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Welcome

Dinner Short Courses

Immuno-Oncology

Novel Approaches for Cancer

Sponsor & Exhibit Opportunities

Hotel & Travel Information

Registration Information

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CancerBiotherapeutics.com

Cambridge Healthtech Institute's Inaugural

# Cancer Biotherapeutics

14-16 March 2016 DoubleTree by Hilton Hotel - Docklands Riverside, London UK

Exciting developments, in-depth discussions, and focused short courses from academia and industry

Final Weeks to Register!

Featured Presenters: \_\_\_\_\_



**Sergio A. Quezada, Ph.D.**  
Professorial Research Fellow,  
Research Haematology, University  
College London Cancer Institute



**Dario Neri, Ph.D.**  
Professor, Chemistry and Applied  
Biosciences, Swiss Federal Institute of  
Technology (ETH), Zurich



**John McCafferty, Ph.D.**  
CEO, IONTAS



**Martin Pule, Ph.D.**  
Senior Lecturer, Haematology,  
UCL Cancer Institute



**Stefan Dübel, Ph.D.**  
Managing Director and Professor,  
Biotechnology, Technische  
Universität Braunschweig

Conference Tracks: \_\_\_\_\_

14-15 March

## > Immuno-Oncology

*Harnessing the Immune Response and  
Overcoming Inhibitory Factors*

15-16 March

## > Novel Approaches for Cancer

*Target Selection, Engineering, Optimisation  
and Development of Bispecifics, Fusion  
Proteins and ADCs*

This Event Features: \_\_\_\_\_

- An equal balance of academic and industry presentations
- In-depth coverage of immunotherapy in both tracks
- Targets and lead selection
- ADCs, fusion proteins and models for translation studies
- Located beside the river in a modern, vibrant part of London

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250 First Avenue, Suite 300,  
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# Hotel & Travel Information

## Host Hotel:

DoubleTree by Hilton Hotel - Docklands Riverside, London, UK  
265 Rotherhithe Street, London,  
SE16 5HW, United Kingdom  
Phone: +44- 207-231-1001

## Discounted Room Rate:

£139 s/d (\$215 US)  
includes breakfast  
February 8, 2016

## Discounted Room Rate Cut-off Date:

Please visit the travel page of  
[www.cancerbiotherapeutics.com](http://www.cancerbiotherapeutics.com)  
for additional information and  
to book your hotel.

## Reasons to Stay at the DoubleTree by Hilton Hotel London - Docklands Riverside:

- Complimentary internet in guest rooms
- Complimentary Breakfast
- Complimentary hotel ferry service to Canary Wharf business district and Thames Clipper



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# Dear Colleague,

Research in Cancer Biotherapeutics is progressing in leaps and bounds with rapid and exciting developments taking place with many different approaches. Cambridge Healthtech Institute, who bring you PepTalk and PEGS Protein & Antibody Engineering Summits, Imvacs and more, are responding by introducing a European event concentrating solely on this topic.

Both tracks focus strongly on immunotherapy, with case studies on immune checkpoint inhibitors, agonistic and immunomodulatory approaches, immunocytokines, chimeric antigen receptors, retargeting T cells, immunomodulatory bispecifics, oncolytic immunotherapy, and the role of dendritic cells. We also broaden the scope with presentations on targets and lead selection, fusion proteins, ADCs, and on recreating the tumour microenvironment for translational studies.

For this inaugural event we have chosen central London, knowing that this will appeal to academics and industry experts. Our venue is right beside the river in Docklands, now a very modern and vibrant location.

Sincerely,

**Nicole Lyscom, Ph.D.**  
Senior Conference Director  
Cambridge Healthtech Institute

# Cancer Biotherapeutics

“I very much like the broad scope of the program, with some very innovative approaches. Moreover, it is good to see the “Immunomodulatory Bispecifics” topic emerging so quickly. //”

*Stefan Dübel, Ph.D., Managing Director and Professor, Biotechnology, Technische Universität Braunschweig*

“You have put together an amazing meeting. //”

*Sergio A. Quezada, Ph.D., Professorial Research Fellow, UCL Cancer Institute*



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# Dinner Short Courses\*

TUESDAY, 15 MARCH, 2016, 18:30 – 21:30

“A really great line up of speakers and topics”

