APPLIED PHARMACEUTICAL TOXICOLOGY

May 18-20, 2016

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ORGANIZER'S WELCOME

Welcome to the 2016 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.

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Chair-Elect: Padma Narayanan, Ionis Pharmaceuticals

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Jonathan Heyen, Pfizer
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Christine Karbowski, Amgen
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Vito Sasseville, Novartis
Timothy MacLachlan, Novartis
Brian Vuillemenot, Genentech

APT 2016 CONFERENCE AGENDA

WEDNESDAY, MAY 18

7:30 - 8:30 Registration & Breakfast

8:30 - 8:35 Conference Opening
Dylan Hartley, Array BioPharma

8:35 - 9:20 **Plenary Talk: Developing a Human Embryonic Stem Cell-Derived Cardiomyocyte Therapeutic**
Scott Thies, University of Washington

DISCOVERY WORKSHOP

SESSION I: Tox Challenges of Cancer Metabolism Pathways

Chairs: Dolo Diaz, Genentech and Michelle Horner, Amgen

9:20 - 9:25 **Session Intro**

9:25 - 9:55 **Nonclinical Assessment of Hematopoietic, Cardiac, and Retinal Toxicities of Small Molecule Inhibitors of Nicotinamide Phosphoribosyltransferase (NAMPT)**
Dinah Misner, Genentech

9:55 - 10:10 Break

10:10 - 10:40 **Mitochondria in Cancer-Potential Targets-Potential Liabilities**
Yvonne Will, Pfizer

10:40 - 11:10 **Inhibition of Phosphatidylinositol 3-kinase for the Treatment of Cancer – On and Off Target Safety Challenges**
Michelle Horner, Amgen

11:10 - 11:40 **Vendor Talk: Use of 3D InSight™ Human Liver Microtissues as a Tool for Prediction of Drug-Induced Liver Injury**
Judi Wardwell-Swanson, InSphero

11:40 - 1:20 Lunch

SESSION II: Translatability of In Vitro Models - Translational Biomarkers & New In Vitro Models

Chairs: Michael Santostefano, Merck and Christine Karbowski, Amgen

1:20 - 1:25 **Session Intro**

1:25 - 1:55 **Human Genetics as a Means of Identifying Clinical Safety Biomarkers and Endpoints**
Paul Nioi, Amgen

1:55 - 2:25 **Qualification of New Translational Safety Biomarkers for Drug Development**
Warren Glaab, Merck

2:25 - 2:45 Break

2:45 - 3:15 **Translational Biomarker-Based Approaches for Evaluation of Drug Induced Liver Injury in Clinical Trials**
Jiri Aubrecht, Pfizer

3:15 - 3:45 **Evaluating Cellular Impedance as an Integrated Assay for Drug Effects on Beating of Stem Cell Derived Cardiomyocytes**
Matthew Peters, AstraZeneca

3:45 - 4:15 **Extracellular Vesicles as Biomarkers of Cardiovascular Toxicity**
John Nolan, The Scintillon Institute

4:15 - 5:15 **Reception** sponsored by abbvie

THURSDAY, MAY 19

8:00 - 9:00 Breakfast

9:00 - 9:05 **Plenary Speaker Introduction**
Timothy MacLachlan, Novartis

9:05 - 9:55 **Plenary Talk: Think like a Regulator: Considerations for Preclinical Testing Programs for Stem Cell-based Products**
Alexander Bailey, FDA

SESSION III: Stem Cell Therapies

Chairs: Padma Narayanan, Ionis Pharmaceuticals and Yi Yang, AbbVie

9:55 - 10:00 **Session Intro**

10:00 - 10:40 **Developing a Clinical-Grade Cell Therapy from an Academic Laboratory's Published Research Methods**
Benjamin Fryer, University of Washington

10:40 - 11:00 Break

11:00 - 11:30 **Challenges and Opportunities in Skeletal Muscle Cell Therapy and In Vitro Models of Skeletal Muscle Function**
Raymond Page, Worcester Polytechnic Institute

11:30 - 12:00 **Unleashing Stem Cell Trials in Companion Animal Disease Models**
Andrew Hoffman, Tufts University

12:00 - 1:15 Lunch

DEVELOPMENT TOXICOLOGY WORKSHOP

SESSION IV: Stem Cell Therapies/Gene Therapies

Chairs: Michael Placke,Alnylam and Vito Sasseville, Novartis

1:15 - 1:25 **Workshop Introduction**
Heather Dowty, Pfizer

1:25 - 1:30 **Session Introduction**

1:30 - 2:00 **Developing Gene Therapy for Sensorineural Hearing Loss**
Richard Colvin, Novartis

2:00 - 2:30 **Modified Messenger RNA as a Therapeutic Modality**
Joseph Senn, Moderna Therapeutics

2:30 - 2:50 Break

2:50 - 3:20 **Safety & DMPK Evaluations of Cell Based Therapies: Strategies and Tactics**
Uri Herzberg, Celgene

3:20 - 3:40 **Panel Discussion**
Richard Colvin, Joseph Senn, and Uri Herzberg

FRIDAY, MAY 20

8:00 - 9:00 Breakfast

DEVELOPMENT TOXICOLOGY WORKSHOP

SESSION V: The Microbiome

Chairs: Heather Dowty, Pfizer; Paul Cornwell, Eli Lily; and Christina de Zafra, Amgen

9:00 - 9:05 **Session Introduction**

9:05 - 9:40 **Overview of the Microbiome**
Eric Alm, MIT

9:40 - 10:15 **Impact of the Microbiome on Reproducibility of Preclinical Studies**
Aaron Ericsson, Department of Veterinary Pathology, Univ of Missouri

10:15 - 10:35 Break

10:35 - 11:10 **Exploring the Gut Microbiome to Improve Treatment of Inflammatory Bowel Disease**
Bradford McRae, AbbVie

11:10 - 11:45 **Nonclinical Considerations for Developing Microbiome Therapies**
Lisa Schopf, Vedanta Biosciences

11:45 - 12:45 Lunch

SESSION VI: In Vivo Translatability/Clinical Translation

Chairs: Florence Lorget, Genentech; Kristina Chadwick, BMS; and Brian Vuillemenot, Genentech

12:45 - 12:50 **Session Introduction**

12:50 - 1:20 **Preclinical Safety Evaluation of Zinc Finger Nuclease Genome Editing Therapeutics**
Kathy Meyer, Sangamo

1:20 - 1:50 **Translatability of Nonclinical Observations to the Clinical Setting for the Development of Ocular Protein Therapeutics**
Eric Wakshull, Genentech

1:50 - 2:20 **Palucorcel (CNTO 2476): The Development of a Cell Therapy for the Treatment of Geographic Atrophy**
Jessica Lynch, Janssen BioTherapeutics

2:20 - 2:25 **Closing Remarks**

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ABSTRACTS

PLENARY

Developing a Human Embryonic Stem Cell-Derived Cardiomyocyte Therapeutic

Scott Thies, University of Washington

The development of human pluripotent stem cell-derived therapies presents unique challenges, but offers the potential for significant advances in the field of regenerative medicine. In early clinical trials for heart disease, adult stem cell therapeutics have resulted in modest improvements based on the trophic effects of these cells. The impact of a cardiomyocyte therapeutic is expected to be more profound, if the cells appropriately integrate and provide an enduring contribution to contractile function. It is with this goal in mind that the UW Medicine Heart Regeneration Program is developing an allogeneic cryopreserved hESC-cardiomyocyte therapeutic. From a discovery toxicology perspective, large animal studies are in progress to evaluate the efficacy and safety of this therapeutic in early stages of product development. With the completion of product optimization, IND-enabling studies are anticipated to evaluate efficacy, biodistribution, toxicology, and tumorigenicity.

