Welcome to the 2018 HT-ADME Conference. Our organizers have gathered another excellent group of speakers for the annual HT-ADME 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 HT-ADME experience. Thank you for your participation.

ORGANIZING COMMITTEE

PRESIDING OFFICERS
Conference Chair:
Joseph Tweed, Pfizer

Conference Chair Elect:
Stephen Johnston, Broad Institute

COMMITTEE MEMBERS
Dallas Bednarczyk, Novartis
Dieter Drexler, BMS
Maria Fitzgerald, Sanofi
John S. Janiszewski, Sound Analytics
Ian Knemeyer, Merck
Steven Louie, BioIVT
Wilson Shou, BMS
Ron Xu, ACEA Biosciences
THURSDAY, JUNE 21

7:30 - 8:30  Registration & Breakfast

8:30 - 8:40  Conference Opening
Joseph Tweed, Pfizer

SESSION I: Developing Strategies in the ADME Discipline
Session Chairs: Stephen Johnston, Broad Institute and Steven Louie, BioIVT

8:40 - 8:45  Session I Introduction

8:45 - 9:15  ADME SAR: The Origination, Current State and Future Possibilities, Shaped by Strategy, Science and Technology
Matthew Troutman, Pfizer

9:15 - 9:45  Incorporating Human Dose Projection in Early Lead Optimization; Good or Bad Idea?
Sean Kim, Blueprint Medicines

9:45 - 10:15  Adapting and Readapting in the Outsourcing Era
Sujal Deshmukh, Novartis

10:15 - 10:35  Break

SESSION II: New Technologies and Approaches in ADME Science
Session Chairs: Ian Knemeyer, Merck and John Janiszewski, Sound Analytics

10:35 - 10:40  Session II Introduction

Hui Zhang, Pfizer

11:10 - 11:40  Leveraging in silico ADMET Models and Influence to Increase the Probability of Success in Discovery
Elizabeth Joshi, Merck

11:40 - 12:10  High Content Metabolic Stability Assay for Drug Discovery
Marina Slavsky, Sanofi Genzyme
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<td>12:10 - 1:10</td>
<td>Complimentary Lunch</td>
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<td>1:10 - 1:40</td>
<td><strong>VENDOR PRESENTATION</strong></td>
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<td>Albert P. Li, InVitro ADMET Laboratories</td>
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<td>Translational DMPK Applications of Tissue Chip Technologies</td>
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<td>Murat Cirit, MIT</td>
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<td><strong>Mass Spectrometry Imaging: Revealing Tissue</strong></td>
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<td>Secrets for Early Drug Efficacy and Risk Assessment</td>
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<td><strong>PLENARY LECTURE</strong></td>
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<td>Concentrations: A Proteomics and PET Imaging Approach</td>
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<td>Kenneth Koeplinger, Merck</td>
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<td><strong>ADME Characterization of Antibody Drug Conjugates</strong></td>
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<td>5:15 - 5:20</td>
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SESSION I

ADME SAR: The Origination, Current State and Future Possibilities, Shaped by Strategy, Science and Technology
Matthew Troutman, Pfizer

In this discussion, we will cover the key remit for the ADME SAR discipline in Drug Discovery and how we have seen this data be used strategically to make organizational impact from ADME SAR’s early days, to present state, and how we see this potentially evolving to shape the future. Within this, we will additionally discuss the how strategy and emerging sciences and technologies combined to shape our impact, efforts and capabilities in the ADME SAR discipline. Finally, we will additionally touch on how organizational approaches have influenced the nature of the ADME SAR discipline to date and in the future as well.

Incorporating Human Dose Projection in Early Lead Optimization – Good or Bad Idea?
Sean Kim, Blueprint Medicines

Prediction of human efficacious dose is a critical component of drug development, especially for the candidates entering human clinical trial. In the past, human PK and dose projection were performed only for development candidates as an accurate prediction requires rich data set of in vitro ADME and in vivo pharmacokinetic information in preclinical species. However, advancement in sophistication of ADME assays, modeling tools/methodologies and understanding of PD requirement for efficacy from marketed drugs allow us to deploy human dose projection in early lead optimization in certain class of targeted therapies. Such early adoption of human dose may benefit integrated assessment of compound viability and/or provide an insight on what properties are critical in optimizing the series to reach ‘Development Candidate’ status. This presentation will provide an overview of early human dose projection approaches and highlight potential advantages and disadvantages.