*Kerry Chester, Ph.D., Professor, UCL Cancer Institute*



## SC1: Cancer Immunotherapy

*Sergio A. Quezada, Ph.D., Professorial Research Fellow, Research Haematology, University College London Cancer Institute*

*Andrea van Elsas, Ph.D., CSO, BioNovion B.V.*

Distinct from other paradigms in medical oncology, cancer immunotherapy aims to treat the patient's immune system. During the past few years, antibodies targeting T-cell checkpoint proteins demonstrated unprecedented clinical responses and long-term benefit in patients diagnosed with melanoma and other advanced cancers. Beyond anti-PD-1 and anti-CTLA-4, other pathways and therapeutic agents are rapidly being translated to clinical practice alone or in combination approaches.

**Attend this short course to obtain an overview of:**

- Clinically validated and novel targets and modalities
- What we can learn from clinical success and failure
- Current understanding why some patients are responding to checkpoint inhibitors and others are not
- Personalised cancer vaccines
- Rational combinations and why these are necessary
- Outlook for immunotherapy as a treatment for cancer

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14-15 March 2016

# > Immuno-Oncology

*Harnessing the Immune Response and Overcoming Inhibitory Factors*

## MONDAY, 14 MARCH

### 07:30 Registration and Morning Coffee

### 08:30 Chairperson's Opening Remarks

*Robert Williams, Ph.D., Chief Drug Development Scientist, Cancer Research UK Centre for Drug Development*

## AGONISTIC APPROACHES

### 08:40 CARS and "Armoured" CARS

*Renier Brentjens, Ph.D., Director, Cellular Therapeutics Centre, Memorial Sloan Kettering Cancer Centre*

### 09:10 Preclinical Development of the Human CD40 Agonistic Antibody ADC-1013

*Peter Ellmark, Ph.D., Principal Scientist, Alligator Bioscience*

Increasing the response rate while minimising toxicity can be achieved by directing the immune activation to the tumour. Alligator Bioscience currently evaluates intratumoural administration of a CD40 agonistic antibody (ADC-1013) in the clinic. The mode of action of ADC-1013, as well as the anti-tumour effects of combinations with other immune modulating antibodies have been evaluated in hCD40 transgenic mice in multiple syngeneic tumour models.

### 09:40 Preclinical Evaluation of an Anti-ICOS Agonist Antibody

*Jennifer Michaelson, Ph.D., Director, Research, Tumour Biology, Jounce Therapeutics*

Jounce is developing an agonistic antibody to the co-stimulatory molecule ICOS (Inducible CO-Stimulator molecule). Preclinical studies demonstrate that anti-ICOS antibodies are efficacious in syngeneic tumour models, with enhanced efficacy observed in combination with PD-1 inhibition. Mechanistic studies demonstrate agonistic effects of the antibody on T effector cells as well as preferential reduction of T regulatory cells. Together these data provide the rationale for development of a candidate antibody to be evaluated in the clinic in monotherapy and combination therapy settings. The lead anti-ICOS antibody is currently in IND-enabling studies.

### 10:10 Rapidly Screening a Novel Affinity Scaffold Library for PD-L1 Inhibitors Using the iQue Platform

*Matt Johnson, Ph.D., CTO, Avacta Life Sciences*

### 10:25 Costimulatory T-cell Engagement by Bispecific CD137 Agonists PRS-343 (CD137/HER2) and PRS-342 (CD137/GPC3)

*Andrea Allersdorfer, Senior Group Leader, Protein Analytics, Pieris Pharmaceuticals, Inc.*

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We have generated CD137-targeting bispecifics designed to promote CD137 clustering by bridging CD137-positive T cells with HER2- or GPC3-positive tumor cells, thereby providing a potent costimulatory signal to tumor antigen-specific T cells. Data supporting the mode of action and favorable drug like properties of PRS-343 and PRS-342 will be presented.

### 10:40 Coffee Break with Exhibit and Poster Viewing

## ADDITIONAL IMMUNOSTIMULATORY APPROACHES

### 11:20 Role of Isotype in Immunomodulatory Antibody Function

*Ann White, Ph.D., Senior Research Fellow, Faculty of Medicine, Cancer Sciences Unit, University of Southampton*

Monoclonal antibodies (mAb) that stimulate the immune system are revolutionising cancer treatment, delivering durable responses in previously untreatable disease. However, not all patients and tumours respond and toxicity can be problematic. In this talk I will review recent data examining the role of mAb isotype and Fc GAMMA receptor interaction in dictating mAb activity and discuss ways to optimise immunostimulatory agents through mAb engineering.

