



APPLIED PHARMACEUTICAL TOXICOLOGY

May 5-7, 2026
ABBVIE | CAMBRIDGE, MA

PROGRAM GUIDE

PRESENTED BY OUR SPONSORS:



ABOUT OUR SPONSORS



STEMCELL TECHNOLOGIES supports toxicologists and drug developers with high-quality tools, cells, and services for more predictive, human-relevant in vitro assays. With over 30 years of experience providing the biological components that support new approach methodologies (NAMs), we supply fresh and frozen human primary cells, iPSC-derived cells, and specialized cell culture media, including reagents for organoids and other complex models. Our portfolio of cell isolation kits and culture systems helps streamline workflows, improve reproducibility, and generate decision-driving data across toxicology and drug discovery programs. For groups seeking to outsource, our Contract Assay Services team can partner with you to design and execute custom studies using primary cell- and organoid-based systems. By combining reliable cell sourcing, innovative culture solutions, and expert scientific support, STEMCELL helps you build more predictive models to assess toxicological hazards.



APCONIX Our lab team conduct hERG and CiPA cardiac screening assays and have developed an in vitro assay to better understand seizure liability (iSLA®). We continue to carry out research in other fields relevant to efficacy and safety in the CNS.

The ApconiX Safety Science Team combines toxicology expertise and advanced data science, offering customized Acuity® target safety assessments (TSAs). The team also conducts modality or asset focused reports and will support you in understanding and optimizing project safety profiles.

Our consultancy team provide a flexible nonclinical drug safety and DMPK support to your discovery and development team.



CYPROTEX Founded in 1999, Cyprotex (www.cyprotex.com) has grown to become an industry leader in in vitro and in silico ADME-Tox. The company, with sites in the UK and USA, was acquired by Evotec (www.evotec.com) in 2016. The Evotec Group offer expert support from early discovery through to clinical development.



SOUTHERN RESEARCH is a nonprofit research institute with 85 years of experience and nearly 200 employees turning scientific discovery into real-world impact. We collaborate with industry, government, and academic partners to accelerate the development of life-saving therapies. Our legacy includes landmark contributions in cancer treatment, infectious disease, and translational medicine, and with expanding state-of-the-art facilities and deep expertise in drug discovery and translational science, we continue to drive biomedical innovation and bring new treatments closer to those who need them.



TOXPLUS MONITORING (www.TOXPLUS.com) provides flexible, global, end-to-end nonclinical support to help biotech and pharmaceutical teams move their drug development programs forward with confidence.

We partner with companies from early discovery through IND-enabling studies and beyond to provide toxicology support, study management, study monitoring, vendor qualification and audits, regulatory writing, and data QC. Our focus is to help teams progress their timelines efficiently while maintaining strong scientific rigor and regulatory readiness. Our team brings decades of experience supporting programs across the U.S., EU, and Asia.

We'd be happy to connect and explore how we can support your nonclinical drug development team.



VIVOSIM LABS is a biotechnology company advancing human-safety decision-making in drug development through its proprietary NAMkind™ 3D liver and intestine models, which use primary human cells to deliver more predictive, human-relevant toxicology data than traditional 2D or animal-based approaches. As a New Approach Methodology (NAM) provider, VivoSim partners with drug developers at three decision-critical points—prospective screening during hit-to-lead and lead optimization, translational bridging through candidate nomination and IND-enabling studies, and on-demand investigative toxicology when unexpected findings arise—offering bespoke study designs, species-specific variants, and modular assay panels spanning hepatocyte function, barrier integrity, oxidative stress, inflammatory markers, gene expression, and histopathology. By flagging human-specific liver and GI liabilities before costly animal studies or clinical trials, VivoSim helps sponsors de-risk compound selection, clarify cross-species relevance, and advance promising candidates with greater confidence and speed.

ORGANIZERS' WELCOME

Welcome to the 2026 Applied Pharmaceutical Toxicology Conference.

Our organizers have gathered another excellent group of speakers for the annual APT conference. The program is arranged to incorporate extensive audience participation and discussion. We encourage attendees to take full advantage of the opportunity to engage in discussion in order to receive the maximum benefit from the APT experience. Thank you for your participation.

ORGANIZING COMMITTEES

Presiding Officers

Chair: Kathryn Fraser, Merck

Chair-Elect: Michael Kerins, Eli Lilly

DISCOVERY

Toxicology Workshop Organizers

Chair: Kathryn Fraser, Merck

Chair-Elect: Michael Kerins, Eli Lilly

Committee:

Jodi Goodwin, Takeda
Jonathan Heyen, Treeline Bio
Satoko Kakiuchi-Kiyota, Genentech
Prathap Kumar Mahalingaiah, AstraZeneca
Rama Pai, Merck
Sunjay Sethi, IDEAYA Biosciences
Yoav Timsit, Novartis
Gina Yanocho, Johnson & Johnson
Helen Yu, Vertex

DEVELOPMENT

Toxicology Workshop Organizers

Chair: Yuan Lu, CinRx Pharma

Chair-Elect: Betty Pettersen, Alexion

Committee:

Surekha Akella, AbbVie
Satheesh Anand, Boehringer Ingelheim
Joe Cichocki, Vertex
Birgit Fogal, Sanofi
Emma Karey, AstraZeneca
Yu-Mee Kim, Genentech
Heather Kowalski, Organon
Jon Maher, Pliant
Christine Mollica, Amgen
Daniella Pizzurro, Merck
Michael Santostefano, Merck
Radha Sura, Gilead
Nardos Tassew, The Janssen
Pharmaceutical Companies of Johnson &
Johnson

APT 2026 CONFERENCE AGENDA

TUESDAY, MAY 5

DISCOVERY TOXICOLOGY WORKSHOP

- 8:00 - 9:00 **Registration & Breakfast**
- 9:00 - 9:10 **Conference Opening and Plenary Speaker Introduction**
Kathryn Fraser, Merck
- 9:10 - 9:50 **PLENARY LECTURE:**
DILI Risk Prediction: Focus on Mechanism
Jack Uetrecht, University of Toronto

SESSION I: Obesity Drugs - Toxicology Insights for GLP-1 and Peptide Therapeutics

Moderators: Michael Kerins, Eli Lilly & Rama Pai, Merck

- 9:50 - 9:55 **Session Introduction**
- 9:55 - 10:20 **Body Weight Modulation: Contributors and Cardiometabolic Health Consequences**
Qi Sun, Harvard
- 10:20 - 10:45 **Navigating the Nuances: Key Considerations in Peptide Toxicology Strategy**
Wei Wang, Eli Lilly
- 10:45 - 11:10 Break
- 11:10 - 11:35 **Addressing Safety Concerns of GLP-1 Receptor Agonists - A Case Study**
John Vahle, Eli Lilly
- 11:35 - 12:00 **VENDOR PRESENTATION:**
Intestinal and Hepatic Organoid Systems: In Vitro Models of Drug Toxicity
Riya Sharma, Stemcell Technologies
- 12:00 - 1:15 Lunch
- 1:15 - 1:25 **VENDOR PRESENTATION:**
Southern Research Institute: The Oldest US CRO?
Bill Coode, Southern Research



SESSION II: Incorporating the Immune System into Discovery Toxicology

Moderators: Prathap Kumar Mahalingaiah, AstraZeneca; Kathryn Fraser, Merck, and Jonathan Heyen, Treeline Bio

- 1:25 - 1:30 **Session Introduction**
- 1:30 - 1:55 **Immune System Evaluation and Immunopathology Considerations in Discovery Toxicology**
Tracey Papenfuss, StageBio

- 1:55 - 2:20 **Integrating T-Cell Engagers: Evolution, Preclinical Safety Packages in Oncology**
Nirav Patel, AstraZeneca
- 2:20 - 2:45 **Exploring Hapten Formation in Anti-Drug Antibody Development**
Sophie Tourdot, Pfizer
- 2:45 - 3:10 Break

SESSION III: AI in Toxicology - From Prediction to Oversight/Decision-Making

Moderators: Jodi Goodwin, Takeda & Yoav Timsit, Novartis

- 3:10 - 3:15 **Session Introduction**
- 3:15 - 3:40 **Redefining How We Discover Safer Medicines with AI and NAMs**
Russ Naven, Novartis
- 3:40 - 4:05 **AI-enabled Prediction of DILI with Transcriptomics**
Matt Wagoner, Takeda
- 4:05 - 4:30 **AI-powered Translational Safety Intelligence to Anticipate Drug Safety**
Ramon Flores, Clarivate
- 4:30 - 4:55 **From Cell Morphology to Human Safety: Predictive Liver Toxicity Across Cell Types Using Cell Painting and Machine Learning**
Runxi Shen, Broad Institute
- 4:55 - 5:00 Closing Remarks