Adapting and Readapting in the Outsourcing Era
Sujal Deshmukh, Novartis

Outsourcing of ADME assays has become an integral part of the pharmaceutical industry. Over the last decade there has been an evolution in the assays, quality, cost and services provided by the outsourcing partner. Various big and small pharmaceutical companies have embarked on the outsourcing bandwagon at different times based on company strategies and requirements. Although it is well recognized that managing outsourcing is an ongoing process, the dynamic environment both internally and externally influences the operating model and defines the strategic landscape. General strategies such as cost savings, freeing internal resources, and maximizing external resources are key drivers for outsourcing. However, ongoing internal and external changes and discoveries post-outsourcing have resulted in several other strategies that have emerged to a significant level of importance. These strategies and other consideration essential to the success of ADME support will be discussed.

SESSION II

Acoustic-OPP-MS: The Next Generation BioAnalytical Platform for Drug Discovery with Ultra-High Throughput
Hui Zhang, Pfizer

Label-free LC/MS based screening technology is routinely used in pharmaceutical industries for hit discovery and various ADME profiling applications. Although the current analysis speed of less than 30 seconds per sample is quite promising, it still cannot match the throughput provided by plate-reader based HTS platforms. Acoustic dispensing is a droplet transfer technology capable of high speed, reproducibility and
absolute accuracy. In this work, we successfully integrated acoustic transducer and the open-port probe (OPP) for direct sampling into a standard ESI ion source. Screening speeds of up to 0.4 seconds-per-sample were demonstrated with superb sensitivity (attomole loading), good quantitation capability (>3 orders of magnitude), and broad compound coverage (from small molecule pharmaceuticals to peptides and antibodies). The great performance was demonstrated with a Drug-Drug Interaction (DDI) assay, where various substrates/metabolites were monitored. Analysis speeds of 1.7 seconds per sample (~12 minutes per 384-well plate) were achieved with baseline separation between samples. The determined IC50s matched the results from fast LC-MS analysis (30 seconds/sample) very well. In addition, the Acoustic-OPP-ESI-MS platform provided ~15X screening throughput increase and reduced the sample consumption reduced by 4000 fold and solvent consumption by 100 fold.

**High Content Metabolic Stability Assay for Drug Discovery**  
Marina Slavsky, Sanofi Genzyme

Prediction of human pharmacokinetics from in vitro assays and pre-clinical data is an integral part of drug discovery. The aim of this approach is to identify potential development liabilities of new chemical entities (NCEs) as early as possible, thereby minimizing the risk of late failure of new drug candidates. Highly metabolized compounds can suffer from low oral bioavailability and short half-lives leading to inadequate therapeutic effect. NCEs that are primarily metabolized by a single enzyme can be prone to inter-individual pharmacokinetic variability, and potential drug-drug interactions.

A Labcyte Echo® acoustic dispenser was utilized to reduce both compound volume and solubility requirements for the assay via nanoliter scale non-contact dispensing. A Tecan EVO® automated liquid handler was used allowing for fully automated, high-throughput sample handling in 384-well plate format. A Thermo Q Exactive™ high resolution mass spectrometer was operated employing full scan mode with data dependent fragmentation. GMSU, Mass-Metasite, and Webmetabase applications were employed for calculating intrinsic clearance, CYP450 contribution, and metabolic soft spot identification.

A single, multiplexed, high throughput assay has been developed to concurrently assess the intrinsic metabolic clearance, CYP3A and CYP2D6 contribution, and metabolic soft spot identification. Obtaining this data earlier in the drug discovery process aids project teams in their scaffold identification and subsequent optimization efforts.

**VENDOR PRESENTATION**

**Novel Hepatocyte and Enterocyte Technologies for the Evaluation of Human Drug Metabolism, Drug-Drug Interactions, and Drug Toxicity**  
Albert P. Li, InVitro ADMET Laboratories

Human-based in vitro experimental systems can be applied during preclinical stages of drug development for the assessment of human-specific drug properties. In this presentation, novel human hepatocyte and enterocyte-based systems included 999Elite™ cryopreserved human hepatocytes (90% viability, >90% confluency, >9 days in culture), MetMax™ cryopreserved human hepatocytes (permeabilized, cofactor-supplemented cryopreserved human hepatocytes), cryopreserved human enterocytes, and cryopreserved human intestinal mucosal epithelium (CHIM) and their application to evaluate hepatic and enteric drug metabolism, drug-drug interactions, and drug toxicity will be discussed.