### 11:50 Hexavalent TNFR-Superfamily Agonists for Cancer Treatment and Immune Modulation: TRAIL, CD27L, CD40L and Beyond

*Oliver Hill, Ph.D., Vice President, Molecular Biology, Apogenix GmbH*

Apogenix has developed a fusion protein technology to create hexavalent agonists targeting individual members of the TNFR-superfamily. Compared to conventional approaches using agonistic antibodies, Apogenix compounds mimic the three-dimensional organisation of the natural ligands (the TNFSF proteins). Consequently, their activity does not rely on secondary crosslinking events *in vitro* nor *in vivo*. We will present the molecular engineering concept and the current results obtained for the TRAIL-R-, CD40- and CD27-agonists.

### 12:20 Humanized Mice for Evaluation of Immuno-Oncology Therapeutics

*Brian Soper, Ph.D., Technical Information Scientist, The Jackson Laboratory*

JAX *In Vivo* Pharmacology Services has combined the human CD34+ hematopoietic stem cell engrafted NSGTM (005557) and NSGTM-SGM3 (013062) mice with human patient derived xenograft (PDX) to create two new platforms for humanized preclinical studies in immuno-oncology. Non-HLA matched PDX tumors grow well, despite concerns over transplant rejection. When treated with Keytruda® (pembrolizumab), an antibody that blocks PD1/PD-L1 binding, tumor growth was significantly diminished. This showed human T cells could be induced to respond to PDX following treatment with a check-point inhibitor. The humanized mouse platform enables further research into both the basic biology and development of therapeutics in human immuno-oncology.

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**12:50 Luncheon Presentation** (*Sponsorship Opportunity Available*) or  
**Lunch on Your Own**

**13:20 Session Break**

## IMMUNE CHECKPOINT INHIBITORS

**14:15 Chairperson's Opening Remarks**

*Björn Frendeus, Ph.D., CSO, BiolInvent International AB*

### » KEYNOTE PRESENTATION



#### 14:20 Immune Regulation at the Tumour Site Defining the Interplay between Therapy and the Tumour Microenvironment

*Sergio A. Quezada, Ph.D., Professorial Research Fellow, UCL Cancer Institute*

In recent years, a number of publications have demonstrated the essential role that the tumour microenvironment and Fc Receptors play in the *in vivo* activity of checkpoint targeting antibodies. In this talk we will discuss novel developments in this area relating to the mechanism of action and the development of immune modulatory antibodies, and combinations that promote intra-tumoural Treg with maximal modulatory activity.

**14:50 Identification of Checkpoint Inhibitors to Antibody Therapy Regulatory T Cells and Myeloid-Derived Precursors**

*Björn Frendeus, Ph.D., CSO, BiolInvent International AB*

A patient-centric phenotypic discovery platform for identification of antibody:target pairs with superior immune cell modulatory activity is described. F.I.R.S.T™ utilizes the high-affinity human antibody library n-CoDeR®, primary cancer-patient's cells, differential biopanning, and state-of-the-art *in vitro* and *in vivo* oncoimmunology models, to identify novel receptors and receptor functions. Preclinical PoC has been obtained through identification of the antibody checkpoint inhibitor (FcγRIIB) as a prime target to overcome antibody drug resistance in lymphoma. Current focus is on identifying targets and mAb capable of specifically deleting cancer Treg cells, or re-educating tumor-associated myeloid cells, to help improve anti-cancer immunity.

**15:20 Refreshment Break with Exhibit and Poster Viewing**

**16:00 Monoclonal Antibodies Targeting Innate Immunity Checkpoint Receptors**

*Nicolai Wagtmann, Ph.D., CSO, Innate Pharma*

NK cells can recognise and kill tumour cells, while sparing healthy tissues. In patients with Acute Myeloid Leukemia, NK cells can prevent tumour relapse and significantly prolong survival, providing a rationale for developing targeted therapeutics that boost NK cell-mediated anti-tumour activity. The talk will describe the rationale and mode-of-action of some of the first-in-class therapeutic antibodies targeting NK cell checkpoint receptors that Innate Pharma is developing for treatment of cancer.