Discovery Workshop

SESSION I

Nonclinical Assessment of Hematopoietic, Cardiac and Retinal Toxicities of Small Molecule Inhibitors of Nicotinamide Phosphoribosyltransferase (NAMPT)

Dinah Misner, Genentech

Nicotinamide adenine dinucleotide (NAD) is an essential co-factor in glycolysis. Cancer cells have increased energy demands due to excessive proliferation and have a highly increased rate of glycolysis (Warburg effect; reviewed by Heiden et al, 2009). NAMPT catalyzes the rate-limiting step of NAD synthesis and protein is up-regulated in many cancer types. NAD can also be generated de novo from nicotinic acid via alternate pathways. NAMPT inhibitors (NAMPTi) are being investigated as anti-cancer agents. Literature reports of clinical trials with earlier NAMPTi, FK866 and CHS828, indicate that these molecules failed to demonstrate sustained efficacy due to dose-limiting thrombocytopenia. In vivo rodent toxicity studies also showed evidence of retinal and cardiac toxicity. We developed a mechanistic context and human relevance using in vitro cellular models. We also examined the potential for nicotinic acid to pharmacologically mitigate these toxicities when co-administered with NAMPTi. Overall, our data demonstrates that the retinal and cardiac effects are on-target (related to pharmacological potency of NAMPTi). We have observed complete correlation of both in vitro and in vivo effects. Our data suggest that nicotinic acid co-administration may be appropriate to rescue platelet but not retinal or cardiac toxicity.

Inhibition of Phosphatidylinositol 3-kinase for the Treatment of Cancer – On and Off Target Safety

Michelle Horner, Amgen

Inhibition of the phosphatidylinositol 3-kinase (PI3K) pathway is currently being pursued for oncology indications based on the premise that PI3K is essential for the growth and survival of cancer cells. In addition, genetic alterations in the form of PI3K mutations lead to dysregulation of PI3Kdependent pathways which is implicated in several human cancers. Due to the involvement of PI3K in the regulation of various metabolic pathways, potential on target-associated safety liabilities may be of concern, even in the oncology setting. Known class effects of PI3K inhibitors include dysregulated glycemia with associated cardiovascular changes, bone changes, bone marrow toxicity, and reproductive organ toxicity. A series of potent class Ia PI3K inhibitors were evaluated in exploratory toxicology studies. The toxicology strategy included an initial single dose rat study to determine the dose level at which glucose/insulin homeostasis was significantly impacted to predict a maximum tolerated dose. Repeat dose studies were then conducted in rats, dogs, and non-human primates to identify a molecule with acceptable exposure safety margins. For one series of compounds, the lead molecule was associated with off-target hepatobiliary toxicity. By applying a metabolite-based structure-activity relationship approach, successful identification of a PI3K inhibitor devoid of off-target liver toxicity was achieved. Overall, a comprehensive safety strategy for PI3K inhibitors should include evaluation of both on-target and potential off-target liabilities.

SESSION II

Qualification of New Translational Safety Biomarkers for Drug Development

Warren Glaab, Merck

Improving the ability to detect drug-induced tissue injuries using

novel safety biomarkers will provide a tool for preclinical and clinical monitoring to better ensure patient safety. These new safety biomarkers are needed to supplement current endpoints that are both insensitive and nonspecific, and qualification through regulatory agencies for use in both preclinical drug development and translation to the clinic is essential to further enable drug development. Data will be presented for new kidney and skeletal muscle biomarkers, using preclinical studies with histopathology outcome to determine their relative performance in monitoring drug-induced degeneration/necrosis. The strategy and preliminary data to support the clinical qualification of these biomarkers will also be presented. The regulatory endorsement from the FDA and EMA will be highlighted demonstrating their preclinical utility as well as the potential translation to the clinic.

Evaluating Cellular Impedance as an Integrated Assay for Drug Effects on Beating of Stem Cell Derived Cardiomyocytes

Matthew Peters, AstraZeneca

Experience using cellular impedance as a screen to assess drug effects on the beating of human iPSC-derived cardiomyocyte will be shared. Evaluation metrics discussed will include beat rate vs. amplitude, contractility and deconvoluting mechanisms of kinase inhibitor functional cardiotox.

Extracellular Vesicles as Biomarkers of Cardiovascular Toxicity

John Nolan, The Scintillon Institute

All living cells release extracellular vesicles (EVs), small (~70-200 nm) membrane bound particles, and biofluids such as plasma contain EVs from many different cell types. Because EVs carry molecular cargo from their cells of origin, there is great potential to use these to determine the physiological status of those cells. Because EVs are small and dim they are hard to measure by methods conventionally used to study cells. We have developed flow cytometry instruments, reagents, and assays to enable the sensitive and rapid measurement of individual EVs and their cargo. We are using these new tools to study the dynamics of the cardiovascular system response to insults and identify potential biomarkers of cardiovascular toxicity.

PLENARY

Think like a Regulator: Considerations for Preclinical Testing Programs for Stem Cell-based Products

Alexander Bailey, FDA

The conduct of an investigative clinical trial is governed by the Code of Federal Regulations (CFR) Title 21, Part 312. According to 21 CFR 312.23 (a)(8), adequate information derived from pharmacology and toxicology studies is needed in order to support a conclusion that the trial is reasonably safe and scientifically feasible to conduct. Thus, data obtained from preclinical studies are used to guide the design of certain elements of early-phase clinical trials, including: 1) extrapolation of a safe starting dose, dose-escalation scheme, and dosing schedule; 2) determination of a potential safe route of administration; 3) identification of potential target tissues of toxicity and activity; 4) selection of appropriate subject eligibility criteria; and 5) establishment of an adequate clinical monitoring plan. In addition, data generated from the preclinical studies may support the scientific rationale for the use of the proposed investigational product in the specified clinical indication. The administration of a stem cell-based therapy (SCT) for clinical use often requires flexible approaches in preclinical studies to first assess product safety and activity. The same biological properties of stem cells that make them attractive candidates for therapeutic development – such as their capacity for self-renewal, proliferative potential, and plasticity – may also pose regulatory challenges for evaluation of the potential associated risks. Regulatory guidance concerning the design of preclinical studies for SCTs is based on both the product-specific properties and the proposed clinical trial design. Factors that should be considered when designing preclinical studies include cell type and source, product interactions with the host immune system, biological relevance of the proposed animal species/model, route/anatomical site of product administration, translation of dose levels and dosing regimens from animals to humans, cell distribution to target and non-target tissues, organ pathology, and the potential for tumor or ectopic tissue formation. This presentation will provide an overview of CBER's current regulatory practices regarding the preclinical development of SCT products, as well as discuss potential regulatory and scientific challenges in designing IND-enabling preclinical studies to assess the safety and activity of these diverse products.