**Translational DMPK Applications of Tissue Chip Technologies**  
Murat Cirit, MIT

In vitro models have been developed and utilized in various stages for the preclinical development. Compared to animal models, in vitro models have advantages such as high-throughput capability, low cost, well-controlled experimental parameters and fewer ethical concerns etc. However, the simplicity of the conventional in vitro models makes them
incapable of achieving adequate physiological relevance for mimicking the human body, which is a dynamic system that has complex three-dimensional microenvironment, intracellular communications and organ interactions. Hence, there is an urgent need to develop more physiologically relevant in vitro systems for better simulating the human body in response of drugs and providing more reliable in-vitro in-vivo translation (IVIVT) from preclinical results to clinical outcomes.

Tissue chip technologies are to provide an improved approach for more predictive preclinical drug discovery via a highly integrated experimental/computational paradigm. Success will require quantitative characterization of MPSs and mechanistic analysis of experimental findings sufficient to translate resulting insights from in vitro to in vivo. We describe a systems pharmacology perspective on this problem, incorporating more mechanistic detail for tissue chip studies than traditional pharmacokinetic (PK) and pharmacokinetic/pharmacodynamic (PK/PD) models yet within broadly comprehensive scope. These systems pharmacology approaches offer new insight into design of experiments, data interpretation and organ-specific responses, which can be translated to in vivo responses, such as patient-to-patient variability, drug efficacy and toxicity.

Mass Spectrometry Imaging: Revealing Tissue Secrets for Early Drug Efficacy and Risk Assessment

Stefan T. Linehan, Blue Tail Regenerative Therapeutics

In vivo drug efficacy and toxicity evaluations are key areas of drug development. It is crucial to evaluate how much drug arrives to a given site of action; and also to determine the positive and adverse effects that drugs may have on organs or cell function.

MALDI MSI is a new approach to accelerate drug discovery, with the possibility of yielding valuable biodistribution information about new candidate pharmaceuticals early, without labeling the test compounds. This technique can be both qualitative and quantitative. It also allows for the simultaneous localization of the parent compound, and its metabolite(s) if formed, as well as any other endogenous metabolites of interest, on a tissue section. MSI supports in vivo or ex vivo preclinical data in some of the following ways:

1. PK information: Specific distribution of drug and its metabolites - Quantification of these molecules - metabolism, clearance, exposure studies of drug candidate in tissue without labeling in combination with histology;
2. Target engagement information: Drug distribution and quantification with its target using MSI technique;
3. PD information: Tracking biomarkers of efficacy or toxicity - Can be combined with PK and target engagement studies;
4. Toxicity information: Drug distribution and metabolites correlated to pathologist information (histology) to validate mechanism of action.

Pursuing the Holy Grail of Predicting and Verifying Tissue Drug Concentrations: A Proteomics and PET Imaging Approach

Jashvant (Jash) Unadkat, University of Washington

Tissue concentrations determine efficacy and toxicity of a drug. Transporter expression at the tissue: blood barrier (e.g. liver: blood or brain: blood barrier) can result in “asymmetry” or disconnect in tissue: blood concentration. In humans, except for Positron Emission Tomography (PET) or other imaging methods, it is impossible to measure tissue drug concentrations. For this reason, methods to predict such concentrations and to verify the predictions are needed. Therefore, we have developed a proteomics-based approach to predict tissue drug concentrations through PBPK modeling and simulation. In addition, we have developed PET imaging methods to measure and verify the model-predicted tissue drug concentrations in humans. Data will be presented to show the promise of this approach using rosuvastatin as a model drug. Once our proteomics-informed approach has been verified with additional probe substrates that interrogate a variety of transporters, it can be used to routinely predict tissue concentration of drugs under development. Supported by UWRAPT funded by Genentech, Merck, Biogen, Gilead, BMS, Pfizer and Takeda.
ADME Implications of Chimeric Protein Degrader Druggability
Adam M. Gilbert, Pfizer

The use of chimeric protein degraders or PROTACs is a potentially breakthrough approach to treat disease since these agents co-opt the Ubiquitin Proteasome System to degrade targeted proteins rather than inhibiting them. In addition to inhibiting the catalytic functions of proteins, chimeric degraders ablate protein scaffolding function, and the pharmacological effects of these agents persist until the degraded protein is resynthesized. However the development of chimeric degraders has proven challenging due to their high molecular weights, LogD and TPSA values since they are composed of two traditional small molecules (a protein target ligand and an E3 binding ligand) connected by a linker moiety.

