AGIOS is focused on discovering and developing novel investigational medicines to treat cancer and rare genetic diseases through scientific leadership in the field of cellular metabolism. In addition to an active research and discovery pipeline across both therapeutic areas, Agios has an approved oncology precision medicine and multiple first-in-class investigational therapies in clinical and/or preclinical development. All Agios programs focus on genetically identified patient populations, leveraging our knowledge of metabolism, biology and genomics. For more information, please visit the company’s website at www.agios.com.

IMMUNOGEN is a clinical-stage biotechnology company that develops targeted cancer therapeutics using its proprietary ADC technology. The Company’s lead product candidate, mirvetuximab soravtansine, is in a Phase 3 trial for FRD-positive platinum-resistant ovarian cancer, and is in a Phase 1b/2 trial in combination regimens for earlier-stage disease. ImmunoGen has three additional clinical-stage product candidates, two of which are being developed in collaboration with Jazz Pharmaceuticals. ImmunoGen’s ADC technology is also used in Roche’s marketed product, Kadcyla®, and in programs in development by Amgen, Bayer, Biotest, CytomX, Debiopharm, Lilly, Novartis, Sanofi and Takeda.
ORGANIZERS’ WELCOME

Welcome to the 2018 Acute Myeloid Leukemia Medical Symposium. Our organizers have gathered an excellent group of speakers for the first annual AML symposium. 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 AML experience. Thank you for your participation.

ORGANIZING COMMITTEE

Presiding Chairs
Academic Chair: Daniel J. DeAngelo, Dana Farber Cancer Institute
Chair: Bikash Verma, Celyad

Committee Members
Terry J. Fry, Center for Cancer Research, National Cancer Institute
David Sykes, Massachusetts General Hospital
Patrick A. Zweidler-McKay, ImmunoGen
AML 2018 SYMPOSIUM AGENDA

Thursday, March 15

7:00 - 8:00  REGISTRATION
8:00 - 8:05  Conference Opening
            Bikash Verma, Celyad

SESSION I: The Current Landscape

8:05 - 8:10  Session Introduction
            David Sykes, Massachusetts General Hospital

8:10 - 8:35  Current Standard of Care Guidelines
            Daniel J. DeAngelo, Dana Farber Cancer Institute

8:35 - 9:00  Genomics of Myeloid Malignancies
            Coleman Lindsley, Dana Farber Cancer Institute

9:00 - 9:25  AML after Transplant: Are We Becoming High Maintenance?
            Yi-Bin Albert Chen, Massachusetts General Hospital

9:25 - 9:45  Break

9:45 - 10:15 Panel Discussion

SESSION II: State of the Art Research and Treatment Updates

10:15 - 10:20 Session Introduction
         Daniel DeAngelo, Dana Farber Cancer Institute

10:20 - 10:45 Immunotherapeutic Approaches for AML
              Terry J. Fry, Center for Cancer Research, National Cancer Institute