**16:30 Anti-Regulatory T Cells: An Alternative Approach to Target Immunosuppressive Mechanisms**

*Mads Hald Andersen, Ph.D., D.Sc. Tech., Professor, Director, Centre for Cancer Immune Therapy, Copenhagen University Hospital*

We have recently described how these naturally-occurring specific T cells recognise both regulatory immune cells as well as malignant cells. The ability of self-reactive T cells to react to and eliminate regulatory immune cells can influence general immune reactions. Thus, utilisation of e.g. IDO- or PD-L1-derived T-cell epitopes may represent an attractive vaccination strategy for targeting cancer cells and for boosting the clinical effects of additional anti-cancer immunotherapy.

**17:00 Problem Solving Roundtable Discussions**

**Table 1: Novel Diagnostics to Determine the Mechanism of Anti-PD1/PDL1 Failure**

*Moderator: Holbrook E. Kohrt, M.D., Ph.D., Assistant Professor, Oncology, Stanford University*

- Multiplex Ion Beam Imaging (MIBI)
- T-cell receptor (TCR) analysis
- Single cell gene expression profiling
- Nanostring technology

**Table 2: Fcγ Receptors and Therapeutic Antibody Function**

*Moderator: Ann White, Ph.D., Senior Research Fellow, Faculty of Medicine, Cancer Sciences Unit, University of Southampton*

- Antibody isotype and therapeutic function
- Activatory versus inhibitory FcγR binding
- Target deletion, blocking and agonistic receptor engagement
- Combination therapies: Can multiple mechanisms be exploited?

**Table 3: Pros and Cons of Immunocytokine-Based Immunotherapeutics**

*Moderator: Dario Neri, Ph.D., Professor, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology (ETH), Zurich*

- Rationale for choice of immunocytokines and how they can act in synergy
- MOA of the immunocytokines in inducing both local and systemic responses
- Benefits of using immunocytokines as opposed to ADCs
- Means of overcoming the challenges of dose limitation and side effects

**Table 4: Challenges with Targeting Immune Checkpoint Inhibitors**

*Moderator: Sergio A. Quezada, Ph.D., Professor and Research Fellow, UCL Cancer Institute*

- Different ways in which the immune response is "checked" in cancer
- Screening antibodies to the desired target
- Finding appropriate mouse models for proof-of-concept
- Finding good antibody-screening assays

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### Table 5: Challenges of CART-Cell Immunotherapies

Moderator: Martin Pule, Ph.D., Senior Lecturer, Haematology, UCL Cancer Institute

- Different CAR T-cell approaches and their limitations
- Target selection, screening and validation for targeted delivery
- Means of overcoming the need for a customized approach
- Platform development, and product optimization
- Biomarkers for safety and efficacy
- Risk of cytokine release syndrome

18:00 Welcome Reception with Exhibit and Poster Viewing



19:00 End of Day One of Immuno-Oncology

## TUESDAY, 15 MARCH

### 08:30 Chairperson's Remarks

Sergio A. Quezada, Ph.D., Professor and Research Fellow, UCL Cancer Institute

## CHIMERIC ANTIGEN RECEPTOR TECHNOLOGY

### »» FEATURED PRESENTATION



#### 08:35 Engineered T Cells Focusing on Advanced CAR Engineering

Martin Pule, Ph.D., Senior Lecturer, Haematology, UCL Cancer Institute

### 09:05 Cutting Off the Supply Lines: Engineering T Cells to Target the Tumour Vasculature

Steven P. Lee, Ph.D., Senior Research Fellow, Institute of Immunology and Immunotherapy, University of Birmingham

### 09:35 Controlling CAR-T Cell Function *in vivo* Using Molecular Switches

Aaron Foster, Ph.D., Senior Director, Product Discovery, R&D, Bellicum Pharmaceuticals

Regulating CAR-T survival, persistence and expansion *in vivo* following adoptive transfer is critical for maximising therapeutic efficacy while also managing CAR-T-related toxicity. We present two molecular switches, inducible Caspase-9 (iCasp9) and inducible MyD88/CD40 (iMC), which can be used as "Off" and "On" signals, respectively, to control T-cell behaviour *in vivo* using systemic administration of the small molecule dimerising ligand, rimiducid.

