With a focus on the development of safe and effective RM products, the workshop will identify critical gaps that must be addressed to enable significant innovation and rapid advancement of RM approaches and will explore issues related to product development and standards, regulatory science, and clinical applications. The framework for Sessions II–IV and VI–VIII is a set of key questions designed to identify the scientific, technical, and operational challenges as well as to highlight strategies for enabling major transformative advances and the development of clinical applications using adult stem cells. These challenges and opportunities will be explored through the lens of scientific overviews and case studies of clinical science and product development in specific scientific areas that will serve as springboards for in-depth discussions while emphasizing cross-cutting issues with broad applicability to many areas of RM clinical research.

AGENDA

DAY 1 – Wednesday, December 6

8:00 AM Session I: Introduction

Welcome

— **Gary Gibbons, MD**, Workshop Co-chair; Director, National Heart, Lung, and Blood Institute, NIH

— **Peter Marks, MD, PhD**, Workshop Co-chair; Director, Center for Biologics and Evaluation Research, FDA

Introductory Remarks

— **Francis Collins, MD, PhD**, Director, NIH

FDA Perspectives

— **Scott Gottlieb, MD**, Commissioner, FDA

Keynote: Promises, Perils, and Public Trust

— **Sally Temple, PhD**, Scientific Director, Neural Stem Cell Institute

9:15 AM Session II: Musculoskeletal Tissues and Integument

Co-moderators:

— ***Stephen Katz, MD, PhD**, Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH*

— ***Martha Somerman, DDS, PhD**, Director, National Institute of Dental and Craniofacial Research, NIH*

Presentation: State of Clinical Science and Case Study

— **Anthony Oro, MD, PhD**, Professor, Dermatology, Stanford University

Presentation: State of Product Development and Case Study

— **Anthony Ratcliffe, PhD**, President and CEO, Synthasome, Inc.

Panel Perspectives

— **Constance Chu, MD**, Professor and Vice Chair Research, Department of Orthopedic Surgery, Stanford University

— **Janice Lee, MD**, Clinical Director, National Institute of Dental and Craniofacial Research, NIH

— **Pamela Robey, PhD**, Chief, Skeletal Biology Section, National Institute of Dental and Craniofacial Research, NIH

— **Dennis Roop, PhD**, Professor, Dermatology, University of Colorado Denver

— **B. Lynn Allen-Hoffman, PhD**, Senior Vice President Regenerative Medicine, Stratatech—A Mallinckrodt Company; Professor, Department of Pathology and Department of Surgery, University of Wisconsin School of Medicine and Public Health

— **Joshua Hare, MD**, Director, Interdisciplinary Stem Cell Institute, University of Miami

— **Steve Bauer, PhD**, Chief, Cellular and Tissue Therapies Branch, Division of Cellular and Gene Therapies, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA

Discussion of Key Questions

Open Q&A

11:00 AM Break

11:15 AM Session III: Endocrinology

Co-moderators:

— ***Nancy Bridges, MD**, Chief of Transplantation Branch, Division of Allergy, Immunology, and Transplantation, National Institute of Allergy and Infectious Diseases, NIH*

— ***Griffin Rodgers, MD**, Director, National Institute of Diabetes and Digestive and Kidney Diseases, NIH*

Presentation: State of Clinical Science and Case Study

— **José Oberholzer, MD**, Director, Charles O. Strickler Transplant Center, University of Virginia Health System

Presentation: State of Product Development and Case Study

— **Felicia Pagliuca, PhD**, Co-Founder and Vice President of Cell Biology Research and Development, Semma Therapeutics

Panel Perspectives

— **Bernhard Hering, MD**, Professor of Surgery and Medicine and Eunice L. Dwan Chair in Diabetes Research, University of Minnesota

— **Jon Odorico, MD**, Professor of Surgery, Director of Pancreas Transplantation, Co-Director of Islet Transplantation, Division of Multi-Organ Transplantation, University of Wisconsin—Madison

— **Klearchos Papas, PhD**, Professor of Surgery, University of Arizona

— **Daniel Pipeleers, MD, PhD**, Professor, Director Diabetes Research Center, Brussels Free University—VUB, Belgium