SESSION III

Developing a Clinical-Grade Cell Therapy from an Academic Laboratory's Published Research Methods

Benjamin Fryer, University of Washington

Significant proof-of-concept research from Chuck Murry's group recently (Nature 2014, Chong et al) showed that a human embryonic stem cell derived cardiomyocyte cell therapy could engraft and potentially repair the damage caused by a myocardial infarction (heart attack). The "research grade" process described in the article for generating cardiomyocytes can not be used to make sufficient amounts of a "clinical grade" product. Consequently the published methods must be

translated and transferred to a process that can be used in IND and toxicology supporting studies, human clinical studies, and eventually a commercial product. In order to generate that product an aseptic and well controlled manufacturing process must be developed. This begins with proper raw material sourcing via secure and trust worthy supply chains, and material validation via identity and in-process testing. Planning ahead in early stage development should facilitate development of a scalable cold supply chain cell therapy product that can be used and adapted for supplying the increasing demands of a clinical grade product.

Challenges and Opportunities in Skeletal Muscle Cell Therapy and In Vitro Models of Skeletal Muscle Function

Raymond Page, Worcester Polytechnic Institute

Currently, many skeletal muscle diseases including volumetric muscle loss, age related muscle loss and genetic disorders such as muscular dystrophies lack effective clinical treatments. To aid with the testing of pharmaceutical solutions, functional in vitro models of human skeletal muscle can provide a pre-clinical testing platform. There is also a need for regenerative or cell/tissue therapy options to actually replace tissue lost to due trauma or disease. Developing model systems that accurately recapitulate native muscle function in vitro and large scale amplification of patient specific myogenic cell populations for cell/tissue therapy is challenging. Salient features of native muscle that must be emulated include: cellular and extracellular environment, myotendonous junctions anchored tissue and electromechanical stimulation of engineered tissue to improve its maturation. In addition, traditional cell culture systems fail to enable large scale amplification of cell populations derived from adult human skeletal muscle without loss of myogenic capability. This talk will address our approach to these challenges by reviewing our work on cell culture system development, biomaterial development to direct regenerative responses in vivo and development of high-content 3D engineered tissue models of skeletal muscle function to augment the therapeutic product development process, which has application to a variety of myopathies.

Unleashing Stem Cell Trials in Companion Animal Disease Models

Andrew Hoffman, Tufts University

The pre-clinical evaluation of stem cells and thus predictive value of those trials would be improved with more realistic animal models. Companion animals (dogs, cats, horses, etc) develop many human-like diseases spontaneously, therefore constituting a great opportunity to study cell based therapies in real patients. Examples from the literature of diseases for which stem cell trials have been performed in companion animals include: osteoarthritis, spinal disc herniation, dilated cardiomyopathy, inflammatory bowel disease, Crohn's fistulitis, meningoencephalomyelitis (multiple sclerosis-like), keratoconjunctivitis sicca (Sjogren's syndrome-like), atopic dermatitis, tendonitis, and chronic (end-stage) kidney disease. Stem cells evaluated in these studies included mesenchymal stem-stromal cells, olfactory ensheathing cells, or neural lineage cells derived from bone marrow MSC with most studies performed in canines. There are special ethical and logistic considerations in conducting clinical trials in companion animals, which in many respects are expedited, low-cost versions of human trials. Furthermore there is new FDA guidance for stem cell based therapies in client-owned animals, which describes the process of investigational exemptions for INAD, in addition to preexisting guidelines for pre-IND inclusion of companion animals. The talk will describe the issues with study design, initiation, participant engagement, infrastructure, and regulatory compliance of stem cell clinical trials in companion animals.

Development Workshop

SESSION IV

Modified Messenger RNA as a Therapeutic Modality

Joseph Senn, Moderna Therapeutics

The concept of mRNA-based therapy states, in principal, any protein can be produced in vivo by delivery of the corresponding mRNA into the cells and has been suggested as early as 1990 (Wolff, Malone et al. 1990). Distinct from gene therapy, mRNA is a transient carrier of information. There is a broad range of potential mRNA-based applications including protein replacement therapies, production of multi-clonal therapeutic or prophylactic antibodies and vaccines.

However, there are challenges with the clinical use of therapeutic mRNA. Exogenous mRNA is a pathogen-associated molecular pattern (PAMP) and can stimulate activation of the innate immune system (Kariko, Buckstein et al. 2005; Desmet and Ishii 2012). The recognition or activation of these sensors to exogenous mRNA can be modified by selective modification of nucleotides or the polyA tail (characteristic of eukaryotic mRNA) (Kariko, Ni et al. 2004; Koski, Kariko et al. 2004). Additionally, mRNA is unstable in biological matrices and is rapidly degraded by ribonucleases. Therefore, formulations for delivery and protection of mRNA are needed. These delivery systems require additional qualification and possess their own safety risks.

Although there are several "innate" hurdles to the realization of the potential for therapeutic use of mRNA, this system provides

a "platform" approach wherein a new drug only requires the alteration of the base sequence of mRNA. Risk assessment and characterization of these molecules will require the assessment of mRNA effects, delivery system effects and subsequent assessment of the protein produced. Several examples and questions will be discussed to illustrate this approach.

Safety & DMPK Evaluations of Cell Based Therapies: Strategies and Tactics

Uri Herzberg, Celgene

Cell based therapeutics can be viewed as the most pleiotroptic pharmacological intervention and also as the most dynamic one. As such, this therapeutic intervention presents opportunities to treat complex diseases along with challenges in development. Specifically, in-vivo Preclinical assessment of cell based therapies faces several challenges: the inherent xenogeneic setting often confounds interpretation of most of the data, in addition allometric scaling is not yet feasible. Also, the dynamic state of the injected therapeutic is inherent to this type of treatment. Thus, the route of administration, as well as disease state (in animal models and possibly in patients) are likely to play major roles in "cell therapy PK/PD". The presentation will discuss an overall approach that bridges the concepts of Safety and ADME from "traditional" drug development to the development of cell based therapeutic, and creates a framework to support early clinical development. This framework is intended to address regulatory requirements, facilitate our scientific understanding of cell based therapies, and supports decisions about indication selection and dosing regimens. Case studies describing animal models that proved useful for safety assessment and models used to demonstrate Efficacy, Distribution, and PK for cell based therapies will follow.