In this seminar, the ADME implications of assessing protein degrader druggability will be discussed using simulations as well data from a series of chimeric degraders of BTK. Moreover we will address the question of what properties are required in chimeric protein degraders to create an effective therapeutic agent.

Pharmacologic Target Validation Utilizing siRNA-Mediated Knock Down of Hepatic Genes
Kenneth A. Koeplinger, Merck

Lipid nanoparticle (LNP) mediated delivery of siRNA is an effective and selective means of knocking down the expression of targeted hepatic genes in preclinical species (rodent and non-human primates). We have used this approach for direct evaluation of the effect of reduced expression of hepatic target proteins with respect to both pharmacology and safety endpoints in preclinical pharmacology and safety studies.

In addition to new pharmacology target genes, we have also utilized LNP mediated delivery of siRNA to evaluate reduced hepatic expression of ADME target genes including hepatic transporters, UDP glucuronosyl transferases (UGT), and cytochrome P450s (CYP). Often early discovery lead compounds exhibit undesirably high clearance and selective and/or broad knock-down of ADME genes enables sufficient increases in exposure for observation of pharmacologic proof of concept. In addition to selective KD of single ADME genes, an approach for pan-reduction of CYP or UGT activity is reduction of pathways supporting production of necessary electron transport or enzyme co-factors. Pan knock-down of cytochrome P450 activity was achieved by targeting hepatic cytochrome P450 reductase together with cytochrome b5. Pan-reduction of UGT activity was achieved by targeting UDP glucose dehydrogenase (UDPG DH) which is the rate limiting step in UDPGA biosynthesis.

ADME Characterization of Antibody Drug Conjugates
Nagendra (Nag) Chemuturi, Novartis

Antibody Drug Conjugates (ADCs) are, slowly but surely, establishing themselves as a potent modality in treatment of cancer. They aspire to combine the selectivity of antibodies with the potency of small molecule to selectively deliver potent cytotoxins to tumors. The current talk will be focused on what ADCs are, where ADCs are in the clinic, and the role of DMPK in ADME characterization of ADCs, including the role of transporters in the disposition of ADCs.
BIOGRAPHIES

DALLAS BEDNARCZYK, PH.D., Novartis, Dr. Dallas Bednarczyk is an Investigator in the Department of Metabolism and Pharmacokinetics at Novartis. He earned his doctorate under the supervision of Steve Wright at the University of Arizona. Dallas began his career in the pharmaceutical industry developing and implementing transporter assays as a Post-Doctoral Scientist at Sanofi-Synthelabo in 2002. Since then he has investigated aspects of transporter-mediated absorption, distribution, and excretion of drugs, as well as drug-drug interactions involving transporters. His current role at Novartis involves developing strategy around transporter issues and identifying and implementing suitable solutions to address project teams’ needs regarding the transporter-mediated flux of molecules including, potential drug interactions, BBB penetration, liver targeting, and addressing in vitro/in vivo clearance disconnects due to transport.

NAGENDRA CHEMUTURI, PH.D., Novartis, Dr. Chemuturi received his Bachelor Degree in Pharmacy with Distinction from Kakatiya University in India. He then worked as a pharmaceutical salesman for Zydus-Cadila in India, before pursuing his Ph.D. at the University of Iowa. He was awarded the AAPS Graduate Symposium Award in 2005 for his dissertation work on the role of drug transporters and metabolism in the preferential uptake of dopamine from the nose into the brain. He started his career in the US at Vertex Pharmaceuticals in MA in 2005. Since then, he has worked at Alcon-Novartis and Seattle Genetics and is currently a Senior Investigator-I at Novartis Institutes of BioMedical Research Inc., working on biologics and cell & gene therapies. During his career he has served as DMPK lead on several small and large molecule projects and has led efforts to understand the role of drug transporters in ophthalmology and ADCs. He has given podium presentations at several scientific conferences, is active in IQ consortium, leading the MABEL working group and has authored/co-authored several articles and book chapters.