### 10:05 The Humoral Immune Response in Cancer and Translational Implications for the Design of Antibody Therapies



Sophia N. Karagiannis, Ph.D., Senior Lecturer in Translational Cancer Immunology, and Head, Cancer Antibody Discovery and Immunotherapy, St. John's Institute of Dermatology, Division of Genetics and Molecular Medicine, King's College London

The nature and roles of the B cells and the antibodies they produce

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in solid tumours remain largely unexplored. We provide evidence to support the presence of an active B cell immune surveillance in tumours and the contribution of mature memory B cells with distinct immunoglobulin isotype-biased profiles. Shedding light into the humoral immune compartment in cancer can inform the design of more effective immunotherapies.

### 10:35 Coffee Break with Exhibit and Poster Viewing

## CYTOKINES / ONCOLYTIC IMMUNOTHERAPY

### 11:10 Advances with IL-2-Based Cancer Immunotherapies

Onur Boyman, M.D., Professor, Chairman and Director, Immunology University Hospital Zurich

Interleukin-2 (IL-2) immunotherapy has resulted in some remarkable long-term responses with advanced cancer, but at the high doses used for cancer immunotherapy, it can cause adverse effects mediated via its binding to IL-2 receptor  $\alpha$  (also termed CD25), leading to endothelial cell damage and expansion of CD4+ regulatory T cells. I will report on studies on avoiding contact of IL-2 with CD25, while preserving IL-2's immune stimulatory anti-tumour effects. The current state of the art of IL-2-based cancer immunotherapies, implications, and future research directions will be discussed.

### 11:40 ADAM17: A Gatekeeper in Immuno-Oncology?

Peter Lowe, Ph.D., Project Leader, Molecular and Cellular Biology, Institut de Recherche, Pierre Fabre

ADAM17 a cell surface sheddase, releases a wide range of membrane bound growth factors, receptors, adhesion molecules, cytokines and chemokines. Deregulated ADAM17 shedding of EGFR ligands including amphiregulin, epiregulin, TGF $\alpha$  and HB-EGF has been implicated in a range of cancers. Recent discoveries demonstrate that ADAM17 also sheds at least fifteen immunoregulatory proteins, enhancing immune suppression and permitting tumour escape from immune surveillance. These will be reviewed in this presentation.

### 12:10 Immune Responses Following Intrapleural Administration of the Oncolytic Immunotherapeutic HSV, Seprehvir, in Patients with Malignant Mesothelioma.

Joe Conner, Ph.D., CSO, Virttu Biologics Ltd.

Seprehvir is a clinically active oncolytic immunotherapeutic HSV administered to 93 patients via intratumoural, locoregional and intravenous delivery routes. Preclinical data supports Seprehvir's oncolytic and immunotherapeutic MoA and its potent combinatorial activities with other cancer therapies including Immune Checkpoint Inhibitors and ACT. Our current phase 1/2a trial of Seprehvir given intrapleurally in MPM is providing fascinating insights into patient immune responses to oncolytic immunotherapy with increased Th1 cytokines and localised immune cell recruitment.

### 12:40 End of Immuno-Oncology

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15-16 March 2016

# > Novel Approaches for Cancer

*Target Selection, Engineering, Optimisation and Development of Bispecifics, Fusion Proteins and ADCs*

**TUESDAY, 15 MARCH**

## RETARGETING T CELLS WITH BISPECIFICS

**13:00 Conference Registration**

**14:00 Chairperson's Opening Remarks**

*Stefan Dübel, Ph.D., Managing Director and Professor, Biotechnology, Technische Universität Braunschweig*

**14:05 Preclinical Evaluation of a CD3/CD33-Bispecific T-Cell-Engaging Antibody with Potential for Treatment of Acute Myelogenous Leukemia**

*Matthias Friedrich, Ph.D., Director, Nonclinical Development, Amgen Research (Munich) GmbH*

CD33 has been frequently selected as target antigen for acute myeloid leukemia therapy. AMG 330 is a Bispecific T-cell engager (BiTE®) antibody construct mediating redirected lysis of CD33-positive cells by cytotoxic T cells. *In vitro* and *in vivo* studies support clinical development of AMG 330 for the treatment of acute myeloid leukemia.