WEDNESDAY, MAY 6

DISCOVERY TOXICOLOGY WORKSHOP

- 8:00 - 9:00 **Registration & Breakfast**

SESSION IV: NAMs - Case Studies & Practical Application

Moderators: Gina Yanochko, Johnson & Johnson; Satoko Kiyota, Genentech, and Helen Yu, Vertex

- 9:00 - 9:05 **Session Introduction**
- 9:05 - 9:35 **New Approach Methodologies (NAMs): Role of Nonclinical Scientists**
Radha Sura, Gilead
- 9:35 - 10:00 **Use of NAMs to Support Early Safety Assessment in Drug Development**
Rebecca Kohnken, AbbVie
- 10:00 - 10:25 **From Discovery to Safety: Human-relevant Complex In Vitro Models as Fit-For-Purpose Decision Tools**
Xinming Tong, Genentech

10:25 - 10:50 Break

DEVELOPMENT TOXICOLOGY WORKSHOP

SESSION I: NAMS and the FDA Roadmap: Regulatory Evolution & Industry Practice

Moderators: Betty Pettersen, Alexion; Yuan Lu, CinRx Pharma; Birgit Fogal, Sanofi, and Radha Sura, Gilead

10:50 - 10:55 **Session Introduction**

10:55 - 11:35 **PLENARY LECTURE:**
Right-Sizing The Use of Animals In The Nonclinical Safety Assessment
Ron Wange, Alcario Pharmaceutical Development Group/former FDA

11:35 - 12:00 **Nonclinical Toxicology Package To Support The Clinical Development of a T-Cell Engager**
Zhechu Peng, AstraZeneca

12:00 - 12:25 **In vitro Developmental Toxicity Testing of PROteolysis-TArgeting Chimeras (PROTACs)**
Giel Hendriks, Toxys Netherlands

12:25 - 1:40 Lunch

1:40 - 1:45 **Vendor Talk Introduction**

1:45 - 2:10 **VENDOR PRESENTATION:**
Benefits of Early In Vitro Screening for Seizure Liability in Problem Solving and Decision Making
Kim Rockley, AconiX



2:10 - 2:25 Break

SESSION II: Expect the Unexpected: Regulatory Curveballs in Today's Nonclinical Development

Moderators: Satheesh Anand, Boehringer Ingelheim; Surekha Akella, AbbVie; Michael Santostefano, Merck, and Heather Kowalski, BlueRock Therapeutics

2:25 - 2:30 **Session Introduction**

2:30 - 2:55 **Alternative Approaches During T Cell Engager Development: Regulatory Interactions, Scientific Rigor and Reduced NHP Usage**
Petra Lutterbuese, Amgen

2:55 - 3:20 **IQ Survey - Strategies to Reduce NHP Use in the Nonclinical Development of Oncology Therapeutics**
Kaushik Datta, Merck

3:20 - 3:50 **Lost In Translation: From ePPND Study to Label**
Marie Lemper, UCB

3:50 - 4:10 **Round table discussion**

4:10 - 5:25 **Reception**

THURSDAY, MAY 7

8:00 - 9:00 **Breakfast**

DEVELOPMENT TOXICOLOGY WORKSHOP

SESSION III: Next-Generation Biotherapeutics & Complex Modalities

Moderators: Yu-Mee Kim, Genentech; Emma Karey, AstraZeneca, and Nardos Tassew, The Janssen Pharmaceutical Companies of Johnson & Johnson

9:05 - 9:05 **Session Introduction**

9:05 - 9:30 **Nonclinical Safety Considerations for RNA based Complex Biologics**
Sheroy Minocherhomji, Eli Lilly

9:30 - 9:55 **Insights From Evaluations of Two Next-generation Trastuzumab Auristatin Conjugates - Trastuzumab-MMAU and Trastuzumab-AS269**
Onyi Irrechukwu, Johnson & Johnson

9:55 - 10:25 **T Cell Engagers for Non-Oncology Indications: Bench to Bedside Considerations for Dose and Safety**
Kavita Raman, Amgen & Ryan Polli Novartis

10:25 - 10:45 **VENDOR PRESENTATION**
Leveraging NAMs to Derisk Cardiac and Neurotoxicity
Christopher Strock, Cyprotex



10:45 - 11:15 **Break**

SESSION IV: Breaking It Down: Preclinical Development Strategies for Targeted Protein Degraders

Moderators: Jon Maher, Pliant; Christine Mollica, Amgen, and Daniella Pizzurro, Merck

11:15 - 11:20 **Session Introduction**

11:20 - 11:45 **Evolving Discovery Toxicology Strategies for Targeted Protein Degraders**
Rhiannon Harwick, BMS

11:45 - 12:10 **CRBN-Based Degradar Specificity Eliminates Potential Developmental Toxicity**
Matthew Lalonde, Kymera Therapeutics

12:10 - 12:35 **A Novel Bile Duct Toxicity In Dogs Associated With a Heterobifunctional Protein Degradar**
Lise Loberg, AbbVie

12:35 - 12:40 **Conference Closing Remarks**

ABSTRACTS

DISCOVERY TOXICOLOGY WORKSHOP

SESSION I

PLENARY LECTURE

DILI Risk Prediction: Focus on Mechanism

Jack Uetrecht, University of Toronto

Many drug candidates fail during clinical trials because of an unacceptable risk of idiosyncratic drug reactions, especially idiosyncratic drug-induced liver injury (iDILI). Methods to predict iDILI risk during drug development require an understanding of the basic mechanisms involved. It is now clear that iDILI is immune-mediated. Although the adaptive immune response involved is complex, the dominant cell involved in hepatocyte cell death is the cytotoxic CD8+ T cell. The major factors that make iDILI idiosyncratic are the requirement of specific HLA haplotypes to present drug-associated antigens to specific T cell receptors. The idiosyncratic nature of iDILI makes studies difficult. However, an innate immune response to activate antigen presenting cells (APCs) is necessary but not sufficient to activate specific cytotoxic T cells. Unlike the adaptive immune response, the innate immune response is unlikely to be idiosyncratic and could provide biomarkers to predict the risk that a drug candidate will cause iDILI. In most cases the drug, or more likely a reactive metabolite will cause changes in gene expression and the release of damage-associated molecular pattern molecules (DAMPs) from hepatocytes that can activate antigen presenting cells. Such DAMPs can represent biomarkers of iDILI risk. However, some drugs can directly activate APCs, in some cases because they are oxidized by myeloperoxidase in APCs to reactive metabolites. We have found several drugs that cause iDILI cause an increase in the expression of genes such as GDF-15, Dusp-t, Cebpd, etc that likely represent risk biomarkers. In other cases, such as isoniazid and ximelagatran, the drug itself appears to activate APCs. The development of accurate biomarkers of iDILI risk would have a profound effect on drug development.

Body Weight Modulation: Contributors and Cardiometabolic Health Consequences

Qi Sun, Harvard

Obesity has become the leading cause of chronic diseases and premature deaths in the U.S. and exerts tremendous burden to the health care system. Numerous research has been dedicated to understanding the causes and consequences of excess weight gain. Collectively, it becomes a consensus that excess weight gain may stem from unhealthy diets, sedentary lifestyles, genetic predispositions, psychosocial factors, built-environment, as well as their complex interactions. Emerging evidence also suggests the role of environmental pollutants or obesogens, as well as the human gut microbiome, in the etiology of obesity. Meanwhile, effective interventions, ranging from dietary and lifestyle modifications to the GLP-1 receptor agonists, are available for individuals living with obesity to manage their weight. However, despite the effectiveness of achieving short-term weight loss by these approaches, the compliance may diminish over time and weight regain upon the cessation of the interventions is extremely common. Interestingly, the consequences of intentional weight loss and subsequent weight regain can be diverse, at least partially depending on the body weight status before weight loss attempts. This lecture will provide an overview of the primary predictors of excess weight gain, with a special focus on diets, environmental pollutants, and the gut microbiome. The consequences of intentional weight loss and weight regain will be discussed as well.