SESSION V

Impact of the Microbiome on Reproducibility of Preclinical Studies

Aaron Ericsson, Department of Veterinary Pathology, Univ of Missouri

The gut microbiota provides several beneficial functions to the host and influences human health and disease susceptibility. Similarly, the gut microbiota has a strong influence on the phenotype of many animal models and should be considered as an intercurrent variable capable of impairing study reproducibility. Many common variables associated with animal husbandry, including caging, bedding, diet, animal source, and shipping (among others), can greatly influence the composition of the gut microbiota. Data will be presented demonstrating the influence of those variables on the GM, and examples given of the impact those differences can have on the phenotype of models of inflammatory bowel disease, colorectal cancer, behavior, and other conditions. Moreover, other tissues previously considered free of bacterial colonization in health are now recognized to harbor complex but uniform microbial populations. These findings will be discussed in the context of their use as potential biomarkers of disease susceptibility, through tissue-specific dysbiosis

Exploring the Gut Microbiome to Improve Treatment of Inflammatory Bowel Disease

Bradford McRae, AbbVie

Bacteria and human hosts have developed a symbiotic relationship over eons of evolution. In recent years, a new paradigm has emerged for how these symbiotic microbes interact with the immune system. Much of this work has been based on the observation that in animals raised in the absence of bacteria (i.e., germ free conditions) immune cells types including T regulatory cells and some innate cell types are absent. These data suggest that the gut microbiota interacts with the immune system providing signals to promote the maturation of immune cells and the development of normal immune function. Conversely, loss of beneficial microbes and reduced microbial diversity are associated with chronic inflammation in conditions such as inflammatory bowel disease, obesity, and diabetes. A better understanding of the role of the gut microbiome in health and disease may provide opportunities to develop novel therapeutic approaches for the treatment of chronic inflammatory diseases. Several strategies for using microbes in drug discovery and biomarker development will be discussed.

SESSION VI

Palucorcel (CNTO 2476): The Development of a Cell Therapy for the Treatment of Geographic Atrophy

Jessica L. Lynch, Janssen BioTherapeutics

Palucorcel (CNTO 2476) is a novel cell therapy currently being evaluated for the treatment of Age Related Macular Degeneration. Subretinal administration of palucorcel was associated with decreased visual function loss in the RCS rat model of human retinal disease. In an early clinical study utilization of a microcatheter delivery system via an ab externowas associated with an unacceptably high rate of adverse events. To circumvent these issues anovel method for subretinal delivery of palucorcel using a subretinal access kit (SRAK-02) device via a suprachoridal surgical approach was developed. To test the safety of this procedure a bridging study with palucorcel and

analogous pig umbilical derived tissue cells (pUTC) aws conducted. This study also evaluated surgical healing over time, characterized post-dosing disposition of administered fluorescent vehicle and carboxyfluorescein diacetate succinimidyl ester (CFSE)-labeled cells and to differentiate the potential immune responses in the context of a xenogeneic (palucorcel) or allogenic (pUTC) setting. Cells and vehicle were successfully administered using the SRAK-02 device and procedure in all animals. Immediately post-dose, the CFSE-labeled cells or fluorescent vehicle were visible within the subretinal bleb. There was no evidence of leakage into the vitreous. There were no unscheduled deaths and no changes in body weights, food consumption, electroretinography, or clinical pathology parameters. Ophthalmic exams showed procedure-related ocular changes that resolved over time. Focal elevation in the area of subretinal delivery was observed transiently post-dosing. No retinal detachments or vitreous traction bands (based ophthalmologic examination) were identified. Microscopic changes observed were considered related to the dosing procedure and were not related to administration of cells. Small focal retinal granulomas were observed after 3 months in 2 of 3 eyes that were administered palucorcel (xenogeneic), whereas no granulomas were observed in eyes receiving pUTC (allogeneic) or vehicle. Anti-palucorcel antibodies were detected in 2 of 6 minipigs receiving cells. No anti-pUTC antibodies were detected in minipigs receiving pUTC.

BIOGRAPHIES

Jiri Aubrecht, Pharm.D., Ph.D., Pfizer Jiri Aubrecht is a Senior Director and Group Lead of Safety Biomarker Laboratories at Pfizer Worldwide Research and Development in Groton, CT. His research interests are development and application of translational biomarker strategies with emphasis on qualification of novel biomarkers for risk assessment. Dr. Aubrecht completed postdoc fellowship in molecular toxicology at Harvard School of Public Health, has experience in biotech an pharmaceutical industry and authored over 55 peer-review publications in leading biomedical journals, as well as six book chapters, has one issued patent and several patent applications. Dr Aubrecht serves as a co-director of Predictive Safety Testing Consortium at the Critical Path Institute and as a lead of Genomic Biomarker Qualification Working Group at the ILSI HESI. He is a member of the Society of Toxicology and a vice president of Clinical and Translational Toxicology Specialty Section. Dr. Aubrecht served as chair of the Technical Committee on Application of Genomics to Mechanism-Based Risk Assessment at the ILSI Health and Environmental Science Institute and was a member of the scientific advisory board of the EU project CarcinoGenomics.

Alexander Bailey, Ph.D., FDA The Pharmacology/Toxicology Branch (PTB) is responsible for the regulatory review of all preclinical studies submitted to CBER/OCTGT to support the safe use of an investigational cell therapy, gene therapy, or tissue-engineered product in human clinical trials. As a Team Leader in PTB, Alex Bailey leads a team of experienced Pharmacology/Toxicology reviewers and provides scientific and regulatory oversight of the review of regulatory submissions. Alex has served as the office and center representative to various committees within FDA, and for the last three years has chaired a series of interactions between CBER pharmacology/toxicology staff and members of the Special Biologics Expert Working Group of the Biotechnology Industry Organization (BIO) to discuss preclinical testing strategies for CBER-regulated products. Alex was previously a Commissioner's Fellow (Class of 2010), where he conducted regulatory review work in CBER and the Center for Devices and Radiological Health (CDRH), as well as designed a database of product development and preclinical testing strategies for cell-based products to assess data quality, identify trends, and stratify products based on their potential for tumor formation. While at the FDA, Alex has co-authored 10+ regulatory and technical publications and presentations regarding US FDA requirements for biologics, as well as contributed to the FDA guidance titled, Guidance for Industry: Preclinical Assessment of Investigational Cellular and Gene Therapy Products (2013).

Christina de Zafra, Ph.D., DABT, Amgen Dr. de Zafra received her PhD in Toxicology from the University of Rochester in 1998, and conducted a post-doctoral fellowship at the University of Colorado from 1998-2000; her research utilized rodent models to study the impact of toxins (lead) or neurodegenerative disease (Parkinson's disease) on dopaminergic pathways in the central nervous system. From 2000-2016, Christina was a member of the Safety Assessment department at Genentech, and in February 2016 she joined the Comparative Biology and Safety Sciences department at Amgen as a Principal Scientist. Christina has extensive experience in large molecule oncology drug development, and is currently responsible for the toxicology evaluation of several Immuno-Oncology molecules. She also has a passion for product quality risk assessment and nonclinical abuse liability assessment. Christina is a member of the Society of Toxicology, the Society for Neuroscience, and the Association for Research in Vision and Ophthalmology, and is a Diplomate of the American Board of Toxicology.