— **Mo Heidaran, PhD**, Cell Therapies Branch, Division of Cellular and Gene Therapies, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA

Discussion of Key Questions

Open Q&A

1:00 PM Lunch

2:00 PM Session IV: Ophthalmology

Co-moderators:

— ***Nitin Gogtay, MD**, Director, Office of Clinical Research, National Institute of Mental Health, NIH*

— ***Paul Sieving, MD**, PhD, Director, National Eye Institute, NIH*

Presentation: State of Clinical Science and Case Study

— **Dennis Clegg, PhD**, Professor, Center for Stem Cell Biology and Engineering, University of California, Santa Barbara

Presentation: State of Product Development and Case Study

— **David Gamm, MD, PhD**, Associate Professor, Ophthalmology and Visual Sciences, University of Wisconsin–Madison

Panel Perspectives

— **Leonard Levin, MD, PhD**, Professor and Chair, Department of Ophthalmology, McGill University, Montreal, Canada

— **Kapil Bharti, PhD**, Stadtman Investigator, National Eye Institute, NIH

— **Derek Hei, PhD**, BlueRock Therapeutics

— **Sophie Deng, MD, PhD**, Professor of Ophthalmology, University of California, Los Angeles

— **Don Fink, PhD**, Cell Therapies Branch, Division of Cellular and Gene Therapies, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA

Discussion of Key Questions

Open Q&A

3:45 PM Break

4:00 PM Session V: Regulatory Considerations for Stem Cell-Based Product Development

Moderator:

— ***Steven Oh, PhD**, Deputy Director, Division of Cellular and Gene Therapies, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA*

FDA Presentation: Stem Cell-based Therapies: FDA Regulatory Perspectives

— **Deborah Hursh, PhD**, Senior Investigator, Cellular and Tissue Therapies Branch, Division of Cellular and Gene Therapies, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA

Academia/Industry Perspective Presentation: Preclinical and Translational Steps to Facilitate Clinical Testing of Cell-Based Therapies

— **Michael Matthay, MD**, Professor, Medicine and Anesthesia, University of California San Francisco

Panel Perspectives & Discussion of Session Questions

What are the major product development challenges that must be overcome to accelerate progress in the stem cell field?

— **Deborah Hursh, PhD**, Senior Investigator, Cellular and Tissue Therapies Branch, Division of Cellular and Gene Therapies, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA

— **Anthony Ting, PhD**, Vice President of Regenerative Medicine, Head of Cardiopulmonary Programs, Athersys, Inc.

— **Michael Matthay, MD**, Professor, Medicine and Anesthesia, University of California San Francisco

— **Martha Lundberg, PhD**, Program Director, Program Director, Tissue Engineering and Regenerative Medicine, National Heart, Lung, and Blood Institute, NIH

— **Kelley Rogers, PhD**, Federal Technical Program Manager, Office of Advanced Manufacturing, National Institute of Standards and Technology

Panel Questions

i. Where is there opportunity for collaboration among stakeholders to support product development with adult stem cells, e.g., how can government agencies best partner with each other and stakeholders to move this field forward?
ii. What government underwritten networks, consortia, or other resources would be of value in this space (e.g., PACT)?
iii. What are the key regulatory science questions for stem cell based products that would facilitate translation in this field?
iv. Are there additional guidances FDA could provide that would provide clarity to sponsors?
v. Are there assay methods that are ripe for standardization in this field?
vi. What aspects of government funding and/or regulation affect ability to predict commercial development in this field?

Open Q&A

5:30 PM Adjourn

DAY 2 – Thursday, December 7

8:00 AM Session VI: Neurology

Co-moderators:

— ***Candace Kerr, PhD**, Program Officer, Division on Aging Biology, National Institute on Aging, NIH*

— ***David Owens, PhD**, Acting Deputy Director, Division of Extramural Research, National Institute of Neurological Disorders and Stroke, NIH*

Presentation: State of Clinical Science and Case Study

— **Robert W. Mays, PhD**, Vice President of Regenerative Medicine and Head of Neuroscience Programs, Athersys, Inc.