Navigating the Nuances: Key Considerations in Peptide Toxicology Strategy

Wei Wang, Eli Lilly

Peptide therapeutics continue to expand across therapeutic areas, bringing distinct nonclinical safety assessment challenges that differ from traditional small molecules and large-molecule biologics. Their unique pharmacological and physicochemical properties demand thoughtful, fit-for-purpose toxicology strategies rather than a one-size-fits-all approach. This presentation will explore key strategic considerations in designing and interpreting nonclinical safety programs for peptides, including species selection, study design, managing exaggerated pharmacology, and distinguishing on-target from off-target findings. Real-world examples will be used to

illustrate how these considerations influence decision-making and shape the path from candidate selection through IND-enabling studies. The goal is to foster an open exchange of practical experience and emerging thinking among toxicologists navigating this evolving space.

Addressing Safety Concerns of GLP-1 Receptor Agonists – A Case Study

John Vahle, Eli Lilly

Incretin-based therapies have emerged as highly effective agents for treating cardiometabolic diseases, including type 2 diabetes and obesity. Despite being widely perceived as a recent breakthrough, the study of incretins spans decades, during which numerous scientific challenges had to be overcome in both basic research and clinical development. Among the most significant in the early development of the GLP-1 receptor agonists were safety concerns related to thyroid C-cell tumors, identified through traditional rodent carcinogenicity studies, and pancreatic toxicity, prompted by clinical observations and academic rodent research. This presentation uses a case study approach to describe how both traditional and investigative toxicity studies were employed to evaluate the clinical significance of these findings and guide the safe development of this therapeutic class.

VENDOR PRESENTATION

Southern Research Institute: The Oldest US CRO?

Bill Coode, Southern Research

General overview of Southern Research Institute and current capabilities, including GLP and non-GLP toxicology support, BSL-2/3 vivariums and wet labs, full bioanalytical and biomarker assay support from research grade methods to full validations, a nonhuman primate PK colony, and a world-class quality system.

SESSION II

Immune System Evaluation and Immunopathology Considerations in Discovery Toxicology

Tracey Papenfuss, StageBio

With the rapid and continued growth of complex immune-impacting therapies, it is increasingly important to incorporate and integrate immune system findings early in development

to identify and understand potential risks and immunosafety considerations. An initial understanding of efficacy and potential safety concerns first occurs in the discovery phase of therapy development and can have important and direct implications in later phases of drug development. In this talk, immune system evaluation, immunopathologic changes and immune-mediated events that are important in drug development and can be incorporated into discovery toxicology will be presented.

Integrating T-Cell Engagers: Evolution, Preclinical Safety Packages in Oncology

Nirav Patel, AstraZeneca

T cell engagers (TCEs) are antibody-based molecules that transiently redirect cytotoxic T lymphocytes to eliminate target cells by binding both the T cell receptor and a specific antigen on the target cell. Over the past 12 years, 12 TCEs have been approved by regulatory agencies including the US FDA and EMA, with nine treating hematologic cancers and three for solid tumors. More than 150 TCEs are currently in clinical trials, expanding into autoimmune disease indications. Approved TCEs exhibit diverse molecular designs and biochemical profiles, demonstrating flexibility in development. Clinically, important aspects include varying targets, dosing regimens, side effect profiles, and mitigation strategies. TCEs offer high monotherapy response rates in blood cancers, and growing efficacy in solid tumors and autoimmune diseases, making them a promising therapeutic approach. The presentation will cover the ongoing efforts for TCEs since the first approval in 2014 and discuss preclinical safety assessments, including in vitro and in vivo models addressing immune-related safety challenges in oncology settings.

Exploring Hapten Formation in Anti-Drug Antibody Development

Sophie Tourdot, Pfizer

The development of anti-drug antibodies (ADAs) remains a significant challenge in the advancement of biotherapeutics, with important implications for patient safety and treatment outcomes. Immunogenicity of antibody drug conjugates (ADCs) can be influenced by multiple factors, among which hapten formation has been proposed as a potential contributor. This presentation examines the underlying mechanisms by which chemical entities may elicit CD4 T cell responses, subsequently leading to antibody generation against ADC payload components. Strategies for identifying and mitigating hapten-related risks during the drug design in support of proactive immunogenicity risk management will be discussed.

SESSION III

Redefining How We Discover Safer Medicines with AI and NAMs

Russ Naven, Novartis

In silico and in vitro NAMs promise faster and safer drug discovery, yet persistent rates of preclinical attrition indicate that these tools continue to underdeliver when applied outside of controlled validation paradigms.

Clinical safety data is often treated as the gold standard for NAM development. Whilst essential for patient protection, such data may not be well aligned with the requirements to establish NAMs in preclinical decision-making. Data is sparse with late stage-signals that are often collapsed to binary adverse event outcomes and already biased through established preclinical testing. By contrast, preclinical in vivo studies together with in vitro ADMET datasets produce rich, compoundlinked, organ and timeresolved toxicity data that is well suited for interrogation by AI and datadriven approaches. Early analysis of this data reveals two fundamental limitations. First, toxicity findings in preclinical datasets are frequently less organspecific than implied by conventional annotations, challenging the value of organcentric prediction frameworks. Second, the richness and depth of toxicological information demands new, biologically meaningful representations to fully leverage AI and develop fit-for-purpose in vitro NAMs.

This presentation argues that one key limitation in predictive toxicology lies in how preclinical toxicity data is digitally represented and integrated with the full spectrum of safety data. Given the scale and multidimensional complexity of this data, AI-enabled approaches offer a new opportunity to realistically capture and exploit its full predictive potential.

AI-enabled Prediction of DILI with Transcriptomics

Matt Wagoner, Takeda

Mechanisms of drug-induced liver injury are vast and varied, requiring more complex in vitro models to detect and de-risk DILI preclinically. Here we compare traditional preclinical DILI assays against an AI-enabled whole transcriptome analysis. We find that the AI-enabled transcriptomic assay is able predict DILI driven by innate, immune and cholestatic mechanisms across >100 drugs and drug candidates. This screening strategy enables both early detection, mechanistic insight and predicted margins to clinical hazards.

AI-powered Translational Safety Intelligence to Anticipate Drug Safety

Ramon Flores, Clarivate

Preclinical and clinical safety liabilities continue to be major drivers of attrition in drug research and development, with particularly high economic impact and increased risks to patient safety when they emerge at later stages. In parallel, the volume and diversity of safety relevant data continue to grow, often distributed across fragmented and heterogeneous sources. Effectively integrating insights from these data into timely, evidence-based safety assessments—and keeping them current as new information emerges—remains a significant challenge for drug safety professionals.

This presentation will explore how AI-enabled approaches, grounded in expertly curated safety data from discovery to post-marketing, can support the anticipation and interpretation of safety risks for novel targets and drug candidates. Topics will include the correlation of preclinical findings with clinical outcomes, the contextualization of new observations based on related drugs, targets, or modalities, and the generation of mechanistic hypotheses relevant to risk assessment. Through illustrative examples, the talk will highlight how these approaches can complement and accelerate established toxicology workflows, with the objective of supporting earlier and more informed safety related decision-making.

From Cell Morphology to Human Safety: Predictive Liver Toxicity Across Cell Types Using Cell Painting and Machine Learning

Runxi Shen, Broad Institute

Preclinical models remain poor predictors of human drug-induced liver injury (DILI), a leading cause of attrition and post-market withdrawal. Here, we apply Cell Painting across four cell systems spanning a gradient of species and liver relevance: U2OS, HepaRG, primary human hepatocytes, and primary rat hepatocytes. Profiling roughly 1,200 compounds through the OASIS Consortium, we evaluate how morphological profiles predict human DILI, rat in-vivo hepatotoxicity, cytotoxicity, mode-of-action, and general bioactivity. Across all endpoints, morphology-based predictions consistently outperform baselines derived from cell count alone. Unexpectedly, a non-liver line (U2OS) matches or exceeds liver-relevant models for hepatotoxicity prediction, and rat hepatocytes perform comparably to human hepatocytes for DILI. These results indicate that tissue origin and species may be less deterministic than assumed, and position image-based profiling as a core component of new approach methodologies (NAMs) for

modern safety assessment.