Dolo Diaz, Ph.D., Genentech Dr. Diaz is currently an Associate Director and head of Small Molecule Discovery Toxicology at Genentech, where she oversees lead optimization and safety assessment strategies for the small molecule discovery portfolio across therapeutic areas. Dolo received her PhD in Toxicology from the University of Washington in 2001 in the field of oxidative stress and metal toxicology, followed by post-doctoral work at the Fred Hutchinson Cancer Research Center in the area of mitochondrial function and apoptosis. In 2003 Dolo joined CEREP Inc., where she built and became the Group Leader for In-vitro Toxicology; following a 4-year tenure, she joined Genentech's Safety Assessment group in 2007. Dolo has authored/co-authored many peer-reviewed publications in the field of toxicology and she is a Diplomate of the American Board of Toxicology. Dolo is a member of the Society of Toxicology and several specialty sections. Dr. Diaz will be the Chair-Elect of the APT 2016 Toxicology workshop.

Heather Dowty, Ph.D., DABT, Pfizer Heather Dowty is currently an Associate Research Fellow and Drug Safety Team Lead in Drug Safety Research and Development at Pfizer in Andover, MA. Heather enjoys her portfolio role as a project team representative responsible for assessment of target safety liabilities, developing the nonclinical safety strategy for individual project teams from discovery through development, and supporting due diligence efforts for potential in-license programs. She has held previous roles in management of the General Toxicology Discipline, leading a team of In Vivo Study Scientists, Study Directors, and Project Team representatives to design, conduct and report in vivo exploratory toxicity studies in support of Pfizer's research portfolio. She initially supported the Pfizer DSRD

site in Saint Louis, MO and later was selected to lead the successful buildup and implementation of the General Toxicology Laboratory in Massachusetts. She received a BS in Pharmacology and Toxicology from the University of Wisconsin-Madison School of Pharmacy and a PhD in Toxicology at the Kettering Laboratories, Department of Environmental Health, University of Cincinnati. Heather began her career in toxicology as a Scientist in the Drug Safety Assessment Department at Procter & Gamble Pharmaceuticals gaining increased experience and responsibilities as a Study Director, Team representative, and PhRMA Genetic Toxicology working group member. She attained board certification from the American Board of Toxicology and is a Full Member of SOT and ACT. Heather has sincerely enjoyed her role as Chair of the 2016 APT Development sessions and looks forward to supporting the next Development Co-Chair and transitioning the Chair role to Michael Placke in 2017.

Aaron Ericsson, DVM, Ph.D., University of Missouri Dr. Ericsson is a Research Assistant Professor at the University of Missouri (MU) and Director of the MU Metagenomics Center. He also serves as lead scientist for microbiome research for the NIH-funded MU Mutant Mouse Resource and Research Center (MMRRC) and Rat Resource and Research Center (RRRC). He is a member of the American Association for Laboratory Animal Science and the American Society for Microbiology. Dr. Ericsson received a BA from the University of Iowa, and a DVM and PhD in Pathobiology from the University of Missouri. He also completed a residency in laboratory animal medicine through the MU Comparative Medicine Program, where he now serves as a core faculty member in this T32-funded post-DVM training program. Aside from his role as Co-I on the MMRRC and RRRC grants, he holds independent funding through the NIH (K01) and USDA (Animal Health Formula Funds) and has published extensively on the role of the microbiome in animal health and animal models of human disease.

Benjamin Fryer, Ph.D., University of Washington Dr. Fryer is currently the Team Leader of Cell Manufacturing/Processing for the Heart Regeneration Program at the University of Washington School of Medicine in Seattle WA. Ben has worked on product and process development for small molecule, large molecule, and cell therapy combination products and for the last 10 years has developed scalable methods and processes including cell banking, expansion, cryopreservation, and differentiation of pluripotent stem cells to a transplantable mature fate intended for clinical use as cell therapy.

Prior to joining the UW in early 2015 where he is currently responsible for generating cardiomyocytes from human embryonic stem cells, Ben worked at Janssen's BetaLogics venture from 2006 to 2014 developing stirred tank bioreactor processes to generate ("differentiate") beta islet tissue from pluripotent stem cells for treatment of insulin dependent diabetes.

Ben has a PhD in pharmacology, completed a post-doc in stem cell biology with Celeste Simon at University of Pennsylvania, and has 15 years experience working at both large pharma and small bio-tech start-ups.

Warren E. Glaab, Ph.D., Merck Dr. Warren Glaab has worked within Safety Assessment at Merck Research Laboratories for 19 years. Most recently he has served as Director of Systems Toxicology, involved with providing biomarker development support to Safety Assessment, incorporating new model systems and technologies including genomics and proteomics, and investigative toxicology research solutions. Previous experience within the Department of Molecular and Investigative Toxicology group in Safety Assessment included novel assay development and investigational studies to better understand toxicity mechanisms. He earned his Ph.D. in Toxicology at the University of North Carolina at Chapel Hill, conducted research at the National Institute of Environmental Health Sciences in Research Triangle Park, and completed two postdoctoral positions at National Institute of Environmental Health Sciences and at Merck Research Laboratories in West Point, PA.

Dylan Hartley, Ph.D., Array Biopharma Dr. Hartley is currently Director of Drug Metabolism and Pharmacokinetics at Array Biopharma and is a diplomate of the American Board of Toxicology. During his 15 years in industrial drug discovery, Dylan has held various positions in Drug Metabolism and Toxicology at Array Biopharma, Merck Research Laboratories and Genentech. He received his Ph.D. in Pharmaceutical Sciences in 1996 from the University of Colorado where he studied in the laboratory of Dr. Dennis R. Petersen. Dylan was a post-doctoral Toxicology Fellow in the laboratory of Dr. Curtis D. Klaassen at the University of Kansas Medical Center. Dylan's publications record as an author and co-author includes 37 peer-reviewed articles in the areas of toxicology and drug metabolism. Over the last few years, he has presented lectures as an invited speaker to several workshops focused on structure-based predictions of toxicological end points including, the 2011 CHI Drug Safety Summit, the 2012 Applied Pharmaceutical Toxicology Meeting, and the 2013 Society of Toxicology Meeting. With regard to relevant experience in organizing professional meetings, Dylan organized and led a workshop entitled, "*Understanding Structural and Physical Chemical Drivers of Drug Toxicity: Utility and Translatable Value*" for the 50th Society of Toxicology Meetings, and he has served on the organizing committee for the Applied Pharmaceutical Toxicology meetings.