MURAT CIRIT, PH.D., MIT, Dr. Cirit is a principal investigator at MIT & Director of the Translational Center of Tissue Chip Technologies (TC2T). TC2T will combine quantitative experimental biology, computational biology and biostatistics to characterize these complex systems and translate experimental insights into clinical outcomes. Murat completed his PhD at NCSU focusing on systems biology of growth factor-mediated signal transduction pathways. After completion of his PhD, he worked in the pharmaceutical industry focusing on preclinical drug discovery for oncology. He brings an interdisciplinary and systematic approach through his extensive experimental knowledge and computational modeling with an understanding of biological, physiological, and pharmacological processes. His main research experience is systems pharmacology, systems biology, oncology, tissue engineering, cell biology and signal transduction networks.

SUJAL DESHMUKH, PH.D., Novartis, Dr. Deshmukh is responsible for overseeing the Global Enzyme group focused on in vitro clearance and distribution at Novartis Institutes for Biomedical Research – Cambridge, in the PK Sciences department. Formerly, he was DMPK project representative and PKPD Network lead at Merck Research Laboratories – Boston. At Merck, Sujal supported several discovery projects in Oncology, Neuroscience and Immunology. Sujal obtained his PhD in Pharmacology and Toxicology from the University of Texas Medical Brach – Galveston where he investigated the role of human placenta in the metabolism and transport of opioids. Sujal has presented in the area of clearance in vitro-in vivo extrapolation (IVIVE) and continues to pursue his passion for identifying in vitro tools focused on improving prediction accuracy of human clearance.

DIETER DREXLER, PH.D., Bristol-Myers Squibb, Dr. Drexler is a Research Fellow in the Pharmaceutical Candidate Optimization - Analytical Sciences Department at the R&D site in Wallingford, CT where he leads a group providing analytical and mass spectrometric support for Discovery Chemistry and Biology. The projects include the qualitative and quantitative analysis of
endogenous and exogenous small molecules, peptides/proteins, and biologics in various matrices utilizing a variety of analytical techniques. His research interests involve the development of innovative techniques and methodologies applied to the analysis of novel biopharmaceutical modalities and biomarkers.

Dr. Drexler received his Doctorate in Analytical Chemistry at the University of Ulm, Germany. He joined BASF Corporation in Research Triangle Park, NC as a Postdoctoral Research Fellow to investigate pesticide analysis in soil and water. He then moved to Finnigan Corporation in San Jose, CA as a Product Specialist for ion trap and triple quadrupole mass spectrometers supporting research and marketing efforts. During his career at BMS he has taken on projects and positions with increasing responsibility and is currently the laboratory manager for bioanalytical support.

He has authored or co-authored over 100 journal articles, book chapters, oral and poster presentations.

**MARIA FITZGERALD, M.S., Sanofi,** Maria is a Scientific Director and Head of Early ADME, DMPK, Sanofi US based in Waltham, MA. She has been at Genzyme and then Sanofi for more than 15 years and is currently responsible for physicochemical profiling, in vitro drug metabolism and transporter studies for drug discovery and development. Earlier in her career at Genzyme, she was responsible for pharmaceutics and analytical characterization of drug candidates. Prior to Genzyme, Maria was a group leader for the chromatography, environmental and inorganic analysis group in the R&D organization at Polaroid Corporation. Maria earned her Bachelor of Science in Chemistry from LeMoyne College, Syracuse, NY and her Master of Science from Boston College where she studied bio-inorganic chemistry.

**STEPHEN JOHNSTON, PH.D., Broad Institute of MIT and Harvard,** Dr. Johnston is senior group leader within the Center for the Development of Therapeutics (CDoT) of the Broad Institute of MIT and Harvard, leading the analytical chemistry, compound management, and high-throughput screening groups while also managing overall CDoT finances. The analytical chemistry group provides mass spectrometry-based functions for early therapeutic discovery/development of small molecules, which include assessment of the purity of synthesized or purchased small molecules, purification of them when necessary, mass spectrometry-based high-throughput small molecule and fragment screening assays, and in vitro ADME assays. Additionally, the group maintains the open access instrumentation for the chemist community at the Broad. Dr. Johnston received his bachelor’s degree in chemistry from Davidson College, followed by a doctorate in analytical chemistry from the University of North Carolina at Chapel Hill. He joined the Broad Institute in 2007. Prior to the Broad he was a senior scientist at Schering-Plough performing analytical method development and validation for legacy products.