SESSION IV

New Approach Methodologies (NAMs): Role of Nonclinical Scientists

Radha Sura, Gilead

The landscape of drug development and safety assessment is rapidly evolving with the emergence of New Approach Methodologies (NAMs). My talk will focus on NAMs, with particular emphasis on Complex In Vitro Models (CIVMs) such as organ-on-a-chip systems, microphysiological systems, and three-dimensional cellular aggregates. We will examine their current strengths and limitations as tools for advancing drug discovery and safety evaluation. The session will explore why nonclinical safety scientists are essential in this paradigm shift, how they contribute to the optimization and validation of CIVMs, and what role they play in ensuring these models meet regulatory and scientific expectations. Specifically, we will discuss how nonclinical safety scientists collaborate within multidisciplinary teams to guide model design and define the “Context of Use” for CIVMs, characterize cellular and tissue composition for biological relevance, identify and validate predictive biomarkers, and interpret complex morphological and molecular data to build confidence in translatability to human patients. Their involvement is critical for establishing predictivity and regulatory acceptance of NAMs, ultimately reducing reliance on animal studies and accelerating the development of safe therapeutics.

Use of NAMs to Support Early Safety Assessment in Drug Development

Rebecca Kohnken, AbbVie

The utility of new approach methodologies (NAMs) to support the reduction, reuse, and refinement of animals in research has been an enduring strategy for drug developers for decades. In recent years, due in part to increased attention by regulators and the public alike, there has been a resurgence in developing and applying in silico and in vitro models to support nonclinical safety assessment. These efforts have been further bolstered by rapid technological advances, allowing for more complex models that offer a reasonable throughput. The wealth of available models, as well as the lack of clear regulatory guidance for their use, necessitates a thoughtful and strategic approach to model selection and deployment in the investigative toxicology space.

While the overall goal to improve safety prediction is appealing to nonclinical scientists, significant challenges and headwinds to the use of NAMs in safety assessment remain. Despite these, in silico and in vitro models can be used to great effect in support of prospective prediction of safety liabilities based on target and/or modality, as well as retrospective mechanistic investigations. The aim of these approaches may be to identify the mechanism of toxicity, to understand the target relationship of the toxicity, the translatability from preclinical species, or to de-risk future compounds. This talk will feature a strategic paradigm for use of NAMs in safety as well as select case examples.

The author is an employee of AbbVie and may own AbbVie stock. The design, study conduct, and financial support for this research were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the publication.

From Discovery to Safety: Human-relevant Complex In Vitro Models as Fit-For-Purpose Decision Tools

Xinming Tong, Genentech

Complex in vitro models are widely adopted in early drug discovery for rapid candidate screening; however, their use in late-stage safety assessment requires rigorous, regulatory-aligned validation, creating an adoption gap. This presentation outlines a cross-functional strategy that bridges early drug discovery with later-stage development and safety/toxicology assessment to address this challenge. Aligned with the FDA's 2026 Draft Guidance, we demonstrate a framework for transitioning discovery-stage fundamental biology (“Model-omics”) into validated, fit-for-purpose assays within a defined Context of Use (COU). Using examples from Genentech's portfolio, we illustrate how human intestinal organoids can evolve from a screening tool in discovery to a predictive toxicology platform for assessing clinical diarrhea risk. Furthermore, by incorporating advanced functional readouts in airway, adipose, and bone models, we present an integrated approach in which new approach methodologies (NAMs) serve as high-fidelity filters for target rank-ordering. Ultimately, this NAM-enabled strategy ensures that only the safest and most biologically relevant candidates advance to in vivo testing and clinical development.

DEVELOPMENT TOXICOLOGY WORKSHOP

SESSION I

Nonclinical Toxicology Package to Support the Clinical Development of a T-Cell Engager

Zhechu Peng, AstraZeneca

As the field of toxicology evolves to reduce animal use through the application of advanced technologies in nonclinical testing, this talk presents a case example of a T-cell engager program. The talk describes the rationale and decision framework which collectively enabled an oncology clinical trial application without conducting a traditional repeat dose toxicity study. In addition, the talk will examine the subsequent work packages developed to underpin indication expansion for this modality.

In vitro Developmental Toxicity Testing of PROteolysis-Targeting Chimeras (PROTACs)

Giel Hendriks, Toxys Netherlands

Prenatal exposure to teratogenic compounds can lead to significant birth defects. Due to the high variation in drug response amongst species, and the financial and ethical burdens associated with animal testing, the development of advanced human cell-based assays is critical for effectively identifying and classifying potential human teratogens. The ReproTracker assay is a system in which human induced pluripotent stem cells (hiPSCs) are directed through a differentiation pathway towards three germ layer-specific cell types: cardiomyocytes (mesoderm), hepatocytes (endoderm), and neural rosettes (ectoderm). This system enables the assessment of teratogenic potential by tracking alterations in biomarker expression kinetics and observing morphological disruptions in the differentiated cells upon compound exposure.

We evaluated the teratogenic potential and lineage-specificity of a set of seven PROTACs, each utilizing a different E3 ligase (including CRBN, VHL, and MDM2) in ReproTracker. All tested PROTACs, regardless of the E3-ligase specificity, were identified teratogens in ReproTracker at concentrations much lower than those required to exert general cytotoxicity. This case study demonstrates that ReproTracker can reliably assess the teratogenic potential of PROTACs, enhancing the early detection of developmental toxicity risks in these compounds. The assay provides a robust approach for potency ranking and distinguishing lineage-specific toxicity profiles among PROTACs, allowing for more nuanced toxicological evaluations.

Overall, this study expands the applicability of ReproTracker, making it a valuable tool for assessing teratogenicity of PROTACs at early stages of drug development.

VENDOR PRESENTATION

Benefits of Early In Vitro Screening for Seizure Liability in Problem Solving and Decision Making

Kim Rockley, Aconix

Seizure liability remains a significant cause of attrition throughout drug development both in pre-clinical and clinical studies. We have developed an approach utilizing hiPSC-neuronal cell microelectrode array (MEA) and ion channel screening for early seizure prediction. In our MEA assay, seizurogenic compounds were identified correctly with high predictivity, and correlations were observed between the in vitro and clinical exposures of many therapies known to cause seizure. Screening against a panel of seizure-related ion channels has been used to identify hazards in lead optimisation and gain mechanistic insight. In the early phase of nonclinical testing MEA studies can be used to derisk and prioritize a chemical series, whereas later MEA studies can help to understand the results of in vivo studies. This talk will provide example case studies using the in vitro assays and introduce our other work in this area including investigation into structure activity relationships (SAR) of seizure associated ion channels and sedation.

SESSION II

Alternative Approaches During T Cell Engager Development: Regulatory Interactions, Scientific Rigor and Reduced NHP Usage

Petra Lutterbuese, Amgen

Alternative approaches during T cell engager (TCE) development in oncology are increasingly feasible as regulatory expectations evolve and as new approach methodologies (NAMs) mature. This talk describes how an “evidence-first” NAM/weight-of-evidence (WoE) strategy can preserve - or improve - scientific rigor while reducing nonhuman primate (NHP) use in TCE nonclinical development. The talk will summarize the conventional toxicology package for TCEs in oncology and its limitations, including constraints in species relevance, anti-drug antibody-driven loss of exposure, and limited translational value of some animal readouts for first-in-human (FIH) risk assessment. It will then be outlined how

a practical NAM toolbox—human-relevant in vitro functional assays, quantitative modeling (MABEL, PK/PD), robust target biology and expression assessment, and transparent WoE integration—can support targeted animal testing, with the long-term goal of reserving in-vivo studies for cases where they could still inform risk to human safety prior to conduct of clinical trials or marketing approvals. Regulatory interactions and precedents are illustrated through case studies, which highlight both successful acceptances of WoE-based approaches and key “curveballs”, including divergent agency expectations for longer-duration studies. Overall, we propose that thoughtful, science-led packages integrating all available evidence can accelerate decision-making and support a shift toward fewer but more informative animal studies.

IQ Survey - Strategies to Reduce NHP Use in the Nonclinical Development of Oncology Therapeutics

Kaushik Datta, Merck

The use of animals for toxicity testing for pharmaceutical drug development is a balance between providing appropriate data for adequate risk assessment in humans and application of 3Rs principles for animal use. Recent discussions between IQ consortium and US FDA focused on rationalizing nonclinical toxicity testing strategy for oncology therapeutics, taking into consideration of NHP supply constraints and prioritized biomedical research. For the nonclinical development of biologics in oncology indications, prospects were identified for the acceptance of streamlined toxicology packages, without compromising a rigorous safety evaluation, utilizing a) CD3-bispecific antibodies, b) ADCs with cytotoxic payloads and c) biotherapeutics with well characterized targets. Three recent peer-reviewed publications from IQ-DruSafe working groups revealed adequate opportunities to reduce NHP usage by i) optimum study design and ii) assessing the need of studies >1month duration upon comparing toxicity findings between first in human (≤ 1 month duration) and registration enabling (>1 month duration) studies. Overall, these publications indicated that reduced NHP usage is possible upon adequate safety assessment of abovementioned oncology therapeutics.

