2020 Program Themes

Discovery and Basic Research

Theme 1: Bugs, Drugs, and the Microbiome: What's the Hype, What's the Promise?
Keywords: microbiome, engineered bacteria, viruses, phages, bug-mimicking drug carriers, microbiome-associated diseases, microbiome fingerprint

Initially focused on gastrointestinal diseases, manipulating the microbiome is now being considered as a new way to treat cancer, metabolic diseases, neurodegenerative diseases, cardiovascular diseases, and many more. The research on the microbiome has transformed our understanding of how bacteria, fungi, and other microbes affect human health and disease. This theme will cover topics including but not limited to: (1) the role of the microbiome in health and disease; (2) altering the microbiome using small molecules, biologics, and other modalities; (3) bugs as drugs including engineered bacteria, viruses, phages, bug-mimicking drug carriers, other engineered bugs; (4) the microbiome as a diagnostic fingerprint to monitor and detect diseases.

Theme 2: Novel Oncotargets
Keywords: drug resistance, oncotargets discovery, tumor microenvironment, signaling pathways, omics analysis

Identifying novel oncotargets is a continuous challenge to improve the therapeutic outcome and overcome drug resistance. In this session, we will discuss the different approaches (proteomics, genomics, transcriptomics) to discover new oncotargets, the clinical significance of these targets, and the therapeutic outcome associated with their modulation. Additionally, the role of tumor microenvironment in cancer progression and approaches to target the key mediators that incite tumor progression will be discussed.

Theme 3: Innovations in Pharmaceutical Bioengineering
Keywords: bioinstrumentation, biomaterials, biomechanics, tissue and cellular engineering, medical imaging, human factors device engineering

Pharmaceutical bioengineering covers all aspects of drug product design — from drug discovery and preclinical studies to manufacturing, formulation and packaging — and spans various areas including chemical, mechanical and biomedical engineering, as well as pharmaceutical sciences, chemistry and materials science. Examples of submissions may include 1) 3D bioprinting to co-deliver cells and biomaterials with precise control over their compositions, spatial distributions, and architectural accuracy, therefore achieving personalized recapitulation of the shape, structure, and architecture of

target tissues and organs, and 2) bioengineered devices (e.g., tissue chips) for drug screening to improve the process of predicting whether drugs will be safe or toxic in humans. Other innovative examples are encouraged.

Theme 4: Making the Immune System Behave: Vaccines, Immunotherapies and Other Treatments
Keywords: early-stage drug discovery, autoimmune diseases, allergies, vaccines, infectious diseases, novel immunomodulatory drugs and carriers, next generation delivery platforms for vaccines and immunotherapies

This theme will cover early-stage drug discovery research at the cutting-edge of immunotherapeutics and vaccines. Topics will include, but are not limited to: (1) novel immunotherapeutic targets, mechanisms, and disorders of the immune system, (2) personalized immunization technologies and immunomodulatory approaches to treat infectious diseases, autoimmune diseases, allergies, and other diseases, (3) next generation delivery methods for vaccines and immunotherapies: inhalation, nasal delivery, transdermal patches, etc., (4) synthetic technology platforms for expedited vaccine development in response to infectious disease threats.

Theme 5: Taming the Blood-Brain-Barrier in CNS Drug Discovery
Keywords: brain, spinal cord, blood-brain barrier; blood-cerebrospinal fluid barrier, paracellular transport, efflux transporters, endothelial and epithelial interfaces, brain permeability

This theme addresses novel science, insights, tools, and approaches for targeting and bypassing CNS barriers to achieve drug delivery to the brain and spinal cord. Specialized barriers include the blood-brain barrier and the blood-cerebrospinal fluid barriers. Highly limited paracellular transport and the expression of numerous efflux transporters at these key endothelial and epithelial interfaces pose major challenges to successful brain delivery of both small and large molecule therapeutics. Topics may include the physiology and regulation of the CNS barriers, molecular mechanisms of brain permeability and targeting, novel CNS targeting strategies for crossing and bypassing the barriers, predictive models, *in vitro* and *in vivo* correlations.

