Focusing on Targeted Covalent Drugs how to best identify and develop TCIs

Roche, Basel, Switzerland

10 April 2025

Delegate book

Contents

Click to go directly to section – return to Contents via button in footer

Programme - all times are CET

08.30 - 09.00 **Registration and coffee**

09.00 - 09.05 **Welcome by Sherri Dudal, VP, Global Head Translational DMPK-PD and Clinical Pharmacology (TPCP) at Roche**

09.00 - 10.30 **SESSION 1: Introduction to aspects of TCIs and proteomics approaches**
Session Chair: Matthias Wittwer, Roche

- **1-1 Chemoproteomics approaches to assess selectivity and target engagement of covalent drugs**
  Marcus Bantscheff, Roche
- **1-2 CellEKT: a chemical proteomics platform to profile cellular kinase engagement**
  Joel Rüegger, University of Leiden
- **1-3 Proteome-wide reactivity and selectivity of diverse electrophiles**
  Stephan Hacker, University of Leiden

10.30 - 11.00 **Coffee break**

11.00 - 12.30 **SESSION 2: PK and PKPD considerations for TCIs**
Session Chair: Rowan Stringer, Novartis

- **2-1 Predicting human pharmacokinetics for TCIs**
  Rowan Stringer, Novartis
- **2-2 Parameter Sensitivity and Scaling in Translational PKPD Models of Covalent Binders**
  Frederik Rode, Lundbeck
- **2-3 Target half-life and PKPD-considerations**
  Neil Parrott and Jitao David Zhang, Roche

12.30 - 13.30 **Lunch**

13.30 - 15.00 **TCI case-examples**
Session Chair: Holger Scheible, Merck

- **3-1 Discovery and development of remibrutinib**
  Robert Pulz, Novartis
- **3-2 DMPK learning from the discovery of Osimertinib**
  Nicola Colclough, AstraZeneca
- **3-3 Evobrutinib – Insights from DMPK**
  Holger Scheible, Merck

15.00 - 15.30 **Panel discussion (All)**

- **Critical issues with TCIs (e.g., balancing potency and reactivity, clearance prediction and achieving mass balance-recovery >90%) and approaches to address them**

15.30 - 16.00 **Coffee break**

16.00 - 17.00 **Novel approaches and new chemistry**
Session Chair: Stefanie Zimmermann, Bayer

- **4-1 Towards a Chemical Biology platform for the systematic discovery and evaluation of novel covalent drugs**
  Sebastian Essig, Bayer
- **4-2 Warhead Chemistry for Targeted Covalent Inhibitors: What Comes Next?**
  Matthias Gehringer, University of Tübingen

17.00 - 17.15 **Meeting close**

DMDG COURSES

Pharmacokinetics in Drug Discovery course
19 - 22 May 2024
Burleigh Court, Loughborough, UK

Methods for Bioanalysis and Drug Metabolism course
24 – 27 June 2025
Burleigh Court, Loughborough, UK

Fundamentals of DMPK course
7 - 9 October 2025
Burleigh Court, Loughborough, UK

***In Vitro* Technology course**
17 - 20 November 2025
Burleigh Court, Loughborough, UK

MEETINGS & WORKSHOPS

DDI 2024 - Marbach DDI Workshop
1 - 3 June 2025
Supported by DMDG
Marbach Castle, Germany

Early Careers meeting 2025
3 June 2024
Nottingham Trent University, UK

6th Biotransformation workshop
2 – 4 September 2025
Churchill College Cambridge, UK

Open Meeting 2025

2 – 4 September 2025
Churchill College Cambridge, UK

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Click the arrow to return to the Contents

Meeting organisers' biographies *(by last name)*

Lee Crossman, *Labcorp*

Lee has enjoyed a rewarding and diverse career in in vivo drug metabolism spanning over 30 years. Having worked for GSK in the UK and Schering-Plough in the US as an in-vivo Subject Matter Expert, specialising in tissue distribution and human dosimetry he moved to Covance (now Labcorp) in 2009 taking up a position as an in vivo SME - designing and running pre-clinical pharmacokinetic and ADME studies, as well as human AME studies. During this time he has been involved in a number of refinements to techniques and contributed to a number of journal articles and webinars. The CRO environment offers a breadth of different molecules in a wide array of therapeutic areas and encompasses in vivo studies from discovery screening, through regulatory pre- clinical species to GCP phase 1 studies. He is a strong advocate for animal welfare (3Rs) and sits on the Labcorp AWERB committee and been an advocate in more welfare friendly DMPK study designs across multiple species. Previously he fulfilled the role of Secretary for the European Society for Autoradiography and was involved in arranging and running conferences and training courses for over 20 years. Latterly, he has also been instrumental in the organisation and running of the bi-annual DMDG tissue distribution course. As a long-time supporter of the DMDG, he has presented both oral and poster presentations at Open/One day meetings and thinks it's important that the DMDG gives a voice to new scientists as well as the opportunity to meet up with old colleagues.