Lost In Translation: From ePPND Study to Label

Marie Lemper, UCB

Reproductive toxicity studies are conducted to identify, characterize, and mitigate potential risks of pharmaceuticals to fertility, pregnancy, and offspring development. These assessments are typically performed in rodents and rabbits using study designs intended to minimize variability and to cover all stages of gestation. When a therapeutic exhibits

pharmacological activity exclusively in nonhuman primates, an enhanced pre- and postnatal development (ePPND) study is conducted. However, the assessment of pregnancy outcomes in nonhuman primates poses distinct challenges, including high background rates of spontaneous embryo–fetal loss, limited sample sizes, and substantial inter-individual variability. As a result, data interpretation from nonhuman primate studies differs fundamentally from conventional reproductive toxicity evaluations, a distinction that is not always fully recognized during risk assessment. This can influence regulatory decision-making and may unnecessarily constrain the inclusion of pregnant women or women of childbearing potential in clinical development. Case examples from two approved therapies for generalized myasthenia gravis illustrate the importance of integrating biological variability, pharmacological context, and quantitative interpretative frameworks when evaluating nonhuman primate reproductive toxicity data, thereby enabling more consistent and scientifically robust risk assessments.

SESSION III

Nonclinical Safety Considerations for RNA based Complex Biologics

Sheroy Minocherhomji, Eli Lilly

Innovations in genetic medicine are increasingly driven by novel nucleic acid-based therapeutics, particularly those designed to target specific tissues with enhanced precision and safety. Among these, antibody-conjugated oligonucleotides represent a promising modality that have the potential to improve selectivity, targetability, and overall safety by targeting specific cells or tissues. The aim is to improve treatment outcomes for difficult-to-treat diseases with high unmet medical needs, such as neurodegenerative diseases. These complex biologics combine multiple components to achieve targeted delivery of their active payloads to cells or tissues implicated in disease pathogenesis. Their design is intended to increase selectivity and reduce off-target effects, thereby potentially improving the overall safety profile of these genetic medicines. The development of these Bio-conjugated Oligonucleotides (BCOs) requires both large- and small-molecule nonclinical safety attributes and pharmacodynamic evaluations due to their multi-component nature. Key strategies involve understanding the safety margins and the nonclinical toxicity profile of all the components of the BCO, facilitating the transition from preclinical studies to clinical development. These considerations are critical to ensuring the therapeutic's efficacy and patient safety in clinical trials. This presentation will provide an overview of BCOs, nonclinical safety strategies,

and key regulatory and safety margin considerations that enable their clinical development.

Insights from Evaluations of Two Next-Generation Trastuzumab Auristatin Conjugates - Trastuzumab-MMAU and Trastuzumab-AS269

Onyi Irrechukwu, Johnson & Johnson

First-generation antibody–drug conjugates (ADCs) were limited by narrow safety margins likely due to linker and/or conjugation site instability and use of hydrophobic payloads. Here, we evaluate two next-generation trastuzumab (anti-HER2) ADCs—Trastuzumab–monomethylauristatin U (TMMAU), a monomethylauristatin E prodrug with a cleavable, hydrophilic glycopeptide linker conjugated to antibody via stabilized maleimide chemistry, and Trastuzumab–AS269 (ARX788), a monomethylauristatin F derivative with a noncleavable hydrophilic PEG linker conjugated site-specifically to antibody via a stable oxime bond—against the first-generation Trastuzumab–emtansine (TDM1). In highHER2 expressing N87 xenografts, 3 mg/kg TMMAU (DAR4) and 5 mg/kg ARX788 (DAR2) produced 100% and 90% tumor growth inhibition (TGI), respectively, versus ~60% for 5 mg/kg TDM1. In the HER2low JIMT1 xenograft model, ARX788 achieved 79% and 100% TGI at 1 and 3.3 mg/kg, while TDM1 (3.3 mg/kg) was inactive; TMMAU exhibited subnanomolar in vitro potency in JIMT-1 cells. Repeat-dose cynomolgus toxicology studies showed TMMAU was tolerated up to 12 mg/kg (Q3W ×3) with reduced bone marrow cellularity and peripheral hematologic changes; ARX788 was tolerated up to 10 mg/kg (Q3W ×4) with adverse microscopic kidney and rectal findings. Notably, both auristatin conjugates lacked the axonal degeneration observed with TDM1 at doses >3 mg/kg (HNSTD of 10mg/kg, Q3W×4). Clinically, ARX788 delivered 63.8% ORR and a median PFS of 11.3 months versus 43.6% ORR and median PFS of 9.6 months for TDM1 in advanced breast cancer patients who progressed after trastuzumab plus a taxane. ARX-788 demonstrated a more favorable overall tolerability profile with primarily manageable ocular and pulmonary toxicities and markedly lower rates of hematologic and gastrointestinal (GI) toxicity compared to T-DM1 with higher rates of hematologic and GI toxicity and peripheral neuropathy. These results highlight how improved design of linker, payload, and conjugation chemistry in next generation ADCs can widen the therapeutic window and potentially extend activity into lowerHER2 settings while improving tolerability profiles.

T Cell engagers for no-Oncology indications: Bench to Bedside Considerations for Dose and Safety

Kavita Raman, Amgen and Ryan Polli, Novartis

First developed for oncology, T cell engagers (TCEs) are emerging as a promising biotherapeutic class for chronic conditions such as autoimmune and infectious diseases. While they offer potentially transformative benefits, TCEs present distinct safety challenges in the non-oncology space. Current industry practices and regulatory guidance remain largely oncology-focused, leaving important gaps for nononcology indications where patient populations, risk–benefit considerations, and dosing strategies differ substantially. This presentation will attempt to address those gaps by outlining key nonclinical and clinical safety considerations, first-in-human starting dose approaches, and tailored risk mitigation strategies leveraging weight of evidence and model-informed strategies to accelerate development while balancing patient safety and exposure to subtherapeutic doses.

SESSION IV

Evolving Discovery Toxicology Strategies for Targeted Protein Degraders

Rhiannon Harwick, BMS

Targeted protein degraders (TPDs) represent a rapidly evolving drug class that introduces unique toxicology challenges beyond those typically encountered with small molecules. This presentation will highlight key considerations for designing fit-for-purpose toxicology strategies for TPDs, drawing on real-world examples. Topics will include hazard identification, species selection, target profiling, and selectivity assessment, with practical insights into how these factors shape nonclinical decisionmaking.

CRBN-Based Degradation Specificity Eliminates Potential Developmental Toxicity

Matthew Lalonde, Kymera Therapeutics

Cereblon (CRBN)-recruiting targeted protein degraders (TPDs) have emerged as a powerful therapeutic modality, but their development had been accompanied by a key safety concern rooted in the history of immunomodulatory imide drugs (IMiDs). IMiDs such as thalidomide, pomalidomide, and lenalidomide induce degradation of non-native CRBN “neosubstrates,” including transcription factors like SALL4 and PLZF that play critical roles in embryonic development, thereby driving teratogenicity and other toxicities. This neosubstrate-

driven mechanism has raised theoretical concerns that next-generation CRBN-recruiting degraders, many of which share structural features with IMiDs, could similarly induce unintended protein degradation and associated safety liabilities. The breadth and diversity of CRBN neosubstrates, as well as their links to developmental and multi-organ toxicities, highlight the importance of understanding and controlling off-target degradation in this drug class.

Here, we present a case study of KT-474, a selective IRAK4 degrader, to demonstrate how rational design can mitigate these risks. KT-474 was engineered to retain efficient CRBN recruitment while avoiding engagement of known IMiD-associated neosubstrates. Consistent with this design strategy, proteomic analyses across multiple human cell systems showed selective degradation of IRAK4 without measurable effects on neosubstrates implicated in teratogenicity. In vivo, embryo–fetal development studies in rats and rabbits revealed no treatment-related malformations or developmental toxicity at exposures exceeding clinically relevant levels. Together, these findings support the principle that CRBN-mediated teratogenicity is driven by specific neosubstrate interactions rather than CRBN engagement per se, and illustrate that CRBN-recruiting degraders can be purposefully engineered to avoid these liabilities while maintaining therapeutic activity.