Theme 6: Preclinical Biomarker Studies: Connecting Discovery and Clinical Development
Keywords: drug discovery biomarkers, disease progression and drug efficacy, next generation sequencing, single cell sequencing, new target identification, correlations with preclinical models, correlating epigenomic markers to clinical diseases

Biomarkers provide essential bridges between discovery and clinical research. However, the cross-translational potential of biomarkers has not been fully realized, i.e., technological advances in biomarker measurement are not always integrated into the frameworks that are used to identify mechanisms of disease and drug response, and vice versa. Biomarkers are used to demonstrate target engagement, understand pharmacology and mechanism of action, diagnose disease, categorize patient populations, and provide additional evidence in support of clinical efficacy. Biomarkers have untapped potential to drive discovery-based hypotheses regarding the relevance of new targets to disease states. Advanced biomarker technologies, single-cell analysis, next-generation sequencing, functional genomics and other “omics” approaches push the boundaries of what is possible to measure. Biomarkers are used in the earliest stages of discovery to identify mechanism of action, but it is imperative that preclinical biomarker assessment in disease models correlate with clinical conditions. Clinical biomarker research drives reverse-translation, feeding back to discovery. For example, observational studies are being used to drive new target identification. Topics under this theme will include, but are not limited to: preclinical

biomarker strategy, drug discovery biomarkers, next generation sequencing, circulating tumor DNA, soluble biomarkers, single cell sequencing, imaging technologies, RNA-seq, new target identification, preclinical models, epigenomic markers, pre-clinical to clinical translation and reverse-translation.

Preclinical Development

Theme 1: Preclinical Development of Novel Therapeutic Modalities and Approaches
Recent breakthrough advances in basic sciences have led to an explosion of novel therapeutic modalities and approaches beyond traditional small molecules or monoclonal antibodies to treat diseases with significant unmet medical need. Examples include *non-covalent* small molecule inhibitors, small molecules *modifying* RNA, and a plethora of approved novel modalities such as CAR-Ts and anti-sense oligonuleotides. A major breakthrough has been our ability to efficiently modulate previously inaccessible pharmacological targets (eg. DNA). These novel approaches pose unique challenges not commonly encountered in the traditional therapeutic modality space. This theme will focus on strategies, challenges, lessons learned, and case studies in the preclinical development of these novel small molecule and biologic therapeutic approaches. Examples of topics include preclinical development (e.g., biotransformation, efficacy, safety, relevant preclinical models, translational PK/PD) for novel modalities (e.g., cell and gene therapy, siRNA, vaccines, oligonucleotides, bispecifics, ADCs, peptides, millamolecules), novel routes of delivery, design modifications to improve bioavailability and exposure at the site of action, and targeted delivery utilizing endogenous transporters/enzymes.

Theme 2: Innovation and Acceleration of Preclinical Development
Bringing transformative therapeutics to patients faster is a constant endeavor in the pharmaceutical field. Novel *in vitro* and *in vivo* models, as well as computational approaches are making it possible to innovate and accelerate drug development as never before. This theme will focus on novel methods and approaches to optimize drug candidates for ADME, efficacy, safety, identify biomarkers, and translate findings to the clinic to enable better prediction of first-in-human dose, efficacious dose/regimen, and assessment of therapeutic index. Topics include *in vitro* and *in vivo* models for ADME, efficacy and toxicity evaluations, candidate optimization and screening strategies, biomarker development, and imaging technologies. Additionally, innovative computational approaches such as mechanistic PK/PD modeling, predictive toxicology, quantitative systems pharmacology, advanced analytics, artificial intelligence/machine learning, as well as *in vitro* drug development paradigms will be discussed.

Theme 3: Advances in Preclinical Development of Immuno-Therapeutics
Targeting the immune system for numerous diseases including cancer, autoimmune diseases, inflammatory diseases, neurology and ophthalmology has tremendous breakthrough implications for patients. Immuno-therapeutics have expanded into a wide range of formats from biologics, small molecules, and novel modalities. Major advances such as development of micro-physiological systems, experimental pharmacology assays, systems immunology models, and use of “reverse translation” to guide the preclinical development of immune-therapeutics are under intense investigation. There are also several unique challenges in the preclinical development of these therapeutics including relevance of preclinical efficacy and safety models, evolving understanding of mechanism of action, translational experience for monotherapy and combinations, and regulatory considerations. This theme will focus on recent advances and learnings for various immuno-therapeutics and innovative strategies for their

preclinical development. Topics include pharmacokinetics, pharmacodynamics, optimal therapeutic design, biomarkers, biodistribution, imaging, predictive *in vitro*, *in vivo* and *in silico* models for efficacy and safety, assessment of therapeutic index, translational aspects for prediction of human PK, efficacious dose and regimen, combinations, and recent case studies to highlight successes, challenges, and lessons learned.