**14:35 Bispecific TCR-Anti-CD3 Fusions for Potent Re-Directed Killing of Cancer Cells: Safety and Efficacy Evaluation Using Assessment in a Predictive *in vitro* Preclinical Package**

*Luise Weigand, Ph.D., Team Leader, Cell Biology/Research Management, Immunocore Ltd.*

ImmTACs are bispecific pico-molar affinity T-cell receptors fused to an anti-CD3 specific scFv that re-direct a potent T-cell response towards its target. Here we present how we approach our *in vitro* preclinical package, used to evaluate safety and efficacy, and the predictability of this process for our most advanced molecule IMCgp100 currently in a Phase I/II study.

**15:05 A  $\kappa$ body Bispecific Platform Approach that Tethers Blockade of the 'Don't Eat Me' Signal to Cancer Cells**

*Marie Kosco-Vilbois, Ph.D., CSO, Novimmune SA*

To overcome potential pharmacological and clinical liabilities of universally targeting CD47, we have developed bispecific  $\kappa$ l bodies, which selectively target CD47 on cancer cells. These  $\kappa$ l bodies are full-length bispecific IgGs that bind with high affinity and neutralise CD47 on cancer cells expressing a tumor-associated antigen (TAA), thus, focusing cell killing to cancer cells. Currently, various  $\kappa$ l bodies are in development, e.g., for B cell malignancies (CD47/CD19) and mesothelin-positive tumors (CD47/Mesothelin).

**15:35 Sponsored Presentation (Opportunity Available)**

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Some of the most promising emergent biopharmaceuticals for cancer therapy include agents capable of selective homing to the tumor environment, as well as drugs capable of selective activation of the immune system against malignant cells. //

*Dario Neri, Ph.D., Professor, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology (ETH), Zurich*

**15:50 Refreshment Break with Exhibit and Poster Viewing**

## IMMUNOMODULATORY BISPECIFICS

**16:30 Discovery and Characterisation of Immunomodulatory Bispecific Antibodies**

*Mark Throsby, Ph.D., CSO, Merus BV*

The Biclomics® platform is a robust and validated technology suite for the development of human full length IgG bispecific antibodies. In this presentation we will outline how the technology has been applied to generate bispecific antibody candidates against checkpoint inhibitory and costimulatory molecules.

**17:00 Development of a Bispecific Targeting EGFR and CTLA-4**

*Neil Brewis, Ph.D., CSO, F-star Biotechnology Ltd.*

F-star creates unique Fcab™ antibodies by engineering the constant region against a single target, which can be combined with the variable regions of differing antibodies to create a bispecific. This technology was used to generate a constant region against EGFR and combining with the variable domain of CTLA-4. The ensuing EGFR/CTLA-4 bispecific showed efficacy in an *in vivo* model compared to either EGFR or CTLA-4 alone.

**17:30 CEA TCB, a Novel T-Cell Bispecific Antibody for the Treatment of Solid Tumors**

*Marina Bacac, Ph.D., Head, Cancer Immunotherapy, Roche Innovation Center Zurich.*

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CEA TCB is a new generation T-cell bispecific antibody for the treatment of CEA-expressing solid tumors. Its activity correlates with CEA expression level resulting in efficient elimination of high CEA-expressing tumour cells and sparing of primary epithelia. CEA TCB is efficacious *in vivo* in poorly-T-cell infiltrated solid tumors. It converts non-inflamed into highly-inflamed tumors accompanied by T-cell re-localisation from the periphery into tumor bed. The combination with PD-L1 enhances CEA TCB activity.

### 18:00 End of Day One of Novel Approaches for Cancer

### 18:00 Dinner Short Course Registration

### 18:30 – 21:30 Dinner Short Courses\*

#### SC1: Cancer Immunotherapy

*Sergio A. Quezada, Ph.D., Professorial Research Fellow, Research Haematology, University College London Cancer Institute*

*Andrea van Elsas, Ph.D., CSO, BioNovion B.V.*

*\*Separate Registration Required.*

## WEDNESDAY, 16 MARCH

### DEVELOPMENTS WITH FUSION PROTEINS

#### 08:30 Chairperson's Remarks

#### » KEYNOTE PRESENTATION



#### 8:35 Antibody-Cytokine Fusion Proteins (Immunocytokines) for Targeted Delivery: From Bench to Phase III

*Dario Neri, Ph.D., Professor, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology (ETH), Zurich*

Antibody-cytokine fusion proteins ("immunocytokines") are a promising class of immunomodulatory agents, which are currently being considered for the treatment of cancer and of chronic inflammation. In this lecture, I will present aspects of our preclinical and clinical experience with immunocytokines specific to splice isoforms of fibronectin and of tenascin-C.