A Novel Bile Duct Toxicity In Dogs Associated With a Heterobifunctional Protein Degradator

Lise Loberg, AbbVie

This presentation will be a case study of a novel hepatobiliary toxicity observed in a toxicology study in dogs administered a heterobifunctional protein degrader (Compound X). A mechanistic investigation of the toxicity revealed that cholangiocytes were the target of toxicity. Proteome profiling and high-content imaging highlighted a significant disruption to autophagy. An analog degrader with differentiated physicochemical properties, most notably a reduced pKa, was identified with significantly reduced hepatobiliary toxicity despite similar bile concentration. Together, these data indicate that uptake of the large, basic, and lipophilic Compound X into cholangiocyte lysosomes drives a unique bile duct pathology. This mechanism is a further demonstration of how the physicochemical properties of bifunctional degraders may challenge preclinical development, and its elucidation provides a path forward for development of degrader compounds with improved toxicity profiles.

SPEAKER BIOGRAPHIES

Bill Coode, Southern Research Boston-based and supporting sponsors in New England, Bill has helped pharma and biotech bring their drugs to the clinic for over ten years and has contributed to IND-enabling studies, in vivo and in vitro efficacy, clinical and preclinical assay establishment, and CMC assays.

Kaushik Datta, PhD, Merck Dr. Kaushik Datta (KD) is the Oncology Therapeutic Area Leader at Merck Nonclinical Drug Safety, bringing 25 years of experience in the pharmaceutical industry, with a focus on toxicology and nonclinical drug development. Throughout his career, KD supported numerous regulatory submissions (NDA, BLA and other milestone meetings) for different modalities (small molecules, various mAbs, ADCs and TPDs) for the treatment of oncology and inflammatory/autoimmune diseases. In addition, KD has been actively involved in leadership and working group roles within various industry consortia (DruSafe, HESI, EFPIA, AAPS, NC3R collaboration with MEB) and contributed to scientific and regulatory advancements, resulting in several publications including optimal animal use strategies which align with the 3R principle. KD has also served as a topic lead and presenter at the annual FDA-BioSafe-DruSafe meetings, addressing contemporary issues with proposed resolutions in nonclinical drug development.

KD earned his PhD in Toxicology from The University of South Florida followed by completing a postdoctoral fellowship in mechanistic toxicology at The University of Texas at Austin.

Ramon Flores, PhD, Clarivate Dr. Flores is Lead Product Manager for OFFX, Clarivate's Translational Safety Intelligence platform, and brings over 15 years of experience developing solutions to derisk drug development by bridging toxicology, data, and decisionmaking. He holds a Ph.D. in Medicinal Chemistry and began his career as an R&D scientist. At the Prous Institute for Biomedical Research, he contributed directly to the synthesis and early development of JRP655 (now CTH120), a first-in-class neuroplasticity modulator currently in clinical development for Fragile X syndrome.

Rhiannon N. Hardwick, PhD, DABT, Toxys Dr. Hardwick earned her PhD in pharmacology and toxicology from the University of Arizona and completed postdoctoral training at UNC-Chapel Hill. She began her industry career at Organovo, leading efforts to advance a 3D bioprinted liver model, and later served as a discovery and regulatory project toxicologist at Theravance Biopharma. She is currently a Scientific Director in Discovery Toxicology at Bristol Myers Squibb, San Diego, supporting discovery programs across therapeutic modalities and leading a lab team and crossdepartmental complex in vitro model working group. Rhiannon is a Diplomate of the American Board of Toxicology, an Associate Editor for *Toxicological Sciences*, and an active contributor to multiple professional societies and industry consortia.

Giel Hendriks, PhD, Toxys Dr. Hendriks is the founder and CEO of Toxys. He has developed various in vitro assays to ensure the safety of novel medicines, chemicals and consumer products without the use of animals. He is an expert in genetic toxicology, has co-chaired expert working groups within the HESI Genetic Toxicology Technical Committee (GTTC), is the current president of the Dutch Environmental Mutagen Society and vice-president of the European Environmental Mutagenesis and Genomics Society (EEMGS). Giel has a PhD in molecular cell biology from Utrecht University and worked as a post-doctoral fellow in at Leiden University and Leiden University Medical Center.

Onyi Irrechukwu, PhD, Johnson and Johnson Dr. Irrechukwu is an Associate Scientific Director in Preclinical Sciences and Translational Safety at Johnson and Johnson. In this role, she provides portfolio-level leadership for nonclinical safety strategy and execution across therapeutic areas and modalities, supporting programs from portfolio entry through registration. She currently serves as the Nonclinical Safety SME for RNAi therapies and chairs the Nonclinical Hepatotoxicity group. Onyi represents J&J across several external consortia including IQ DILI and IQ-DruSafe. She joined J&J in 2019 as a Principal Scientist in the Mechanistic and Investigative Toxicology Group and later went on to lead a team of 5 scientists in the Complex Model Systems group advancing in vitro and predictive toxicology platforms. Prior to J&J, Onyi led ADME/Toxicology Services at BioVT (formerly Hepregen) and supported strategic client partnerships. Her earlier career included appointments as an Assistant Professor at the University of Maryland and as a Research fellow at the National Institute of Health. Onyi holds a BSc in Chemical Engineering from the University of Maryland, a PhD in Bioengineering from Georgia Institute of Technology and is a Diplomate of the American Board of Toxicology.

Rebecca Kohnken, DVM, PhD, AbbVie Dr. Kohnken is a veterinary pathologist and toxicologist with 8 years of experience in drug development at AbbVie in Chicago. After obtaining her DVM at University of Wisconsin-Madison, she completed a combined anatomic pathology residency and PhD at The Ohio State University. She currently oversees the Molecular Pathology and Complex In Vitro Models Groups within Preclinical Safety at AbbVie. Rebecca has authored over 40 peer-reviewed publications, 2 book chapters, and over 50 abstracts and posters and national and international meetings.

Matthew Lalonde, PhD, DABT, Kymera Therapeutics Dr. Lalonde is Director of Toxicology at Kymera Therapeutics, where he serves as a project toxicologist for small molecule and targeted protein degrader programs for immunological diseases. He specializes in early-stage safety strategy, adoption of new in vitro platforms, and early proof-of-concept in vivo studies. Prior to Kymera, he was a project toxicologist at Blueprint Medicines and Sumitomo Pharma. Prior to his work in toxicology, he was a protein biochemist and molecular diagnostic assay developer. As a toxicologist, he has supported clinical-stage programs, led IND and regulatory strategies, executed several IND-enabling campaigns and successful IND submissions. Dr. Lalonde received his Ph.D. in Biochemistry from Case Western Reserve University and holds a certification from the American Board of Toxicology.

Marie Lemper, PharmD, PhD, DABT, ERT, UCB Dr. Lemper is a distinguished senior toxicologist and the Head of US Toxicology at UCB. With deep expertise across small molecules, biologics, and gene therapy, she leads UCB's US toxicology function and Digital Toxicology Team and spearheads the Global Nonclinical Safety Strategy for Gene Therapy. Prior to joining UCB, Dr. Lemper served as a toxicologist at Genentech, where she provided nonclinical support from early discovery through late-stage development. A recognized leader in the field, she is a Past President of the Society of Toxicology's Drug Discovery Specialty Section and an active member of multiple professional organizations. Dr. Lemper is a frequent invited speaker on topics ranging from lead optimization to label negotiations, reflecting her comprehensive experience across the drug development lifecycle.

Lise Loberg, PhD, DABT, AbbVie Dr. Lise Loberg has over 20 years' experience in drug development as a toxicologist and scientific director in the biopharmaceutical industry. In her current role she leads a team of scientists from Discovery Research and Development Sciences to advance the novel targeted protein degradation platform from discovery to clinical development in oncology, immunology, and neuroscience. Prior to this role, she held positions of increasing responsibility and influence during her career at Abbott/AbbVie. She has had opportunity to work at three R&D sites (Illinois, California, Germany) and spent several years as a Project Manager on drug development teams. She has experience with small molecules and biotherapeutics development across several therapeutic areas and supported preclinical safety evaluation of compounds from lead selection in early discovery to late-stage clinical trials and marketed drugs. She earned her Ph.D. in Toxicology from the Univ. of Cincinnati (1996) and her B.S. in Psychology & Neuroscience at John Carroll Univ. Prior to joining AbbVie, she led a Molecular Toxicology laboratory at IIT Research Institute (1996-1999). She has served as an officer for the Midwest Regional Chapter of SOT, has been on the planning committee for Applied Pharmaceutical Toxicology annual symposia (2012-2023), is currently serving in both IQ and HESI consortia working groups, and has been an invited speaker at national and international conferences.