Felix Huth, *Novartis*

Dr. Felix Huth has a broad scientific background in PK sciences. Originally, a chemist by training with an emphasis on analytical organic chemistry, he has received his PhD from the University of Göttingen, Germany. After a position in a biotechnological start up company, he joined Altana Pharma as PK scientist for biotransformation. He could extend he knowledge in bioanalytics, enzyme and transporter kinetics and PBPK modeling before joining Novartis as team lead PBPK modeling. His current work involves early and late stage transporter science, PBPK modeling and general DDI strategies for projects.

Holger Scheible, *Merck*

Click here to see Holger's bio in the Speakers' section

Rowan Stringer, *Novartis*

Click here to see Rowan's bio in the Speakers' section

Beth Williamson, *MSD*

Beth graduated with a PhD in Pharmacology from the University of Liverpool and now Heads the UK DMPK group at MSD. Previously Beth was the Head of ADME in the DMPK group at UCB where she also represented DMPK on small molecule, PROTAC and peptide projects throughout discovery and development. Prior to UCB, Beth was a DMPK lead at AstraZeneca, focusing on small molecules and PROTACs and leading the DMPK efforts in predictive modelling.

Beth's work has focussed on *in vitro* and *in vivo* ADME assay optimisation and validation within drug discovery, particularly to address bespoke questions. Beth has worked in the fields of oncology, neurology and immunology. Her main research interests include drug-drug interactions, extrapolation of pre-clinical *in vitro* and *in vivo* data for the prediction of human pharmacokinetics and application of AI/ML approaches within DMPK.

Matthias Wittwer, *Roche*

Matthias Wittwer received his PhD in pharmaceutical sciences from the University of Basel in 2010. After a postdoctoral stay at the University of California, San Francisco (UCSF) in the laboratory of Kathy Giacomini, he started his industry career in 2013 at Bayer Pharma in Germany as a lab head and project leader in the department of Research Pharmacokinetics. In 2016, Matthias moved into a new role as drug metabolism and pharmacokinetics (DMPK) lab head and project leader for development projects at Bayer before joining Roche as DMPK and pharmacodynamics (PD) project leader in 2017. He works mostly on small molecule and ASO projects, driving their DMPK optimization and contributing to the successful development of novel drugs in different therapeutic areas.

Stefanie Zimmermann, *Bayer*

Stefanie studied pharmaceutical sciences at the University of Basel, Switzerland and received her PhD in 2013 from the University of Basel and Swiss TPH as a pharmacist. After a postdoc at Bayer AG with the focus on hepatic and intestinal transporters, she started as a lab head in research DMPK at Bayer AG 2015 and supported with her team for a decade drug discovery and lead optimization programs. She is the co-founder of Dual FIIa/Xa BAY 3389934 (currently in Phase I) and facilitates with her second role as protein binding scientific expert the Bayer R&D portfolio.