#### 09:05 Multivalent Antibody-TRAIL Fusion Proteins for Cancer Therapy

*Roland Kontermann, Ph.D., Professor, Biomedical Engineering, Cell Biology and Immunology, University of Stuttgart*

Fusion of TRAIL to antibody fragments has been shown to allow for a targeted delivery and the selective induction of tumour cell death. We have engineered optimised single-chain derivatives of TRAIL and different homodimerisation models to develop novel multivalent antibody-scTRAIL fusion proteins with improved properties. Targeting and controlled dimerisation of scTRAIL fusion proteins provides a strategy to enforce apoptosis induction, together with retained tumor selectivity and good *in vivo* tolerance.

#### 09:35 Problem Solving Roundtable Discussions

##### Table 1: Antibodies that Harness the Immune System

*Moderator: Kerry Chester, Ph.D., Professor, UCL Cancer Institute*

- Target selection criteria
- Engineering challenges
- Relevant animal models
- How to overcome the challenges of scale, safety and efficacy

##### Table 2: Pros and Cons of Armed Antibody Products

*Moderator: Dario Neri, Ph.D., Professor, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology (ETH), Zurich*

- Benefits of different types of product in terms of potency, stability and versatility regarding targets and use in combination therapies
- Pros and cons of intact antibodies versus scaffolds
- Choice of target: membrane proteins versus extracellular matrix proteins
- Delivery considerations

##### Table 3: Screening of Antibody Libraries

*Moderators: John McCafferty, Ph.D., CEO, IONTAS*

*Stefan Dübel, Ph.D., Managing Director and Professor, Biotechnology, Technische Universität Braunschweig*

- Display technologies for the creation of antibody libraries
- Tailored selection and screening strategies
- Antibody library designs for affinity optimisation

##### Table 4: Overcoming the Challenges of ADCs and Technologies for the Construction of Next Generation ADCs

*James Baker, Ph.D., Senior Lecturer, Chemistry, UCL*

- How to select the right linker and toxin for your product
- Challenges with linkers
- Novel drugs and payloads
- Challenges with site-specific conjugation
- Safety concerns and challenges with toxicity
- Optimization of stability, potency, specificity and homogeneity

##### Table 5: Translational Considerations for Development of Biotherapeutics

*Moderator: To be Announced*

- PDXs and challenges
- Personalized medicine in cancer research
- Organoid models
- Circulating tumor cell/models
- Microfluids and future of 3D models

#### 10:35 Coffee Break with Exhibit and Poster Viewing

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## TECHNOLOGIES FOR TARGETS AND LEAD SELECTION

### 11:15 Chairperson's Remarks

Kerry Chester, Ph.D., Professor, UCL Cancer Institute

#### » FEATURED PRESENTATIONS



#### 11:20 Engineering Antibodies and T-Cell Receptors by Mammalian Display

John McCafferty, Ph.D., CEO, IONTAS

Generation of immune-modifying binders is facilitated by the availability of large libraries of antibodies or T-cell receptors expressed on the surface of mammalian cells. We demonstrate the construction and use of mammalian display libraries, facilitated by the use of site-specific nucleases. Such libraries allow the screening of millions of clones by flow sorting while providing information on both the level of expression and the extent of binding within individual clones.



#### 11:50 Comprehensive Human Antibody Libraries and Human Effector Fusions: Impact on Next Generation Cancer Therapeutics

Stefan Dübel, Ph.D., Managing Director and Professor, Biotechnology, Technische Universität Braunschweig

Two decades of antibody engineering have brought substantial gains in knowledge on how to make good human antibodies for therapy, but also on obstacles to their clinical use. It has also become evident that IgG alone cannot cure cancer in most cases, which has sparked the search for additional and novel effector mechanisms. We present our newest advances in both human antibody generation and effectors.

#### 12:20 High Expression of Bispecific Tandem scFvs and Tribody [(Her2)2X CD 16] in CHO Cells Transfected via Scalable Electroporation

Sponsored by MaxCyte

Peer Heine, Ph.D., Field Application Scientist, MaxCyte, Inc.

Success means getting to market fast. Therefore, fast and efficient protein production for drug candidate development, characterization, and selection is

critical. Creating a stable cell line for clinic trial, takes months to more than a year for complicated proteins. High efficiency, scalable electroporation can reduce stable cell line development timelines by up to 50%, even in difficult-to-transfect cell lines. In this presentation, data will show the rapid production of proteins and cell lines at different scales.