Petra Lutterbüse, PhD, Amgen Dr. Petra Lutterbüse is a project toxicologist in the department of Translational Safety & Risk Sciences at Amgen and is based in Munich, Germany. For more than two decades, she has worked on Amgen's Bispecific T cell Engager (BiTE®) technology and its application in the field of cancer immunotherapy. Petra received her PhD in Immunology from the University of Freiburg, Germany and the Max Planck Institute of Immunology, Freiburg in 2003, before joining Micromet, a Munich-based biotechnology company. At the start of her career she supervised a lab responsible for the increasingly sophisticated in vitro and in vivo pharmacologic characterization of BiTE molecules supporting efforts to evaluate their efficacy and bring them to the clinic. She then switched gears, turned towards toxicology and is now a Diplomate of the American Board of Toxicology. With the acquisition of Micromet for its BiTE® platform in 2012, Petra joined Amgen where she now oversees the nonclinical safety assessment of BiTE programs in Amgen's pipeline across various stages of research and development. She has most recently led the nonclinical safety contribution to the Investigational New Drug application for AMG 305, Amgen's first dual targeting T cell engager and is also responsible for pipeline follow-up dual targeting TCEs.

Sheroy Minocherhomji, PhD, ERT, FRSB, Eli Lilly Dr. Minocherhomji is Senior Director of Toxicology at Eli Lilly and Company with 10+ years in pharma spanning regulatory, investigative, and discovery toxicology, including genetic toxicology and across all phases of drug development. He has supported the early to late-stage clinical development of 10+ first-in-class, multi-modality

therapeutics across immunology, oncology, rare genetic diseases, ALS, obesity/T2D, pain, and neurodegeneration. Previously, he was Principal Scientist/Toxicology at Amgen, where he also led the Genetic Toxicology Unit; prior to that he served as Assistant Professor of Genome Stability at the University of Copenhagen. He holds an MSc in Human Molecular Genetics (Imperial College London) and a PhD (University of Copenhagen). A European Registered Toxicologist and Fellow of the Royal Society of Biology, he has secured international funding, authored 25+ peer-reviewed publications (including in *Nature*, *PNAS*, and *Cell Press* journals), is a past President/Chair of the GTA, and is active across GTA, HESI, ACT, EMGS, and SOT societies.

Russell Naven, Novartis Russell Naven leads the Predictive Safety Data Exploration Group at Novartis, where he develops and advances strategies to anticipate and mitigate attrition risks in drug discovery. Russ began his career as a medicinal synthetic chemist and has since spent over two decades focused on how toxicity risk can be better understood, anticipated, and addressed earlier in discovery. One central theme is recognizing that the performance of AI and machine learning models is fundamentally constrained by in vitro biological representation and coverage of underlying in vivo toxicological processes. Rather than treating in vitro safety tools primarily as predictors of organ toxicity, Russ focuses on how they represent functional biological selectivity and how they can be integrated with ADME properties to inform on medicinal chemistry decisions while design flexibility still exists. His vision is to expand predictive safety from a diagnostic function into an AI-enabled steering discipline—one that iteratively improves compound quality during the design stage, increasing their probability of success and enhancing patient safety by elevating the baseline of biological selectivity early in discovery.

Tracey Papenfuss, PhD, StageBio Dr. Papenfuss is a board-certified toxicologic pathologist and Ph.D. immunologist experienced in nonclinical drug development (discovery through safety assessment) with a specific expertise in immunology, pathology and evaluation of discovery and safety assessment studies of immune-impacting and novel immunotherapies. She has previously directed an NIH-funded immunopathology and early discovery immunotherapeutics laboratory studying immunological and anti-inflammatory therapies in a variety of animal models of autoimmunity, immuno-oncology and infectious diseases at The Ohio State University. Since moving from academia, she has worked as a toxicologic pathologist and immunopathology scientific advisor in industry at contract research laboratories including WIL Research, MPI Research, Charles River Laboratories and her current position at StageBio where she evaluates studies across multiple phases of drug development including GLP and non-GLP/discovery studies. Dr. Papenfuss has deep expertise in immunology and pathology which she leverages to promote biomedical research and promotes scientific engagement and consultation across teams to optimize science, operations, business growth, and policy. She is an active member and holds leadership positions in numerous scientific organizations in toxicology, pathology and immunology (e.g. ACT, SOT, STP, ACVP, IATP and HESI-ITC), has published over number articles, book chapters and given numerous presentations both nationally and internationally on immunology, pathology, immunotoxicology and immunosafety.

Nirav Patel, AstraZeneca Nirav Patel is the head of the Immune-Oncology Safety Group within AstraZeneca's Clinical Pharmacology and Safety Science (CPSS), where he directs nonclinical safety strategy for the Oncology immune cell engager portfolio, guides first-in-human and subsequent development packages and provides governance-level reviews while coaching discovery safety scientists and project toxicologists in close partnership with Toxicology Strategy and Regulatory teams. Prior to senior leadership role, he served as Director of the Oncology Discovery Safety Team at AstraZeneca. He established Immunotox platform/tools to address immune-related safety risks and building a fully functional safety laboratory for oncology and nononcology programs. Earlier roles include Associate Director in Investigative Immunotoxicology at Sanofi (2020–2023) and translational immunologist/immunotoxicologist positions at Pfizer beginning in 2015. With 11+ years in biopharma, he is recognized for innovative research, collaborative leadership, and dependable delivery across biologics, ADCs, protein degraders, and cell and gene therapies, with specialization in investigative toxicology, immune safety, immune inflammation, autoimmunity, immunooncology, and AAV modalities, and a strong track record in translational immunotoxicology and immuneoncology safety.

Zhechu Peng, PhD, DABT, AstraZeneca Dr. Peng is a project toxicologist in the immune safety group of CPSS at AstraZeneca, where she leads nonclinical strategy for immunology programs. Prior to this role, she was a project toxicologist at Boehringer Ingelheim and a study director for more than 7 years. Zhechu has supported IND applications and further clinical development for various biologics and small molecule programs.

Ryan Polli, Novartis Ryan Polli is an Associate Director in Pharmacokinetic Sciences within Translational Medicine at the Novartis Institutes for Biomedical Research. His work focuses on translational clinical pharmacology strategies for biologics and immunotherapies, with particular emphasis on multispecific antibodies, CAR-T therapy, and Tcell engaging therapeutics. He specializes in integrating pharmacokinetics, pharmacodynamics, and PK/PD modeling approaches to support first-in-human dose selection, clinical study design, and quantitative understanding of immunemediated drug responses.

Kimberly Rockley, PhD, Apconix Dr. Kimberly Rockley is a Principal Scientist at Apconix. Kim is passionate about reducing animal use in drug development and believes that there is great power in human based translational assays to help develop safer drugs. Whilst at Apconix Kim has developed 2 novel human in vitro assays for early detection of seizure liability that have now been launched commercially. This early high-throughput screening approach will save time, reduce animal use and support optimal drug design.

Riya Sharma, STEMCELL Technologies Riya Sharma is a Senior Scientist in Research and Development at STEMCELL Technologies. She leads the team developing products and workflows to support liver research using tissue- and human pluripotent stem cell-derived hepatic cells and organoids. Riya completed her Bachelor of Science in Biotechnology at the University of British Columbia. Before joining STEMCELL Technologies in 2016, she held research positions in Dr. Alex Scott's lab, where she developed tendon injury models, and in Dr. Paul Rennie's lab, where she screened small molecule therapeutics for the treatment of castration-resistant prostate cancer.

Runxi Shen, PhD, Broad Institute Dr. Shen is a Postdoctoral Associate in the Carpenter-Singh Lab at the Broad Institute of MIT and Harvard. He received his Ph.D. in Computational Biology from Cornell University, with academic training in evolutionary and population genetics. Building on that foundation and prior pharmaceutical industry experience in translational bioinformatics, he now works as a computational biologist integrating quantitative genetics, image-based profiling, and machine learning to address questions in human disease and drug discovery.