Uri Herzberg, D.V.M., Ph.D, M.B.A, Celgene Dr. Herzberg is a Senior Director for Preclinical Development at Celgene Cellular Therapeutic, the Cell Therapy Division of Celgene. Prior to joining Celgene, Uri worked at Johnson and Johnson as a Principal Scientist, leading several projects for post surgical outcomes, and drug-device combination products. While at J&J he advanced to Research Fellow and also led an osteoarthritis project, a consumer product project and efforts in drug delivery. Prior to J&J he worked at Neurogen, where led the in-vivo pain biology program focusing on TRPV1 antagonists. Prior to Neurogen he worked at Cytotherapeutics (the predecessor of Stem Cell Inc.) and then Acorda Therapeutics where he established and managed the company's in-vivo facility and preclinical operations. He received his B.Sc. and D.V.M. degrees from Washington State University, his Ph.D. in Veterinary Biology and Neuroimmunology from the University of Minnesota and his MBA in pharmaceutical development from Fairleigh Dickinson University. His areas of expertise are comparative biology and veterinary medicine of laboratory animals, neuroscience and neuroimmunology, inflammation and chronic pain and the discovery and early development of cell based therapeutics. He is an ad hoc reviewer for the Small Business Innovative Research Grants – NIH, Special Section on Neuropharmacology and Neuroimmunology. He is also a reviewer for the following journals: Physiology and Behavior, Pain, and The Journal of Pain.

Jonathan Heyen, M.S. D.A.B.T., Pfizer Jonathan (Jon) Heyen is currently a senior principal scientist working in the Safety Pharmacology department at Pfizer La Jolla. Jon completed his undergraduate and graduate degrees at the University of Illinois-Champaign Urbana. Jon joined the Searle Company in St. Louis, Missouri where he worked for the Cardiovascular Discovery Group. Within this group Jon investigated the role of the immune system in various cardiovascular diseases and the potential for new therapies. At the completion of the Pharmacia/Pfizer merger in 2003, Jon relocated to La Jolla California and joined his current group: Global Safety Pharmacology as an in vivo cardiovascular lead. Jon's current roles include investigation of the potential effects of novel therapies, with emphasis on oncology, on the cardiovascular system, drug safety team leader for multiple projects and also leading the cardiovascular imaging group within Safety Pharmacology. He is an active member of several ILSI/HESI initiatives, APT and the Safety Pharmacology Society.

Michelle J. Horner, Ph.D., DABT., Amgen Dr. Michelle Horner is currently a Principal Scientist in the Nonclinical Safety Sciences Department at Amgen in Thousand Oaks, CA. Michelle received her PhD in Cellular and Molecular Biology from the University of Nevada, Reno. She subsequently joined Sierra Biomedical (now Charles River Laboratories, Reno) as a Study Director conducting primate toxicology studies for several pharmaceutical and biotechnology companies.

In 2003, Dr. Horner joined Amgen where her work has focused on discovery and regulatory toxicology support for development of biological and small molecule therapeutics, specializing in the Inflammation Therapeutic Area. At Amgen, Michelle contributed to numerous early stage discovery teams providing target liability input as well as safety screening in support of small molecule candidate selection. She has recently transitioned to a management position overseeing preclinical outsourcing and supervision of the program and study management group. Michelle is a past president of the Southern California Chapter of SOT, and is also a Diplomate of the American Board of Toxicology.

Christine Karbowski, Ph.D., Amgen Dr. Christine Hegedus Karbowski is a Senior Scientist in Comparative Biology and Safety Sciences at Amgen, Inc. She is a member of the Society of Toxicology, an organizing committee member for APT since 2014, and a previous member of the American Association for Cancer Research and the Environmental Mutagen Society. Dr. Karbowski received her B.A. in Molecular and Cell Biology and her Ph.D. in Molecular Toxicology, both from U.C. Berkeley. Her research has focused on applying 'Omics technologies such as transcriptomics, proteomics, and metabolomics for hazard identification in preclinical toxicology studies. During her 7 years at Amgen, Dr. Karbowski has served as a subject matter expert utilizing gene expression and genetic data for understanding potential target based liabilities as well as provided guidance for development of internal databases to query and visualize such data. Currently Dr. Karbowski serves as a project team representative for discovery and early stage programs across both large and small molecule modalities.

Lise I. Loberg, Ph.D., D.A.B.T., PMP, AbbVie Dr. Loberg has over 15 years' experience as a toxicologist and project manager in the biopharmaceutical industry. Dr. Loberg supports preclinical safety evaluation of compounds in development, from lead selection to late-stage clinical trials and marketed drugs. She has experience with large molecule biotechnologies and small molecule drugs ranging across several therapeutic areas including neuroscience, oncology and renal disease. Dr. Loberg is a Diplomate of the American Board of Toxicology and has earned the Project Management Professional (PMP) certification. She served as Treasurer (2011-2013) and Councilor (2010-2011) for the Midwest Regional Chapter of SOT and has been on the planning committee for Applied Pharmaceutical Toxicology meetings in 2012-2016. Dr. Loberg is an employee at AbbVie, Inc., previously Abbott Laboratories, where she has worked in Preclinical

Safety at three research & development sites (Ludwigshafen, Germany; Redwood City, California; and Lake County, Illinois) and three years in Drug Development Project Management. Prior to AbbVie/Abbott, Dr. Loberg supervised a Molecular Toxicology laboratory at IIT Research Institute (1996-1999). Dr. Loberg earned her Ph.D. in Toxicology at the University of Cincinnati (1996) and her B.S. in Psychology/ Neuroscience at John Carroll University.

Florence Lorget, Ph.D., DABT, Genentech Dr. Florence Lorget has over 10 years of industry experience. She joined Genentech as a safety assessment scientist at the end of 2013. Her work focuses on the nonclinical development of new therapies and drug delivery strategies for ocular diseases. Prior to Genentech, Florence was working at BioMarin where she was a key contributor to the nonclinical development of Vimizim, an enzyme replacement therapy for Morquio syndrome, a rare lysosomal storage disorder, and of BMN 111, a C-type natriuretic peptide for the treatment of Achondroplasia. Her first industry position was at Amgen Mountain View where she conducted in vitro/in vivo translational PK work.

During her postdoc at the Nestle Research Center and at UCSF, Florence focused on osteoclast and mesenchymal stem cell biology. Florence holds a PharmD and a PhD from the University of Picardie- Jules Verne, France, a Master in bioengineering from the Universty of Technology Compiegne, France and is a Diplomate of the American Board of Toxicology.