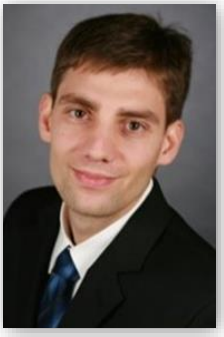
Speakers' biographies *(by last name)*

Marcus Bantscheff, *Roche*

Marcus Bantscheff graduated in Chemistry at the University of Konstanz and obtained his PhD degree from the University of Rostock working with Prof. Glocker on structure-function correlation of bacterial response regulator proteins utilizing mass spectrometric and protein chemistry methods. As a postdoctoral fellow at the Proteome Center in Rostock, Marcus was involved in setting up a proteomics unit and focused on the analysis of synovial fluids and tissue samples derived from rheumatoid arthritis patients and CIA mice. At Cellzome since 2002 he led the proteomics team, and joined GSK upon Cellzome's acquisition in 2012 where he served as Senior Scientific Director and Senior Fellow leading the proteomics/metabolomics platforms within Functional Genomics Department. Marcus' published work focuses on the development and application of proteomics and chemical biology approaches to characterize targets, disease mechanisms and mechanism-of-action of bioactive molecules. He is an inventor on several patents including Cellzome's Kinobeads™ technology, has co-authored more than 100 publications, and serves as a reviewer for reputed journals and funding bodies. His research awards include the Life Science price of the German Society for Mass Spectrometry, in 2016 and the MCP Lectureship, in 2019. In September 2024, Marcus joined Roche as Head of the Proteomics and Metabolomics 360 Lab in Basel.

Nicola Colclough, *AstraZeneca*

Nicola is a principal scientist in oncology DMPK at AstraZeneca, Cambridge, UK and has over 30 years of industrial experience in the drug discovery field. A physical organic chemist by training Nicola gaining her PhD at the University of York, UK working in the group of Professor John Lindsay-Smith studying porphyrins as models for peroxidases and cytochrome P450s. She joined the Structural and Physical Sciences Section at Zeneca at Alderley Park, Cheshire UK where she became Physical Chemistry group leader with responsibility for providing physicochemical property support for all discovery projects at the site including Oncology, Cardiovascular, Respiratory and Inflammation areas. Nicola is currently a DMPK Project Leader within Oncology R & D at AstraZeneca, Cambridge, UK where she works on discovery projects ensuring molecules are designed with good druglike properties. Nicola's interests include the study of ADME properties and understanding their relationship to molecular structure, covalently binding drugs and the design of molecules targeting the brain.



Sebastian Essig, *Bayer*

Sebastian Essig studied chemistry and biology at the University of Heidelberg, Germany and obtained his PhD in organic chemistry in 2013. Subsequently, he joined the group of Prof. Jason Chin at the MRC Laboratory of Molecular Biology in Cambridge, U.K., where he completed his postdoctoral training in chemical biology and synthetic biology. In 2016 he started at Bayer AG as a medicinal chemist where he was involved in different drug discovery programs such as the FXIa inhibitor program leading to Asundexian (currently in Phase III). He is currently Director of Chemical Biology in Bayer's Chemical Biology, Imaging and Omics subcluster focusing on chemoproteomics, covalent chemistry, novel target discovery and target deconvolution strategies.

Matthias Gehringer, *University of Tübingen*

Matthias studied chemistry at the Karlsruhe Institute of Technology (KIT; Germany), the Ecole Nationale Supérieure de Chimie de Montpellier (ENSCM; France), and the University of Heidelberg (Germany). He obtained his doctorate from the University of Tübingen (Germany) where he worked in the group of Prof. Stefan Laufer on reversible and irreversible inhibitors of the protein kinase JAK3. As a postdoc at the Swiss Federal Institute of Technology (ETH) Zürich (with Prof. Karl-Heinz Altmann), he focused on the total synthesis of complex natural products from the mycolactone family. In 2019, he was appointed as Assistant Professor for Medicinal Chemistry at the Institute of Pharmaceutical Sciences, University of Tübingen, and Associate Investigator in the Cluster of Excellence "Image Guided and Functionally Instructed Tumor Therapies (iFIT)". In May 2024, he was appointed as Full Professor and head of the Division for Medicinal Chemistry at the Institute of Biomedical Engineering of the Faculty of Medicine, University of Tübingen. His research in the areas of Medicinal Chemistry and Chemical Biology focuses primarily on covalent protein kinase inhibitors and novel approaches for the covalent targeting of cysteine and other amino acids. He received a variety of awards including the Young Investigator Award of the German Pharmaceutical Society and very recently the Phil Portoghese Lectureship Award of the American Chemical Society MEDI division.

Stephan Hacker, *University of Leiden*

Dr. Stephan M. Hacker performed his PhD studies with Prof. Andreas Marx at the University of Konstanz, Germany, and his postdoctoral research with Prof. Benjamin Cravatt at The Scripps Research Institute in La Jolla, USA. Afterwards, he moved to the Technical University of Munich, Germany, to work as an independent group leader. In 2021, he became an Assistant Professor at the Leiden Institute of Chemistry. Stephan Hacker's group develops chemistries for novel covalent protein ligands targeting diverse amino acids as well as chemoproteomic technologies to study their target engagement with resolution of the modified amino acid residue in proteome-wide studies. His group focuses on the application of these compounds and technologies to identify new druggable target proteins in bacteria.