In his talk, he will present how image-based profiling and machine learning can be applied to predictive toxicology and inform early safety assessment for drug discovery. As an active member of the OASIS Consortium, he leads cross-species benchmarking of Cell Painting for hepatotoxicity prediction, spanning rat in-vivo liver toxicity and human drug-induced liver injury, and develops computational frameworks that translate high-dimensional cellular phenotypes into interpretable signals for nonclinical decision-making.

Chris Strock, PhD, Cyprotex Dr. Strock received his PhD from the University of Maryland, Baltimore and his postdoc at Johns Hopkins School of Medicine. He has been at Cyprotex for the last 15 years where he was involved in the development of in vitro Tox assays and was instrumental in the early development of Microelectrode array assays for Seizure prediction and cardiotox. He is currently the Head of Scientific Operations for Cyprotex US in Framingham.

Qi Sun, PhD, Harvard Dr. Sun is Associate Professor of Medicine at Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School. He is also Associate Professor at Harvard T.H. Chan School of Public Health. Dr. Sun's primary research interests are to identify and examine biomedical risk factors, particularly dietary biomarkers, in relation to type 2 diabetes, obesity, and cardiovascular disease through epidemiological investigations. His research is primarily based on several large-scale cohort studies, including the Nurses' Health Studies and the Health Professionals Follow-up Study. Dr. Sun is also interested in understanding the role of environmental pollutants, such as perfluoroalkyl substances (PFASs) and legacy persistent organic pollutants, in the etiology of weight change and type 2 diabetes. His primary approach is to, through integrating the state-of-the-art of omics technologies and chronic disease epidemiologic approaches, elucidate novel exposure-disease associations and underlying mechanisms relevant to human beings. His research has led to the discovery of endogenous metabolites (e.g., very-long chain fatty acids), endocrine disruptors (e.g., Bisphenol A and PFASs), circulating proteins (e.g., fatty acid binding protein 4 and soluble leptin receptor), and gut microbiome as predictors or modulators of human metabolic diseases. Overall, his innovative research on multiple important topics has enhanced our understanding of the biological mechanisms underlying nutrition and metabolic health and contributed to the US dietary guidelines for chronic disease prevention. His research thus far has led to more than 350 peer-reviewed publications. Dr. Sun is currently leading a few NIH-funded projects that focus on food biomarker discovery

and validation, microbial predictors of diabetes, and environmental pollutants in relation to weight change or cardiovascular disease in human populations.

Radhakrishna Sura, DVM, PhD, Gilead Dr. Sura is Senior Director of Nonclinical Safety & Pathobiology at Gilead Sciences, where he leads preclinical safety strategy and serves as the safety representative and pathologist for immunology and oncology programs. He has over 19 years of experience in pathology, including 16 years in toxicologic pathology, with prior roles at AbbVie and Dow. Dr. Sura is a strong advocate for the 3Rs and has received a 3Rs Advancement Award for contributions to reducing animal use in research. He is an active contributor to the IQ Microphysiological Systems (MPS) initiative and serves as a steering committee member and cochair of the Society of Toxicologic Pathology Special Interest Group on Complex In Vitro Models. He has coauthored more than 30 scientific publications. Dr. Sura holds a DVM (India), an MS from The Ohio State University, and a PhD from the University of Connecticut, and is boardcertified by the ACVP and ABT, and is a Fellow of the IATP.

Xinming Tong, PhD, Genentech Dr. Tong is a Principal System Specialist at Genentech. He is a seasoned expert with over two decades of research experience in tissue engineering, biomaterials, and polymer chemistry. Dr. Tong specializes in developing complex in vitro tissue models and organoid technologies to advance drug discovery. Within the Department of Biochemical Cellular Pharmacology (BCP), he leads the design and implementation of functional in vitro models to evaluate drug candidates across diverse therapeutic areas. He also holds a joint appointment with the Complex In Vitro Systems (CiS) group within Translational Safety, where he serves as a strategic liaison between BCP and CiS to align modeling priorities across portfolio programs. Dr. Tong previously held senior research and instructional roles at Stanford University. He has co-authored numerous high-impact publications in journals, four patents, and has led several research grants. He earned his Ph.D. in Materials Science and Engineering from the Beijing Institute of Technology.

Sophie Tourdot, PhD, Pfizer Dr. Tourdot received her Ph.D. in Immunology from the Université Paris Cité, France and moved to the UK for her postdoctoral training at Imperial College London. She has over 25 years of experience in multiple area of immunology including anti-viral vaccines, cancer immunotherapy, allergy de-sensitization and biologics research and development. As part of the management team, Sophie played a critical role in the success of the ABIRISK a public-private consortium dedicated to the understanding, monitoring and mitigation of biotherapeutics immunogenicity. Sophie joined Pfizer in 2017 and leads a group focused on immunogenicity risk assessment and mitigation of Pfizer's biologic portfolio. She contributes to program development from early stages to dossier submission and is co-chair of the Immunogenicity Advisory Council. In the immunogenicity scientific community, Sophie co-leads a consortium and several working groups regrouping industries, academics and regulators, and act as Director of Scientific Affairs for the European Immunogenicity Platform.

Jack Uetrecht, MD, PhD, University of Toronto Dr. Uetrecht earned a Ph.D. in organic chemistry from Cornell University, an M.D. degree from Ohio State University, an internal medicine residency at the University of Kansas Health Science Center and a clinical pharmacology fellowship at Vanderbilt University. He is currently professor of pharmacy and medicine at the University of Toronto and past Canada Research Chair of Adverse Drug Reactions. He has over 40 years of experience and over 200 publications in the field of idiosyncratic drug reactions. He was awarded the Vos Lifetime Career Achievement Award in Immunotoxicology by the Society of Toxicology. His contributions include identification of several reactive metabolites of drugs associated with idiosyncratic drug reactions. The focus has shifted from reactive metabolites to the role of the immune system in the mechanisms of idiosyncratic drug reactions. He developed an animal model of nevirapine-induced skin rash, and he used PD-1 KO mice to develop models of immune-mediated liver injury. He has found possible biomarkers such as GDF-15 to predict which drug candidates will cause idiosyncratic drug reactions.

John L. Vahle, DVM, PhD, Diplomate ACVP, Eli Lilly Dr. Vahle received his veterinary medical degree from the University of Missouri in 1988 and his doctorate in veterinary pathology from Iowa State University in 1996. He became a Diplomate of the American College of Veterinary Pathologists in 1995 and joined Lilly as a senior pathologist in 1996. He currently serves as a Senior Research Fellow at Lilly.

John has nearly 30 years of experience in pathology and toxicology and has served in a variety of roles including study pathologist, project pathologist, toxicology project leader, and regulatory toxicology advisor. John's areas of interest include carcinogenicity

assessments, toxicologic pathology of biotherapeutics, nonclinical safety assessment of peptides, and bone toxicology and pathology. Dr. Vahle is active in various professional societies and consortia and is current chair of the EFPIA preclinical expert group, a past Councilor of the STP, past Chair of the BioSafe Organization, and a member of the steering committee for the international toxicologic pathology nomenclature initiative, INHAND. Based on his experience in carcinogenicity testing, John served as a member of the ICH Expert Working Group assessing carcinogenicity testing paradigms for pharmaceuticals.

Matt Wagoner, Takeda Matt Wagoner leads the Advanced Biology Lab at Takeda Pharmaceuticals, where their team applies advanced in vitro models and in silico approaches to help make safer, and more effective, medicines. In lieu of hobbies, Matt enjoys chasing his four kids around mountains and helping NASA solve the human health challenges surrounding space flight.

Ron Wange, PhD, Aclairo Pharmaceutical Dr. Wange was a former FDA Associate Director for Pharm/Tox – Office of New Drugs; Former FDA Pharm/Tox Supervisor and Reviewer – Metabolism and Endocrinology; Member Executive Carcinogenicity Assessment Committee; Leadership of Pharm/Tox Subcommittees on Nonclinical Biologics, Emerging Technology, Immunotoxicology and Oligonucleotides; He played key roles in development of nonclinical FDA guidance related to immunotoxicity, oligonucleotides, rare diseases, non-human primate use, platform technology designation, and developmental and reproductive toxicity (including serving as FDA Topic Lead on the EWG for revision of the ICH S5 guidance).

**Thank you to all of our Organizers,
Speakers, Sponsors and Delegates!**

Without your dedication, support and participation APT 2026 would not be possible. We greatly value your comments regarding APT 2026 as well as thoughts or suggestions for improving future conferences. Please take the time to fill out our online survey when we send it to you next week.

Sincerely,



The Boston Society