**ELIZABETH JOSHI, PH.D., Merck,** Dr. Joshi completed her undergraduate studies in chemistry at Mary Washington College in Fredericksburg, VA; then followed up her doctoral training in the Chemistry Department at the University of Virginia investigating chemical mechanisms associated with idiosyncratic drug reactions. Prior to joining Merck, Elizabeth spent 11 years with Eli Lilly & Company in Indianapolis, IN where she served both as a scientific subject matter expert in the area of drug metabolism, as well a departmental project leader supporting ADME discovery/development, primarily in the area of neuroscience. Upon joining Merck in 2013, she has continued to expand her research interests working as a close collaborator with Toxicology to focus on new model development in the area of drug induced liver injury, as well as broadening her discovery expertise in leveraging various ADME models to influence the drug discovery process. More recently, Elizabeth has been leading an early ADME group whose emphasis has been directed as leveraging in silico ADME tools to enhance our screening hit series selection. She has a number of publications covering her respective area of expertise, as well as a variety of invited presentations and posters.

**SEAN KIM, PH.D., Blueprint Medicines,** Dr. Kim is Director of DMPK at Blueprint Medicines in Cambridge, USA. Formerly, he
was a group leader in Metabolism and Pharmacokinetics at Novartis Institute of Biomedical Research and before that, Senior Research Investigator in Metabolism and Pharmacokinetics at Bristol-Myers Squibb. Dr. Kim received his B.S. in biology from the Sogang University in Korea and Ph.D. in toxicology from Rutgers, The State University of New Jersey. He has represented DMPK function in multiple disease areas, including Oncology/IO, Ophthalmology, Neuroscience and Anti-infectives and led P450 induction lab. He has published over 25 peer-reviewed articles and two book chapters in the areas of carcinogenesis, P450 induction and human PK projection as well as discovery of new chemical entities.

IAN KNEMEYER, PH.D., Merck, Dr. Knemeyer obtained his PhD in Pharmaceutical Chemistry from The Ohio State University prior to joining Schering-Plough and subsequently Merck. He has 15 years of drug discovery, preclinical, and clinical development experience, most recently in oncology and immunology therapeutic areas. His areas of specialty and research interest include application of in silico-in vitro-in vivo correlation (ISIVIVC), human PK prediction, drug-drug interaction modeling, and applications development of metabolizing liver (bio)mimetics.

KENNETH A. KOEPLINGER, PH.D., Merck, Dr. Koeplinger worked extensively in the diverse fields of ADME/PK, protein science and molecular biology while employed at The Upjohn Co (later known as Pharmacia) and Merck Research Laboratories. Diverse experience with both large and small molecule therapeutics. ADME lead for Merck Research Laboratory discovery/development teams for nucleoside based antivirals, lipid nanoparticle-mediated siRNA delivery, and oral delivery of peptide based protein-protein interaction (PPI) inhibitors.

STEFAN LINEHAN, Blue Tail Regenerative Therapeutics, Mr. Linehan is currently the Director of Innovation and Outsourcing at Blue Tail Regenerative Therapeutics. He was the Director of North American and Head of Japan at ImaBiotech, where he was responsible for overseeing and directing sales operations in North America, including business development as well as establishing and building a team responsible for selling mass spectrometry imaging (MSI) services out of the ImaBiotech Corp facility in Billerica, MA. Stefan Linehan has more than fifteen years of experience in the ADME (DMPK), Toxicology, and Discovery areas. He is also well known for his development and expertise with the 3D cryo-imaging and autoradiography techniques. Linehan has held previous positions at inviCRO, XenoBiotic Laboratories, and WIL Research Laboratories; where he set up and managed the quantitative whole body autoradiography (QWBA) capabilities and conducted mass balance/pharmacokinetic studies. He has also worked at Wyeth Pharmaceuticals, where he developed the 3D cryo-imaging techniques and conducted regulated tissue distribution, mass balance, and pharmacokinetic studies. Linehan received his Masters in Clinical Biochemistry from Griffith University in Queensland, Australia and his Bachelors in Biology from Colorado State University, CO. He has lived overseas in both Australia and Japan, which has provided him with a deep understanding of business and culture on a global scale. Stefan Linehan was the last President of the Society for Whole Body Autoradiography (SWBA) and has held multiple Executive Committee Officer Positions since 2003. He is also a Founding Executive Committee Officer for the Imaging Mass Spectrometry Society (IMSS); which was incorporated in 2017.