#### 12:50 Luncheon Presentation (Sponsorship Opportunity Available) Or Lunch on Your Own

#### 13:20 Session Break

#### 14:00 Chairperson's Remarks

Kerry Chester, Ph.D., Professor, UCL Cancer Institute

## DEVELOPMENTS WITH ADCs

#### 14:05 Chemical Platform for the Construction of Highly Defined Therapeutic Antibody Conjugates

James Baker, Ph.D., Senior Lecturer, Chemistry, UCL

A powerful and general chemical platform technology is described for the construction of highly defined antibody conjugates by site-selectively targeting and bridging the interchain disulfide bonds. This approach allows access to antibody-drug conjugates, designed to release potent cytotoxins specifically at targeted cancer cells, with a controlled drug to antibody ratio (DAR) and high serum stability. Insights will also be given into the scope for further applications e.g. in bispecifics, imaging, radioimmunoconjugates etc.

#### 14:35 Development of Natural Product Derived Splicing Inhibitors as Antibody Drug Conjugate Payloads

Sujiet Puthenveetil, Ph.D., Principal Scientist, Medicinal Chemistry, Pfizer, Inc.

Analogues of the natural product spliceostatin are highly potent spliceosome inhibitors with a novel mechanism of action that are currently being explored as payloads for antibody drug conjugates (ADCs) for the treatment of cancer. A medicinal chemistry initiative was greatly facilitated by an optimized fermentation process that produced gram quantities of these payloads allowing for subsequent linker attachment, conjugation and screening to yield highly efficacious ADCs. We will describe the early challenges with efficacy and safety of this class of molecule and how these were overcome by synthesis and conjugation efforts.

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CancerBiotherapeutics.com](#)**15:05 Endogenous Vaccination: Kadcyla Renders HER2+ Breast Cancer Highly Susceptible to Immune-Checkpoint Blockade**

*Philipp Müller, Ph.D., Lab Head, Biomedicine University & University Hospital of Basel*  
ADCs such as Kadcyla harbour the potential to act as an endogenous anti-tumour vaccine. In this presentation I will demonstrate that Kadcyla is particularly effective in eliciting anti-tumour immunity in a HER2-expressing, orthotopic tumour model and breast cancer patients. Our data reveal a novel immunological mechanism of action for this class of ADC and provide a strong rationale for clinical combinations with immune-checkpoint blockade.

**15:35 Refreshment Break with Exhibit and Poster Viewing****ROLE OF DENDRITIC CELLS IN IMMUNOTHERAPY / ROBUST MODELS FOR TRANSLATIONAL STUDIES****16:00 Clinical Trials with mRNA Electroporated Dendritic Cells for Stage III/IV Melanoma Patients**

*Kris Thielemans, Ph.D., Professor, Immunology & Oncology, Vrije Universiteit Brussel*

We present convincing data of the clinical responses induced by a “next generation” dendritic cell based immunotherapy, in combination with checkpoint blockade and in an adjuvant setting.

**16:30 Close of Conference**

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## Cancer Biotherapeutics

14-16 March 2016

DoubleTree by Hilton Hotel - Docklands Riverside  
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### Pricing & Registration Information

#### DINNER COURSE PRICING

	Commercial	Academic, Government, Hospital-affiliated	Student*
1 Short Course	£449	£249	£99
15 March 2016   18:30 – 21:30	15 March 2016   18:30 – 21:30		
SC1: Cancer Immunotherapy	SC2: Engineering and Optimisation of Antibody Products		

#### CONFERENCE PACKAGE PRICING

**STANDARD PACKAGE - Includes two conferences, excludes short courses**

Registration Rate after 12 February 2016 and on-site	£1899	£899	£349
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**BASIC PACKAGE - Includes one conference, excludes courses**

Registration Rate after 12 February 2016 and on-site	£1399	£649	£249
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*\*Pre-doctoral, full-time student*

14 - 15 March 2016	15 - 16 March 2016
T1: Immuno-Oncology	T2: Novel Approaches for Cancer

#### CONFERENCE DISCOUNTS

Poster Discount	£35	£35	£35
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**Poster Submission:** Poster abstracts are due by 12 February 2016. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact jring@healthtech.com.

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