Neil Parrott, *Roche*

Neil is a distinguished scientist in translational modelling and simulation which is a part of Pharmaceutical Sciences at Roche Basel. Has is with Roche for 27 years where he is a specialist in physiologically based modelling, supporting projects at the preclinical phase with first in human dose predictions as well as for multiple other applications during discovery and development.

Robert Pulz, *Novartis*

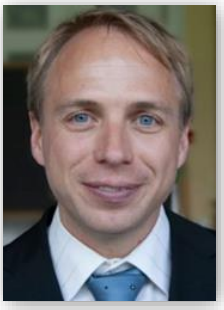
Robert Pulz obtained his chemistry diploma from Technische Universität Dresden, Germany, in 1999 and received his PhD in 2002 from Freie Universität Berlin, Germany, under the supervision of Prof. Hans-Ulrich Reissig. He then moved to the United States for post-doctoral studies with Prof. Robert K. Boeckman at the University of Rochester, NY. In 2004, he joined Novartis Biomedical Research in Basel, Switzerland as a medicinal chemist. There, he contributed to various discovery projects in the fields of musculoskeletal, respiratory, and autoimmune diseases, including leading the MedChem discovery project that resulted in the identification of the covalent BTK inhibitor remibrutinib. He is currently a Director and group leader in the Discovery Chemistry department.

Frederik Rode, *Lundbeck*

Frederik is a senior principal scientist at Lundbeck in Copenhagen. With 21 years of post-PhD experience, he specializes in using pharmacokinetics (PK), pharmacodynamics (PD), quantitative systems pharmacology (QSP), and AI tools to drive dose predictions from early research through first-in-human studies.

Joel Rüegger, *University of Leiden*

Joel began his scientific career with a three-year apprenticeship in medicinal chemistry at Roche Basel, followed by a Bachelor's in Molecular Life Sciences (Muttenz, Switzerland) and a Master's in Chemistry (Leiden, Netherlands). He completed his PhD in the Molecular Physiology group at Leiden University under Prof. Mario van der Stelt, developing a chemical proteomics platform to profile kinase inhibitors. Joel now continues this work as a Postdoc in a collaboration between Leiden University and Roche.



Holger Scheible, *Merck*

Holger studied pharmacy at the University in Tübingen, Germany. He obtained his PhD in Medicinal Chemistry in 2007 from the University of Tübingen, where he worked in the group of Prof. Stefan Laufer on the pharmacokinetics and metabolism of novel p38 MAP kinase inhibitors. He started his industry career as GLP bioanalytics lab head at the Institute of DMPK of Merck KGaA in Grafing; shortly after joined the metabolism field as principal scientist in Regulatory ADME. In 2015 he moved to the Darmstadt site of Merck Healthcare KGaA, where he was responsible for setting up a discovery Biotransformation lab, and afterwards a development radioactive Biotransformation lab. Holger is currently heading the Biotransformation group within NCE DMPK of Merck as Scientific Director with broad responsibilities and interests from early metabolic stability assays to human mass balance studies.

Rowan Stringer, *Novartis*

Rowan is an Associate Director in the Pharmacokinetic Sciences (PKS) department at Novartis, Basel, Switzerland and has over 30 years of industrial experience in the drug discovery and development. A biochemist by training gaining his PhD at the University of Manchester, UK working in the group of Professor Brian Houston studying in vitro drug metabolism models the prediction of human pharmacokinetics. He joined the PKS department initially in Horsham, UK and in 2014 relocated to Basel Switzerland, providing DMPK support for discovery and clinical projects at the site mainly supporting the Immunology therapeutic area. Rowan is the PKS global scientific lead for targeted covalent inhibitors at Novartis.

Jitao David Zhang, *Roche*

Jitao David Zhang is a computational biologist working since 2011 at Roche Basel. His current research interests are three-fold: first, leveraging protein abundance, turnover, and activity for drug discovery and development; second, predicting ADME and PK profiles of emerging modalities; third, causal analysis of attritions and failures of drug-discovery projects.

