Purpose: The goal of this workshop is to develop a path forward for evaluating an immuno-oncology focused nonclinical and clinical development paradigm. Ideally, this workshop will redefine biological outcome measures and clinical endpoints, leading to innovative clinical trial designs and statistical methods in the development of immuno-oncology clinical trials.

Workshop Co-Chairs:
- Maitreyee Hazarika, MD, Medical Officer, Division of Oncology Products 2, Office of Hematology Oncology Products, Center for Drug Evaluation and Research, FDA
- Marc Theoret, MD, Lead Medical Officer, Division of Oncology Products 2, Office of Hematology Oncology Products, Center for Drug Evaluation and Research, FDA
- Suzanne L. Topalian, MD, Member, AACR Regulatory Science and Policy Subcommittee; Professor, Surgery and Oncology, Johns Hopkins University School of Medicine; Director, Melanoma Program, Johns Hopkins Kimmel Cancer Center; Associate Director, Bloomberg-Kimmel Institute for Cancer Immunotherapy
- Jedd D. Wolchok, MD, PhD, Lloyd J. Old/Virginia and Daniel K. Ludwig Chair in Clinical Investigation Chief; Melanoma & Immunotherapeutics Service Director; Parker Institute for Cancer Immunotherapy at MSK; Associate Director, Ludwig Center for Cancer Immunotherapy; Member, Ludwig Cancer Research; Professor of Medicine, Weill Medical College of Cornell University; Memorial Sloan Kettering Cancer Center

AGENDA
THURSDAY, OCTOBER 13, 2016

8:00 AM Welcome and Introduction
Marc Theoret, MD, FDA

8:15 AM Cancer Immunobiology: Principles and Practice
Suzanne Topalian, MD, Johns Hopkins Kimmel Cancer Center

9:00 – 11:30 AM SESSION I: CONSIDERATIONS IN THE PRECLINICAL EVALUATION OF I-O PRODUCTS
Moderator: Whitney Helms, PhD, CDER, FDA

Considerations in the Nonclinical Evaluation of Immuno-Oncology Products
Whitney Helms, PhD, FDA

Checkpoint Inhibitor Induced Autoimmunity in a Humanized Mouse Model
Kristina Howard, DVM, PhD, CDER, FDA

Activity and Safety of Immunomodulatory Antibodies in Preclinical Models
Alan Korman, PhD, Bristol-Myers Squibb

9:45 – 10:00 AM BREAK
Cancer Immunotherapy: Beyond NOAEL for First in Human Dose Selection
Rodney Prell, PhD, Genentech

Nonclinical Safety Assessment for T-cell Therapies
Timothy MacLachlan, PhD, DABT, Novartis Institutes of Biomedical Research

Development of a Vaccine Based Immunotherapy Regimen
David Clarke, PhD, DABT, Pfizer

11:00 – 11:30 AM PANEL DISCUSSION and AUDIENCE Q&A

SESSION I SPEAKERS AND THE FOLLOWING ADDITIONAL PANELISTS:
- Danuta Herzyk, PhD, Merck Research Laboratories
- Janis Taube, MD, MSc, Johns Hopkins University School of Medicine
- Allen Wensky, PhD, CBER, FDA

11:30 – 12:30 PM LUNCH (on your own)

12:30 – 2:30 PM SESSION IIA: CONSIDERATIONS FOR DOSE-FINDING
Moderator: Geoffrey Kim, MD, CDER, FDA

Introduction
Geoffrey Kim, MD, FDA

Approaches to Dose-Finding for Immuno-Oncology Agents and Combinations
Eric Rubin, MD, Merck Research Laboratories

Challenges in IO-IO Combination Dose Finding: A Case Study of Ipilimumab/Nivolumab in NSCLC
David Feltquate, MD, PhD, Bristol-Myers Squibb

Randomized Dose-Escalation and Dose-Ranging Trial Designs
Mark Ratain, MD, The University of Chicago

Regulatory Considerations - Optimizing Dose Selection for Immuno-Oncology Products
Hong Zhao, PhD, CDER, FDA

2:00 – 2:30 PM PANEL DISCUSSION and AUDIENCE Q&A

SESSION IIA SPEAKERS AND THE FOLLOWING ADDITIONAL PANELISTS:
- Stephanie L. Goff, MD, National Cancer Institute, NIH
- Samir Khleif, MD, Georgia Cancer Center

2:30 – 2:45 PM BREAK

2:45 – 4:45 PM SESSION IIB: EVALUATION OF IMMUNE-MEDIATED ADVERSE EVENTS
Moderator: Jedd D. Wolchok, MD, PhD, Memorial Sloan Kettering Cancer Center

Pathophysiology of Immune-Mediated Adverse Events
David Berman, MD, PhD, MedImmune

Adverse Events in Immuno-Oncology: Academic Perspective
Mario Sznol, MD, Yale University School of Medicine

Unique Aspects of Immune-mediated Adverse Events: A Regulatory Perspective
Diko Kazandjian, MD, CDER, FDA