Jessica Lynch, Ph.D., Janssen Research & Development Dr. Lynch joined Janssen Research & Development as a Principal Scientist in Biologics Toxicology in May 2014. Jessica serves as a project toxicologist contributing scientifically and strategically to toxicology plans and provides support for the execution and monitoring of preclinical toxicology studies. Before joining Johnson & Johnson, Jessica began her career in industry as a Study Director at Charles River Laboratories, where she served as a scientist in the conduct of non-clinical research studies, interpreting and reporting study data and assuring the regulatory compliance of these studies. Before beginning her career in industry, Jessica held a position as a Post-Doctoral Associate at Saint Louis University, where she conducted research examining the transport of proteins across the blood brain barrier of mice. Jessica conducted research examining gender differences and pain in the TMEV mouse model of multiple sclerosis at the University of Minnesota.

Bradford McRae, Ph.D., Abbvie Dr. McRae is a Project Director in Immunology Discovery. He has led both internal drug discovery projects and external collaborations with a focus on therapeutics for the treatment of IBD. His experience in project leadership and in vivo pharmacology ranges from the target identification phase through drug candidate selection and IND. During his 17 year industry career Brad has served in various roles in Discovery research with BASF Pharma, Abbott Laboratories, and Abbvie. He completed his PhD in Immunology at Northwestern University and completed his postdoctoral training at the University of Chicago.

Dinah Misner, Genentech Dinah has been in the pharmaceutical industry for more than 16 years, of which she has spent significant time in the cardiovascular safety assessment and toxicology field. She was originally trained as an electrophysiologist in neuroscience at UCSD and the Salk Institute, but transitioned over to cardiovascular assessment and toxicology shortly after entering the pharmaceutical industry at Roche Palo Alto, where she ran the investigative and safety pharmacology labs and sat on both discovery and development project teams. She then went onto Celgene, where she ran the in vivo toxicology testing group, and also served as a project representative for discovery and investigative teams. She is currently leading the investigative toxicology group at Genentech, where they run primarily in vitro toxicology safety assessment assays for both small molecules and biotherapeutics. She is also a project representative for both discovery and development teams.

Padma-Kumar "Padma" Narayanan, Ph.D., Ionis Pharmaceuticals Dr. Narayanan received a BVSc (DVM equivalent) degree (1986) from College of Veterinary & Animal Sciences, Kerala, India; a Masters' in Veterinary Surgery (1988), Madras Veterinary College, Tamil Nadu, India, and a Ph.D (1995) in Immunopharmacology from School of Veterinary Medicine, Purdue University, West Lafayette, IN. He utilized analytical cytology tools, flow and image cytometry, to gain insights into mechanisms of neutrophil and endothelial pathophysiology on exposure to pro-oxidants and environmental toxins during his graduate training at Purdue University Cytometry Laboratories, West Lafayette, IN. He broadened the scope of this investigation during his post-doctoral fellowship (1995-1997) at Los Alamos National Laboratories, Los Alamos, NM, to understand the role of oxidative stress in radiation-induced DNA damage, cell cycle regulation, silicosis and chronic beryllium disease. Padma later joined SmithKline Beecham (SB), Philadelphia, PA (1997) to establish an analytical cytology core facility in Safety Assessment to support non-GLP and GLP toxicology studies for both large and small molecules. During his tenure at SB and later GlaxoSmithKline, Padma integrated cytometric technologies and cellular pathophysiological endpoints for identification and characterization of drug-induced pharmacologic/toxicologic responses at various stages of development. In addition he was instrumental in designing investigative toxicology studies, general and genetic toxicology, and safety pharmacology studies in support

of research and development compounds. Padma joined Amgen, Inc. in 2006 to establish an Investigative Toxicology group in Seattle and was Director of Cell Signaling and Immunotoxicology Group in Discovery Toxicology, until 2014. In this role at Amgen, Padma provided advice, strategic planning, study design, and effective management of issue resolution and predictive toxicology efforts to support selection and timely development of proteins, monoclonal antibodies, and small molecules. Padma is currently Executive Director of Toxicology at Ionis Pharmaceuticals in Carlsbad, CA.

John Nolan, Ph.D., The Scintillon Institute Dr. Nolan is Professor at The Scintillon Institute in San Diego, where his research group develops and applies new technologies for cytometry. Previously he was Professor at the La Jolla Bioengineering Institute and Director of the National Flow Cytometry Resource at Los Alamos National Lab. He is on the Editorial Boards of Cytometry and Current Protocols in Cytometry, a Fellow of the American Institute of Medical and Biological Engineering (AIMBE), and Past-president of the International Society for Advancement of Cytometry (ISAC). Dr. Nolan received BS degrees in Biology and Chemistry from the University of Illinois and a PhD in Biochemistry from Penn State. Current projects in his lab include spectral flow cytometry, surface enhanced Raman scattering (SERS) in cytometry, and high resolution analysis of natural and synthetic nanoparticles.

Raymond Page, Ph.D., Worcester Polytechnic Institute Dr. Page is Professor of Practice, Biomedical Engineering Department, Worcester Polytechnic Institute, in the USA. Formerly, he was Chief Scientific Officer, Cellthera, Inc, USA, Cyagra, Inc., USA and before that Senior Scientist, Advanced Cell Technology, USA and Senior Scientist, PPL Therapeutics, Inc, USA, Dr. Page is a co-founder and scientific advisory board member, Datar Genetics, India. Dr. Page is a member of the Biomedical Engineering Society, a participating faculty in the KEEN Foundation for Entrepreneurial Engineering Education at Worcester Polytechnic Institute and a Member of the Industrial Visiting Committee for the Chemical and Biomedical Engineering Department, West Virginia University, USA. Dr. Page received his BS and MS in Chemical Engineering at West Virginia University, USA and Ph.D. in Bioengineering from Virginia Tech, USA. He has presented and published extensively in the areas of transgenic and somatic cell nuclear transfer technology and development of cell therapy and regenerative strategies for skeletal muscle disorders.

Jeegar Patel, Ph.D., Kadmon Pharmaceuticals Dr. Patel is an experienced regulatory toxicologist and SME in development of small and large molecules (MAbs, Bispecifics, Fusion Proteins, Antibody-Drug Conjugates) in various therapeutic areas. He is currently Senior Director of Nonclinical Development at Kadmon Pharmaceuticals, a clinical stage biotechnology company in New York City. Previous roles have included Nonclinical Safety Project Leader (Principal Scientist) at ImClone Systems (a wholly owned subsidiary of Eli Lilly and Co) and Toxicology Project Liaison/Study Director (Senior Toxicologist) at Abbott Laboratories.

Matthew Peters, Ph.D., AstraZeneca Dr. Peters is a principal scientist at AstraZeneca Pharmaceuticals in Waltham, MA. He received a Ph.D. in Physiology from University of North Carolina at Chapel Hill followed by a postdoctoral fellowship at Johns Hopkins University. Since joining AstraZeneca in 2001, Dr. Peters has performed diverse roles in early phase drug discovery and toxicity.