A delegate list follows on the next page

Delegate List *(Alphabetical by surname, showing only those who chose not to be excluded)*

Ms Isabelle Anderka Roche	**Switzerland**	**Mr Marcus Bantscheff** F Hoffmann-la Roche Ltd	**Switzerland**
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Dr Lea Bouche Roche	**Switzerland**	**Mr Marco Brandstaetter** Roche	**United Kingdom**
Mr Marco Brandstaetter Roche	**United Kingdom**	**Dr Andreas Brink** F Hoffmann-la Roche Ltd	**Switzerland**
Dr Pietro Brunetti F. Hoffmann-La Roche Ltd	**Switzerland**	**Dr Daria Bulanova** Orion Pharma	**Finland**
Dr Giuseppe Cecere F. Hoffmann-La Roche	**Switzerland**	**Dr Nicola Colclough** Astrazeneca	**United Kingdom**
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Dr Luca Docci F Hoffmann-la Roche Ltd	**Switzerland**	**Mr Cosimo Dolente** Roche	**Switzerland**
Dr Sherri Dudal Roche	**Belgium**	**Mr Zachary Enlo-Scott** Kings College London	**United Kingdom**
Dr Simone Esposito Selvita	**Croatia**	**Dr Sebastian Essig** Bayer AG	**Germany**
Dr Holger Fischer F Hoffmann-la Roche Ltd	**Switzerland**	**Dr Stephen Fowler** F Hoffmann-la Roche Ltd	**Switzerland**
Ms Emilia Francesco Roche	**United Kingdom**	**Dr Christophe Fromont** KALVISTA Pharmaceuticals ltd	**United Kingdom**
Mr Matthias Gehringer University of Tubingen	**Germany**	**Dr Mattias Gheringer** University of Tübingen	**Germany**

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Mr Martin Howard York Bioanalytical solutions	**United Kingdom**	**Dr Felix Huth** Novartis Pharma AG	**Switzerland**
Mr Tobias Kaster Novartis	**Switzerland**	**Dr Ben-Fillippo Krippendorff** Institut De Recherche Pierre Fabre	**France**
Dr Jakob Lang F Hoffmann-la Roche Ltd	**Switzerland**	**Dr Grit Laue** Novartis / BR	**Switzerland**
Dr Hugues Lemoine EDELRIS	**France**	**Dr Yumeng Li** Roche R&D Center (China) Ltd	**China**
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Dr Christian Markert Novartis BR, Global Discovery Chemistry	**Switzerland**	**Dr Robert Marks** Bayer AG	**Germany**
Dr Ilonka Meerts Symeres	**Netherlands**	**Dr Sergio Menta** F. Hoffmann-La Roche Ltd	**Switzerland**
Dr Stephan Menz Bayer AG	**Germany**	**Dr Stefanie Mesch** Hoffmann-La Roche AG	**Switzerland**
Dr Michael Niehues Bayer AG	**Germany**	**Mr Axel Pähler** F Hoffmann-la Roche Ltd	**Switzerland**
Dr Neil Parrott F Hoffmann-la Roche Ltd	**Switzerland**	**Dr David-Pierson Pascale** F Hoffmann-la Roche Ltd	**Switzerland**

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Dr Frederik Rode Mette Rode	**Denmark**	**Mr Fedor Romanov-Michailidis** Roche	**Switzerland**
Mr Joel Ruegger Leiden University	**Netherlands**	**Mr Mark Savage** Unilabs York Bioanalytical Solutions	**United Kingdom**
Dr Heiko Schadt Novartis Pharma AG	**Switzerland**	**Mr Frank Scheffler** Hypha Discovery Limited	**United Kingdom**
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Dr Pascal Schulthess Certara	**Switzerland**	**Dr Simone Schulz** Bayer AG	**Germany**
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Mr Bernd Steinhuber F. HOFFMANN-LA ROCHE AG (Kreditorenbuchhaltung)	**Switzerland**	**Dr Rowan Stringer** Novartis Pharma AG	**Switzerland**
Miss Joana Teigao Novartis	**Switzerland**	**Mr Andreas Topp** F Hoffmann-la Roche Ltd	**Switzerland**
Mr Charles TOURNILLAC F. HOFFMANN-LA ROCHE	**Switzerland**	**Dr Clemens-Jeremias von Buehler** Bayer Pharma AG	**Germany**
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Dr Stefanie Zimmermann Bayer AG	**Germany**	**Mr Bill Zuercher** Roche	**United Kingdom**