Presentation: State of Product Development and Case Study

— **Lorenz Studer, MD**, Director, Center for Stem Cell Biology, Memorial Sloan Kettering Cancer Center

Panel Perspectives

— **Sean Savitz, MD**, Professor and Frank M. Yatsu Chair, Department of Neurology, University of Texas Health Science Center, Houston

— **Su-Chun Zhang, MD, PhD**, Professor, Neuroscience and Neurology, University of Wisconsin—Madison

— **Scott Burger, MD**, Principal, Advanced Cell & Gene Therapy, LLC

— **Ilyas Singeç, MD, PhD**, Head, Stem Cell Research, National Center for Advancing Translational Sciences, NIH

— **Jane Lebkowski, PhD**, Chief Scientific Officer, Asterias Biotherapeutics

— **Thomas Finn, PhD**, Cell Therapies Branch, Division of Cellular and Gene Therapies, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA

Discussion of Key Questions

Open Q&A

9:45 AM Break

10:00 AM Session VII: Hematology

Co-moderators:

— ***W. Keith Hoots, MD**, Director, Division of Blood Diseases and Resources, National Heart, Lung, and Blood Institute, NIH*

— ***Anne Pariser, MD**, Deputy Director, Office of Rare Diseases Research, National Center for Advancing Translational Sciences, NIH*

Presentation: State of Clinical Science and Case Study

— **Donald Kohn, MD**, Professor of Microbiology, Immunology and Molecular Genetics and Pediatric Hematology/Oncology and Director, Human Gene and Cell Therapy Program, University of California, Los Angeles

Presentation: State of Product Development and Case Study

— **Robert Negrin, MD**, Chief, Division of Blood and Marrow Transplantation, Stanford University

Panel Perspectives

— **Harry Malech, MD**, Chief, Genetic Immunotherapy Section, National Institute of Allergy and Infectious Diseases, NIH

— **Kateri Moore, DVM**, Professor, Department of Cell, Developmental and Regenerative Biology, Mount Sinai

— **David Scadden, MD**, Professor of Medicine, Harvard University

— **Linda Kelley, PhD**, Senior Member and Technical Director, Moffitt Cancer Center

— **Robert Sackstein, MD, PhD**, Professor, Dermatology and Medicine, Harvard University

— **Helen Heslop, MD, DSc**, Professor, Medicine and Pediatrics, Baylor College

— **Andrew Byrnes, PhD**, Chief, Gene Transfer and Immunogenicity Branch, Division of Cellular and Gene Therapies, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA

Discussion of Key Questions

Open Q&A

11:45 AM Lunch

12:45 PM Session VIII: Cardiology and Vascular Biology

Co-moderators:

- ***James Anderson, MD, PhD**, Director, Division of Program Coordination, Planning, and Strategic Initiatives, NIH*
- ***Denis Buxton, PhD**, Associate Director, Basic and Early Translational Research Program, Division of Cardiovascular Diseases, NIH*

Presentation: State of Clinical Science and Case Study

- **Eric Rose, MD**, Professor, Department of Population Health Science and Policy, Mount Sinai School of Medicine

Presentation: State of Product Development and Case Study

- **Karen Christman, PhD**, Professor, Bioengineering and Associate Dean, University of California, San Diego

Panel Perspectives

- **Laura Niklason, MD, PhD**, Nicholas M. Greene Professor in Anesthesia and Biomedical Engineering, Yale University
- **Nicanor Moldovan, PhD**, Director of 3D Bioprinting Core at IUSM/IUPUI and Associate Research Professor, Indiana University-Purdue University
- **Doris Taylor, PhD**, Director, Regenerative Medicine Research, Texas Heart Institute
- **Lemuel Moyé, MD, PhD**, Professor, Biostatistics, University of Texas Health Science Center, Houston
- **Deborah Hursh, PhD**, Division of Cellular and Gene Therapies, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA

Discussion of Key Questions

Open Q&A

2:30 PM Break

2:45 PM Session IX: Opportunities in Clinical Trial Design

Moderator

- ***Ilan Irony, MD**, Deputy Director, Division of Clinical Evaluation, Pharmacology, and Toxicology, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA*