Bioanalytics

Theme 1: Will the Context of Use for Each Assay Please Stand Up?
Defining the context-of-use (COU) is essential to establish the purpose in fit-for-purpose biomarker assay validation. This theme will focus on the challenge of defining COU and the impact of COU on the entire process of assay design, development, validation and implementation. How to define COU? What to do when COU information is not available? How to continue the active dialogues between industry and regulatory agencies to shape heath authority expectations? These have been some of the hot topics in the global biomarker community, and we will continue these discussions at PharmSci360.

Theme 2: To Boldly Go Where No Assay Has Gone Before!
Each assay has its own challenges to reach a final method that delivers the needed data. This theme focuses on the solutions; those that are stretching bioanalytical sciences in new directions. What technologies are being developed or adapted to support novel modalities? What new solutions are being applied to address current and emerging challenges?

Theme 3: Are you ready for the laboratory of the future?
The lab of the future needs to be more efficient and adaptive than ever before. What can we do to shorten critical path timelines? How are we ensuring data quality and integrity in a fast-moving, time-sensitive environment? How will we continue to do so with novel technologies being implemented for more complicated molecules?

Clinical Pharmacology

Theme 1: Clinical Pharmacology Driving Innovative Trial Design
Keywords: innovative trial design, machine learning, artificial intelligence, real-world data/real-world evidence, biomarker-driven indications, tumor agnostic indications

Recent technological advancements allow collection of real-world data/real-world evidence and provides an opportunity for clinical pharmacologists to guide real-time monitoring (e.g., adherence, safety, outcome/endpoint measurement), provide opportunities for dose and dosing regimen optimization, or evaluation of benefit/risk in specific populations with no or limited clinical data at the time of approval. With 'big data' expected to play a larger role in health care over the next decade,

machine learning algorithms may be applied to clinical pharmacology and pharmacometric problems. Furthermore, recent approvals based on biomarker or pharmacogenomics-based trials (eg, tumor agnostic indications) highlight the central role that clinical pharmacology can play in explaining sources of variability in exposure and response between the different subgroups for these indications.

Topics related to the role of clinical pharmacology and pharmacometrics in applying real-world data/real-world evidence, machine learning algorithms, or biomarker-driven trial designs will be considered.

Theme 2A: Novel Therapeutic Modalities –Clinical Pharmacology Considerations
Keywords: oncolytic viruses, fusion proteins, nanobodies, immunocytokines, immunotoxins, bi or tri-specifics, oligonucleotides, CAR-T or other cell and/or gene therapies

These symposia will focus on clinical pharmacology considerations related to the development of novel therapeutic modalities. The symposia will cover case studies and discuss challenges and issues in dose selection, therapeutic individualization and overall drug development of novel therapeutic modalities. Examples of relevant new therapeutic modalities include oncolytic viruses, fusion proteins, nanobodies, immunocytokines, bi or tri-specifics, oligonucleotides, CAR-T or other cell and/or gene therapies.

Theme 2B: Novel Approaches Informing Understudied Populations
Keywords: subpopulations, lactation, pregnancy, pediatrics, race and ethnicity, global drug development, pharmacogenomics, renal and hepatic impairment

Patient subpopulations that may be relevant to an intended indication are often excluded from clinical trials during drug development. These subpopulations can include women who are pregnant or lactating, those with advanced degrees of renal or hepatic impairment, pediatrics, adolescents, racial or ethnic subpopulations in support of global registrational plans. Furthermore, patients with rare genetic makeup or comorbidities such as HCV, HBV or AIDS could also be either excluded from trials or enrolled in insufficient numbers for adequate characterization of the benefit-risk profile in these subpopulations. Underrepresentation of these subpopulations presents a challenge in extrapolating findings from the general population to these patient subgroups. This symposium will focus on strategies, experiences and results from studying these subpopulations of patients, and their impact on the drug's approval and use in these populations.

Theme 3: Model Informed Drug Development: 2020 and Beyond
Keywords: MIDD, quantitative approaches, dose/dosing regimen selection, combination regimen, probability of technical success, benefit-risk assessments, population PK, physiologically based pharmacokinetic models, quantitative systems pharmacology, decision-making.

The crucial role of model-informed drug development (MIDD) in effective delivery of novel treatments has been recognized by regulatory authorities, pharmaceutical industry, and academia. MIDD is currently an integral component in drug development. MIDD increases the confidence in decision making across drug development stages, reduces development cost, and/or enables accelerated development for drugs serving unmet medical needs.