Michael Placke, Ph.D., DABT, Alnylam Pharmaceuticals Dr. Placke is a seasoned pharmaceutical drug development executive with over 30 years of pharmaceutical industry experience, including scientific and operational responsibilities for multi-disciplinary pharmaceutical development operations, including Drug Safety and Metabolism (DSM) and Chemical Product Development (CPD) Divisions in large pharmaceutical and biopharmaceutical companies, private equity/venture-funded start-up firms and contract research organizations (CRO). Dr. Placke is currently Senior Vice President of Drug Safety and Metabolism at Alnylam Pharmaceuticals, where he leads non-clinical drug development. In this role he is responsible for providing toxicology, pharmacokinetic, and drug metabolism evaluations of siRNA drug candidates in support of both research and full clinical development programs. Prior to joining Alnylam, he was President & CEO of Ricerca Biosciences, a privately held contract research company, providing integrated non-clinical drug development services to the biopharmaceutical and pharmaceutical companies. Prior to Ricerca, Dr. Placke was VP, Drug Safety at Wyeth Pharmaceuticals (and Pfizer post acquisition), where he had both operational and portfolio responsibilities for non-clinical drug safety. Before joining Wyeth he was VP, R&D of a private equity/venture-funded start-up firm developing novel respiratory drug therapies. He has scientific and executive-level operational experience in developing a wide array of drug product modalities including siRNA therapies, small molecules, biologics, vaccines, and specialty drug products. He is formally trained in experimental pathology and toxicology, earning BS and MS degrees from The Ohio State University and his PhD from the University of Connecticut. He is board certified in general toxicology, and a recent director and officer of the American Board of Toxicology.

Michael J. Santostefano, Ph.D., D.A.B.T., Merck Dr. Michael J Santostefano received a B.S. degree in Biochemistry from the Univ. of Scranton, and a Ph.D. in Toxicology from Texas A&M University. After post-doctoral work at the Univ. of North Carolina, Michael joined GlaxoWellcome,

Inc. as a senior toxicologist and held various roles as a study director/monitor, head of toxicology, project representative, and research investigator until his departure from GlaxoSmithKline (GSK) in Oct, 2006. From 2006-2014, Michael worked as a principal scientist at Amgen and provided advice, strategic planning, study design, and effective management of discovery and development toxicology programs/projects to support the development of biologics and small molecules. In 2014, he joined Merck Research Laboratories in Boston and is currently the therapeutic area leader in preclinical safety assessment supporting the Business Development and Licensing organization and is responsible for working with potential partners in conducting the due diligence reviews of in-licensing candidates and facilitating transfer of information for out-licensing candidates In addition, he has provided oversight for regulatory submissions to international and national regulatory agencies while at Amgen, GSK, and Merck. His academic and pharmaceutical career has generated over 35 peer-reviewed manuscripts in the field of mechanistic toxicology. Michael is a Diplomate of the American Board of Toxicology, and a member of ACT and SOT. He also serves on the editorial advisory board for Toxicology and Applied Pharmacology and has served as a symposium organizer/chairperson for ACT and SOT. He served on the Outreach Committee for ACT and was the vice president of the North Carolina Chapter of the SOT. In addition to his position at Merck, he is currently working on a master's degree in Regulatory Sciences at the Univ. of Southern California.

Joseph J. Senn, Ph.D., DABT, Moderna Therapeutics A board certified toxicologist who received his PhD in Pharmacology and Physiology from the University of Rochester School of Medicine and dentistry. He has held joint faculty positions at the Medical University of South Carolina as assistant professor of pediatrics and pharmacology prior to entering industry. In industry, his focus has been on immunotoxicology, investigative, discovery and development toxicology and in a wide range of therapeutic areas including immune modulators, oncology, neurology, inflammatory and infectious diseases. During the course of his career in industry he has led multiple regulatory filings for modalities ranging from small molecules, biologics and antibody drug conjugates and most recently modified messenger RNA. He is currently the Head of Toxicology and Pathology at Moderna Therapeutics, a modified messenger RNA focused company. Previously, he served as Site Head and Director of Drug Safety for Takeda Pharmaceuticals in Boston, MA.

R. Scott Thies, Ph.D., University of Washington Dr. Thies is Director of Operations for the UW Medicine Heart Regeneration Program. In this role, he is responsible for overseeing the development of a human pluripotent stem cell-derived cardiomyocyte therapy through early clinical testing. Concurrently, he is a consultant in the biotechnology sector. Prior to joining the University of Washington, he was Senior Director of Stem Cell Biology at Fate Therapeutics, and before that, a Director in Stem Cell Therapeutics at Geron and a Senior Scientist in Regenerative Medicine at Genetics Institute/Wyeth. Dr. Thies completed postdoctoral training at UCLA and UCSD after receiving his B.S in biology and chemistry from the University of Miami and Ph.D. in physiology from Duke University.

Brian Vuillemenot, Ph.D., DABT, Genentech Dr. Vuillemenot is a pharmacology/toxicology scientist with eleven years of experience in nonclinical development of biological and small molecule therapeutics. His specialties include development of animal models of disease and direct administration of molecules to the lung and CNS. Brian received his Ph.D. from Tulane University in Molecular and Cellular Biology investigating the pathogenesis of interstitial lung disease. He then conducted a postdoctoral fellowship at Lovelace Respiratory Research Institute on the role of epigenetics in lung cancer. Brian began his career in the biopharmaceutical industry in 2005 at Nektar Therapeutics as a scientist involved with exploratory safety assessment of inhalable insulins and other molecules for lung administration. Brian joined Anesiva in 2007 where he developed in vivo pharmacology models to test therapies for pain. From 2008 to 2014, Brian was employed at BioMarin Pharmaceutical Inc., where he served as a core team member and lead nonclinical scientist on programs developing therapies for orphan diseases. Brian is currently employed as a toxicologist in the department of Safety Assessment at Genentech. Brian is a member of the Society of Toxicology and American College of Toxicology and a Diplomate of the American Board of Toxicology.

Yi Yang, Ph.D., DABT, Genentech Dr. Yang received her MD from Sun Yet-Sen University of Medical Sciences in 1995, her Ph.D. in Toxicology and M.S. in Biostatistics from University of Cincinnati in 2003. Dr. Yang joined Abbott Laboratories/AbbVie in 2003. She is currently a Principle Research Scientist in the Global Preclinical Safety Department at AbbVie, supporting programs from Early Discovery to Full Development. She also serves as a scientific advisor on discovery and investigative toxicology issues. Previous to her current position, she managed the Molecular Toxicology group at Abbott, implemented toxicogenomics, urinary biomarkers, mitochondrial assessment, and target safety assessment strategies in Discovery organization. Dr. Yang has authored over 30 peer-reviewed publications in mechanistic and predictive toxicology, given over 20 invited presentations at conferences, and served as a peer reviewer for several journals in this area. She is actively involved in a number of industry-wide collaborations, including the Predictive Safety Testing Consortium and the HESI committee on the qualification of toxicity biomarkers. Dr. Yang is currently an organizing committee member of the Applied Pharmaceutical Toxicology. She also serves as the president-elect for Midwest Regional Chapter of SOT.

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