STEVEN W. LOUIE, BioIVT, Steven is the Director of Transporter Sciences for BioIVT in Durham, NC. He lives in the Greater Boston Area, and mostly telecommutes to his home base. He was formerly a Senior Scientist in the Department of Pharmacokinetics and Drug Metabolism in Amgen, Cambridge, MA. He did his undergraduate work at the University of Minnesota (Minneapolis/St. Paul, MN) and his graduate work at the University of Iowa (Iowa City, IA). He is a transporter jockey who has been developing and implementing in vitro tools and assays to support drug discovery and development for the last 22 years. He is the 2017-2018 Chair of the AAPS Drug Transport Focus Group (DTFG). He is the 2017 AAPS Pharmacokinetics, Pharmacodynamics, and Drug Metabolism (PPDM) Sections Service Award Recipient, and has the honor of co-organizing the AAPS Workshop “Transporter Boot Camp: Back to Basics,” the eLearning Course “Transporter Knowledge for New Frontiers” and the 2018 AAPS
Transporter Workshop-From Benchside to Bedside. This year he has the honor of contributing to The Boston Society HT-ADME Conference. Prior to joining BioIVT, Steven worked at Amgen, Merck and GSK. His recent research interests include in vitro/in vivo extrapolation to predict transporter-mediated drug-drug interactions. His recent work has contributed to the recent IND-filing, FDA and/or EMA approvals of Corlanor™, Kryprolis™, Parsabiv™.

WILSON SHOU, PH.D., Bristol-Myers Squibb, Dr. Shou is Principal Scientist, Discovery Chemistry Platforms at Bristol-Myers Squibb’s R&D site in Hopewell, NJ, where he leads a bioanalytical group providing support for the enterprise-wide high-throughput in vitro ADME profiling effort. Dr. Shou’s research interests involve the application of mass spectrometry, separation sciences and software/automation tools for the high-throughput bioanalysis of small molecules and peptides in support of lead discovery and optimization. He has authored/co-authored 50 journal articles, 4 book chapters, and more than 70 podium or poster presentations. He was the guest editor for a special issue of Bioanalysis focusing on Discovery Bioanalysis in 2012, and also co-edited an ebook entitled “Eliminating bottlenecks for efficient bioanalysis: practices and applications in drug discovery and development” in 2014. He has served on the organizing committee of HT-ADME since 2011, and was the conference chair in 2013.

MARINA SLAVSKY, M.S., Sanofi Genzyme, Marina Slavsky is a Senior Scientist in Early ADME group in DMPK at Sanofi Genzyme US based in Waltham, MA. She has been at Genzyme and then Sanofi for more than 20 years and is currently responsible for in vitro drug metabolism studies for drug discovery. Marina earned her Master of Science from Moscow State University of Fine Chemical Technologies where she studied analytical chemistry.

MATTHEW D. TROUTMAN, PH.D., Pfizer, Dr. Troutman is Senior Director in the Medicine Design Department at Pfizer, Inc. At Pfizer, he leads the Hit Discovery and Optimization (HDO) group. The HDO group plays a global role in delivering target and lead identification and optimization data in support of Pfizer’s small molecule discovery programs. Current areas of focus for HDO include developing medicinal properties (molecular properties and biopharmaceutics, ADME and safety) assays and paradigms to drive lead matter optimization. Additionally, HDO focuses on mass-spectrometry based ‘omics approaches (proteomics and metabolomics) and high throughput quantitation technologies focused on enabling hit ID and optimization capabilities. Before his current role, Dr. Troutman led groups that profiled mechanistic ADME disposition, and directly supported the portfolio as a principle investigator focusing on permeability, physical properties and drug efflux transporters. Dr. Troutman received his BS in Chemistry and a Ph.D. in Pharmacy, from the University of North Carolina at Chapel Hill. He has worked, presented and published extensively in the area of ADME with a focus on in vitro and molecular plate-based approaches (biology and analytical), and he has recently become active in the fields of pharmacology hit identification and ‘omics.