FDA Presentation: Facilitating Clinical Trial Design

- **Larissa Lapteva, MD**, Associate Director, Division of Clinical Evaluation, Pharmacology, and Toxicology, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA

Panel Perspectives & Discussion of Session Questions

- **Larissa Lapteva, MD**, Associate Director, Division of Clinical Evaluation, Pharmacology, and Toxicology, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA
- **Sean Savitz, MD**, Professor and Frank M. Yatsu, MD Chair, Department of Neurology, University of Texas Health Science Center, Houston
- **Eduardo Marbán, MD, PhD**, Director, Heart Institute, Cedars-Sinai
- **Anne Pariser, MD**, Deputy Director, Office of Rare Diseases Research, National Center for Advancing Translational Sciences, NIH

Panel Questions

i. What are the opportunities with design of studies investigating adult stem cell products?
ii. What are the major challenges for patient recruitment and efficient product development?
iii. What platforms/stakeholders, other than the manufacturing companies and the FDA, are currently in existence to support product development with adult stem cells?

Open Q&A

4:00 PM Session X: A Path to Treatments and Cures

Co-moderators:

— ***Peter Marks, MD, PhD**, Workshop Co-chair; Director, Center for Biologics and Evaluation Research, FDA*

— ***Amy Patterson, MD**, Chief Science Advisor, National Heart, Lung, and Blood Institute, NIH*

360-Degree Panel: Multidisciplinary Discussion of Critical Gaps, Solutions, and Next Steps

— **Rachael Anatol, PhD**, Deputy Office Director, Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, FDA

— **Tom Bollenbach, PhD**, Chief Technology Officer, Advanced Regenerative Manufacturing Institute

— **Ruben Carbonell, PhD**, Chief Technology Officer, The National Institute for Innovation in Manufacturing Biopharmaceuticals

— **John Elliott, PhD**, Cell Systems Science Group Leader, National Institute of Standards and Technology

— **Joshua Hare, MD**, Director, Interdisciplinary Stem Cell Institute, University of Miami

— **Janet Lambert, MBA**, CEO, Alliance for Regenerative Medicine

— **José Oberholzer, MD**, Director, Charles O. Strickler Transplant Center, University of Virginia Health System

— **Anthony Oro, MD, PhD**, Professor, Dermatology, Stanford University

— **Sally Temple, PhD**, Scientific Director, Neural Stem Cell Institute

5:10 PM Closing Remarks

— **Peter Marks, MD, PhD**, Workshop Co-chair; Director, Center for Biologics and Evaluation Research, FDA

— **Amy Patterson, MD**, Chief Science Advisor, National Heart, Lung, and Blood Institute, NIH

5:15 PM Adjourn

Key Questions for Clinical Sessions

For given specific applications:

1. What are the major scientific, technical, and operational challenges that must be overcome to accelerate progress in the field?

2. With regard to cell-based therapies:
    a. What is the optimal stage of cell maturation and differentiation to facilitate safe and efficacious RM therapy?
        i. In what specific areas is research needed to further define and thus guide decisions on the optimal stage of cell maturation and differentiation?
    b. How can cell integration and physiologic function be optimized to promote therapeutic effect?
    c. How can this function be stabilized and sustained?
    d. How can immune tolerance be enhanced?
    e. What tools exist and/or need to be developed to:
        i. Deliver cells to appropriate sites in vivo?
        ii. Monitor cell function in situ?
        iii. Track cell fate in situ?
        iv. Promote self-healing and in vivo repair?

3. What are the primary product development challenges surrounding RM cell-based interventions/products in:
    a. Scaling-up production (increasing batch size)?
    b. Scaling-out manufacturing (replicating batches)?
    c. Single use technologies
    d. Process analytical technologies
    e. Modularization

4. What are key attributes of proposed RM interventions/products that demonstrate their readiness to be advanced into clinical trials?
    a. Critical quality attributes
    b. Critical process parameters
    c. Material attributes

5. What are the key regulatory science questions that should be addressed in the next one, three, and five years?