Complications of CAR T Therapy
David Porter, MD, University of Pennsylvania

CAR T-cell Toxicities - A Regulatory Perspective
Ke Liu, MD, PhD, CBER, FDA
A Global Picture of Immuno-Oncology Adverse Events
Elad Sharon, MD, MPH, CTEP, NIH

4:15 – 4:45 PM PANEL DISCUSSION and AUDIENCE Q&A
4:45 PM DAY 1 SUMMARIZING REMARKS
Jedd D. Wolchok, MD, PhD, Memorial Sloan Kettering Cancer Center
5:00 PM ADJOURN

FRIDAY, OCTOBER 14, 2016

8:00 AM Introduction
Suzanne Topalian, MD, Johns Hopkins Kimmel Cancer Center

8:15 AM Regulatory Pathways for Approval, Considerations for Alternate Endpoints
Maitreyee Hazarika, MD, FDA

8:30 AM Challenges in Interpreting Results Based on Traditional Endpoints
Rajeshwari Sridhara, PhD, CDER, FDA

9:00 – 11:15 AM SESSION IIIA: ENDPOINTS FOR I-O PRODUCTS: CONSIDERATIONS FOR UNIQUE EFFICACY BASED ON UNIQUE BIOLOGY OF CHECKPOINT INHIBITORS
Moderator: Renzo Canetta, MD, Bristol-Myers Squibb (Retired)

Traditional Endpoints, Introduction: An Historical Perspective
Renzo Canetta, MD, Bristol-Myers Squibb (Retired)

Imaging Response Assessment with Immunotherapy
Lawrence Schwartz, MD, Columbia University

Tumor Measurement Based Endpoints: Lesson Learned from the RECIST Database Experience
Sumithra Mandrekar, PhD, Mayo Clinic, Mayo Clinic Cancer Center

Immunotherapy Clinical Endpoints: Challenges and Opportunities
Axel Hoos, MD, PhD, GlaxoSmithKline Pharmaceuticals

10:00 – 10:15 AM BREAK

10:45 – 11:15 AM PANEL DISCUSSION and AUDIENCE Q&A

SESSION IIIA SPEAKERS AND THE FOLLOWING ADDITIONAL PANELIST:
• Shenghui Tang, PhD, CDER, FDA

11:15 – 12:15 PM LUNCH (on your own)
12:15 – 2:45 PM SESSION IIIB: USE OF ALTERNATE EFFICACY ENDPOINTS WITH I-O PRODUCTS
Moderator: Marc Theoret, MD, FDA

Modified Progression-free Survival as a Potential Surrogate for Survival in Immunotherapy Trials
Srisha Mushti, PhD, CDER, FDA

Exploration of a Novel Intermediate Endpoint in Immunotherapy Clinical Studies
Xin Gao, PhD, CDER, FDA
### How We Assess Benefit from Immuno-Oncology Agents
Antoni Ribas, MD, PhD, *University of California, Los Angeles*

### Milestones for Survival: Overall Survival versus Earlier Endpoints
Jan Bogaerts, PhD, *EORTC*

### Non-Classical Response Patterns, Immune-Modified RECIST and Immune-Modified PFS
Daniel S. Chen, MD, PhD, *Genentech/Roche*

### Immune-related Response and Survival
Keaven Anderson, PhD, *Merck Research Laboratories*

### Alternative Survival Endpoints
Tai-Tsang Chen, PhD, *Bristol-Myers Squibb*

#### 1:45 – 2:45 PM  PANEL DISCUSSION and AUDIENCE Q&A

**SESSION IIIB SPEAKERS AND THE FOLLOWING ADDITIONAL PANELIST:**
- Kun He, PhD, *CDER, FDA*

#### 2:45 – 3:00 PM  BREAK

#### 3:00 – 4:30 PM  SESSION IV: CONSIDERATIONS FOR NOVEL TRIAL DESIGNS
**Moderator: Rajeshwari Sridhara, PhD, FDA**

**Phase III Design Considerations for Agents with a Potential Predictive Biomarker**
Ed Korn, PhD, *National Cancer Institute, NIH*

**Immuno-oncology Combinations – Clinical Trial Design Considerations**
Lillian Siu, MD, *Princess Margaret Cancer Centre, University of Toronto*

**New More Rapidly Informative Approaches to Development of Improved Therapy for Advanced Unresectable and High Risk Operable Melanoma**
John Kirkwood, MD, *University of Pittsburgh*

**Designing Late-Stage Randomized Clinical Trials with Cancer Immunotherapy: Can We Make It Simple?**
Tai-Tsang Chen, PhD, *Bristol-Myers Squibb*

**Assay Design: Special Considerations for Immuno-Oncology Companion Diagnostic Tests**
David Rimm, MD, PhD, *Yale University School of Medicine*

#### 4:00 – 4:30 PM  PANEL DISCUSSION and AUDIENCE Q&A

#### 4:30 PM  WORKSHOP CONCLUDING REMARKS
Maitreyee Hazarika, MD, *FDA*

#### 5:00 PM  ADJOURN