These symposia will discuss current and future applications in MIDD methodologies including, but not limited to, population pharmacokinetics, physiologically based pharmacokinetic models and quantitative systems pharmacology, in evaluating the probability of technical success at different drug development

stages, optimizing combination regimens, benefit-risk assessments, dose optimization, health economics, cost-effectiveness, alternative approaches to evidence generation, novel clinical trial designs, and drug approvals.

Manufacturing and Analytical Characterization

Theme 1: Advances in Process Control, Modeling, and Analytics
Recent advances in data analytics and process analytical technologies (PAT) have enabled real-time monitoring and control of parameters, improving quality and robustness for both batch and continuous processes. This theme will cover the current state of process control, modeling, and analytics for the manufacture of biologic and chemical entities. The focus will be on process control, encompassing data analytics, process modeling, machine learning, implementation of PAT and real time release testing (RTRT). Examples could include development and use of data lakes, advanced statistics and process modeling approaches, performance monitoring, and deployment of automated feedback / feedforward control.

Theme 2: Manufacturing and Analytical Challenges of Emerging Therapeutic Modalities and Novel Delivery Systems
With recent approvals for several new therapeutic modalities including chimeric antigen receptor T cells (CAR-T), gene therapy, and oligonucleotide products, manufacturing science is extending beyond the current small and large molecule platforms. This theme will cover the nascent science, analytical characterization and regulatory aspects of manufacturing emerging therapeutic products, devices, drug device combinations, and drug delivery systems. Some examples could include recent advances in cell therapy manufacturing, viral vector / gene therapy manufacturing, in-process control and validation of new modality processes, and facility design considerations. Analytical characterization of cell and gene therapy products, oligonucleotides, and other unique formulations such as aerosols, topicals, liposomes, amorphous materials and customized release products could be covered.

Theme 3: Next Generation Manufacturing Enabling Speed to Patient
For patients facing serious disease, speed is critical. This theme will cover next-generation development and manufacturing approaches for traditional therapeutic products, enabling speed to patient. Topics could include process intensification, speed through deployment of continuous and single-use manufacturing technologies, 3D printed pharmaceuticals and elimination of scale-up and tech transfer. Strategies such as registration-ready clinical campaigns, breakthrough therapy designations, analytical roadmaps, identification / justification of Critical Quality Attributes (CQAs), and stability approaches could be discussed. Health agency guidance and sponsor experience, presented as case studies will be considered for this session.

Formulation and Delivery

Theme 1: Advances and Innovation in Formulation Development
This theme is dedicated to the recent advancements in formulation development and related regulatory considerations. For biomolecules, this theme covers new approaches in low and high concentration formulations, development and use of novel excipients, high-throughput screening, liquid formulation development, lyophilization, and vaccine formulation development. For chemical entities, topics include development and use of novel excipients, prediction and simulation in formulation development and processing, formulation of molecules with poor solubility and bioavailability, biorelevant dissolution methods, formulation technologies for different routes of administration including particle engineering for pulmonary delivery and the use of 3D printing in early drug product development.

Theme 2: Formulation Development Strategies for Novel Modalities
Several novel therapeutic modalities are in different stages of development and commercialization to treat a wide range of therapeutic indications. This theme covers the latest advances in formulation technologies and strategies to develop drug products of novel and emerging therapeutic modalities. Scientific approaches and cutting-edge research to fundamentally understand structure function attributes and their connection to formulation development is considered in this theme. Novel modalities require different thinking than traditional drug product development which is also recognized by regulatory agencies. This theme covers regulatory considerations and related guidance for novel modality development. For biomolecules, topics include formulation aspects of cell therapy, gene therapy, bispecific and trispecific antibodies, BiTE® antibody constructs, diabodies, peptibodies, and oncolytic immunotherapy viruses. For chemical entities, topics include formulation aspects of complex generic drug products, non-biologic complex drugs (NBCDs), synthetic peptides, and oligonucleotides.

Theme 3: Drug Delivery and Device Development
Drug delivery approaches and device development are essential parts of drug product development. Understanding how end user interacts with the final product is also critical. This theme covers advances in drug delivery approaches, medical device development, connectivity between patient experience and device development, and related regulatory topics. This includes specialty delivery systems such as long-acting delivery, ocular and inhalation products, and implants. This theme also covers aspects of drug product handling and administration, advances in primary packaging development including autoinjectors, pre-filled syringes, dual chamber systems, on-body injectors, connected devices, and low temperature storage for emerging modalities.

Career Development

Theme: Tactical and Strategic Approach to Communication and Leadership