JOSEPH TWEED, M.S., M.B.A., Pfizer, Joseph Tweed is a bioanalytical scientist working at Pfizer Inc. located in Groton, CT. Joseph has over 19 years of multi-disciplinary experience in the areas of drug discovery, drug development and pharmacology research. He is actively engaged in pursuing innovative bioanalytical approaches for routine use in the quantitative bioanalysis of small-molecules, antibody-drug conjugates (ADCs), biomarkers and nanoparticles in a regulated GLP/cGLP laboratory. He is also responsible for developing and directing automated bioanalytical techniques that can improve the quality and the efficiency of day-to-day laboratory operations. Joseph received his B.S. from Drexel University, a M.S. from Thomas Jefferson University and his M.B.A from the University of New Haven.

JASHVANT (JASH) D. UNADKAT, PH.D., University of Washington, Dr. Unadkat is the Milo Gibaldi Endowed Professor at the School of Pharmacy, University of Washington, Seattle. He received his Bachelor degree in Pharmacy (B.Pharm.) from the University of London (1977), his Ph.D. from the University of Manchester (1982; advisor Prof. Malcolm Rowland) and
his postdoctoral training at the University of California at San Francisco (1982-85; advisor the late Dr. Lewis B. Sheiner). Dr. Unadkat’s research interest is focused on elucidating the mechanisms of transport and metabolism of drugs. Dr. Unadkat has published more than 190 peer-reviewed research papers. He is a fellow of AAAS, AAPS, JSSX, and the founding co-chair (1999-2001) of the focus group of AAPS on Drug Transport and Uptake. Dr. Unadkat received the AAPS Research Achievement Award in 2012. Dr. Unadkat created and leads the UW Research Affiliates Program on Transporters (UWRAPT), a cooperative effort between the UW School of Pharmacy and pharmaceutical companies. He also leads UWPKDAP, a NIDA funded Program Project grant (P01) on drug disposition during pregnancy.

**HUI ZHANG, PH.D., Pfizer**, Dr. Zhang got his Ph.D in Analytical Chemistry from Iowa State University and he is currently an Associate Research Fellow at Discovery Science department of Pfizer. Hui has worked mostly in early drug discovery settings supporting hit and target identification, compound optimization, and SAR. Hui has extensive experience in Hit ID, ADME, assay developments, and bioanalysis. Hui has always being passionate in developing mass spectrometry based high throughput platforms to improve overall drug discovery efficiency and ROI (return of investment), and he was the pioneer to evaluate and implement MALDI, LDTD, fast multiplexing LC/MS systems etc. within Pfizer. Hui has over 30 peer reviewed journal publications and many invited presentations at various conferences.
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Cryopreserved hepatocytes: High quality cryopreserved human and animal hepatocytes in both suspension and plateable grades. These primary cells can be applied in drug uptake, metabolism, drug-drug interactions, and hepatotoxicity studies.

Cryopreserved enterocytes: We are the first to successfully isolate and cryopreserve human and animal enterocytes to retain drug metabolism activities. IVAL’s enterocytes can be utilized to evaluate intestinal metabolism of orally-administered drugs as well as drug-drug and food-drug interactions in the intestines.

IVAL’s latest innovation: MetMax™ hepatocytes and enterocytes (US Patent 5,474,940). MetMax™ Hepatocytes and MetMax™ Enterocytes: Permeabilized, co-factor supplemented hepatocytes and enterocytes. MetMax™ cells can be used directly after thawing; do not require centrifugation and microscopic quantification of cell viability and cell number, thereby allowing convenient application for routine hepatic metabolism and hepatic drug-drug interaction studies.

Our contract research services include: metabolic stability, metabolite profiling, metabolic phenotyping, P450 inhibition, and P450 induction studies. The following are examples of our proprietary technologies:

ROS/ATP human hepatocyte assay to identify sDILI drugs: This proprietary assay was co-developed with FDA National Center for Toxicological Research. The assay could identify (with >85% specificity and sensitivity) drugs that are known to be associated with severe liver toxicity, leading to deaths or a need for liver transplantation.

Plated hepatocyte relay assay for slowly metabolized chemicals: This patented assay allows in vitro study of drugs with low hepatic clearance that cannot be readily evaluated with routine in vitro approaches. In this assay, compounds are incubated for 24 hrs with plated hepatocytes, with the incubated media transferred to newly plated hepatocyte cultures daily. Time-dependent parent disappearance is analyzed against model chemicals for up to 120 hrs (5 days), with the calculated hepatic intrinsic clearance similar to that observed in vivo.
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