicity, depending on the mechanism of toxicity. The failure of the assay to detect human toxicities was largely attributable to the metabolic incompetence of the cell line used for the assay and immune-mediated toxicity. Most of these toxicities were considered attributable to formation of reactive metabolites that were frequently linked with oxidative stress. Future work needs to focus on developing metabolic competence, using incubation with S9 microsomal fractions and/or using more metabolically competent cells. Additionally, the assay needs to include a measure of oxidative stress. More non-toxic drugs need to be tested to accurately assess the frequency of false positives. Toxicity-attrited compounds and compound sets that have been historically used to evaluate toxicity screens also need to be tested.

Dr Peter J. O'Brien, Head of Discovery Toxicology Biomarkers, Pfizer Global Research & Development, UK

17.35 **Technology Tutorial**
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18.00 Close of day Two