10:45 - 11:10 Novel CAR-T Therapy for AML
              Bikash Verma, Celyad

11:10 - 11:35 Immune Checkpoint and Vaccine Approaches in AML
              Naval Daver, MD Anderson Cancer Center
<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:35 - 12:50</td>
<td>Lunch and Networking</td>
</tr>
<tr>
<td>12:50 - 1:15</td>
<td><strong>ADCs in AML: GO and Beyond</strong></td>
</tr>
<tr>
<td></td>
<td>Patrick A. Zweidler-McKay, ImmunoGen</td>
</tr>
<tr>
<td>1:15 - 1:40</td>
<td><strong>Novel Targeting of AML and T-ALL</strong></td>
</tr>
<tr>
<td></td>
<td>John F. DiPersio, Washington University School of Medicine</td>
</tr>
<tr>
<td>1:40 - 2:05</td>
<td><strong>Approaches to Differentiation Therapy in AML</strong></td>
</tr>
<tr>
<td></td>
<td>David Sykes, Massachusetts General Hospital</td>
</tr>
<tr>
<td>2:05 - 2:35</td>
<td>Panel Discussion</td>
</tr>
<tr>
<td>2:35 - 2:55</td>
<td>Break</td>
</tr>
<tr>
<td>2:55 - 3:35</td>
<td><strong>PLENARY LECTURE</strong></td>
</tr>
<tr>
<td></td>
<td>Can AML Precision Science Become AML Precision Clinical Reality?</td>
</tr>
<tr>
<td></td>
<td>Gwen Nichols, The Leukemia &amp; Lymphoma Society</td>
</tr>
<tr>
<td>3:35 - 3:40</td>
<td><strong>SESSION III: On the Horizon</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Session Introduction</strong></td>
</tr>
<tr>
<td></td>
<td>Patrick Zweidler-McKay, ImmunoGen</td>
</tr>
<tr>
<td>3:40 - 4:05</td>
<td><strong>FDA Work to Expedite the Development of Products to Address Serious</strong></td>
</tr>
<tr>
<td></td>
<td>and Life-Threatening Conditions</td>
</tr>
<tr>
<td></td>
<td>Peter Marks, CBER/US FDA</td>
</tr>
<tr>
<td>4:05 - 4:30</td>
<td><strong>TriLeukeVax: A “Next Generation” Autologous Immunotherapy for Leukemia</strong></td>
</tr>
<tr>
<td></td>
<td>Karin Gaensler, UCSF</td>
</tr>
<tr>
<td>4:30 - 4:55</td>
<td><strong>Novartis Work on AML</strong></td>
</tr>
<tr>
<td></td>
<td>Scott Cameron, NIBR</td>
</tr>
<tr>
<td>4:55 - 5:00</td>
<td>Closing Remarks</td>
</tr>
<tr>
<td>5:00 - 6:15</td>
<td>Evening Reception hosted by The Boston Society</td>
</tr>
</tbody>
</table>
SESSION I: The Current Landscape

Genomics of Myeloid Malignancies
Coleman Lindsley, Dana Farber Cancer Institute

The landscape of common, recurrent somatic alterations in the coding genome of acute myeloid leukemia (AML) has been extensively characterized, revealing a central role for specific mutations in driving distinctive features of disease biology. Genomic studies have shown that AML is typically driven by a multi-step somatic genetic process affecting a core set of genes. By definition, recurrent AML driver mutations all cause clonal dominance, although they can have stereotyped positions in the clonal hierarchy or patterns of co-mutation association and exclusivity. For AML patients, clinical genetic analyses are now employed to improve the accuracy of disease diagnosis, to define molecular taxonomy, to refine prognostic and predictive models, and to identify novel therapeutic strategies.

AML after Transplant: Are We Becoming High Maintenance?
Yi-Bin Albert Chen, Massachusetts General Hospital

Allogeneic hematopoietic cell transplantation (allo-HCT) for patients with acute myeloid leukemia (AML) is increasingly able to impact the historically poor outcomes in this disease. Nonetheless, even with transplant, the rates of post-HCT relapse are unacceptably high, and remain a great challenge in the treatment of patients with AML. Maintenance therapies after allo-HCT, given to patients at high risk of relapse or with evidence of minimal residual disease, may provide a way to reduce relapse rates and improve survival. New therapies may offer acceptable toxicity profiles in the post-HCT setting, and investigations are ongoing using many agents including hypomethylating agents, HDAC inhibitors, immunomodulatory drugs, targeted tyrosine kinase inhibitors, drug-antibody conjugates, and cellular therapies. Future directions in the field of post-HCT therapies may include better risk stratification with MRD, as well as the exploitation of novel mechanisms such as immune checkpoint inhibition and modified CAR T-cells. Although there is great potential for post-HCT agents to improve AML outcomes, these will need to be evaluated prospectively through well-designed large collaborative clinical trials.

SESSION II: State of the Art Research and Treatment Updates

Novel CAR-T Therapy for AML
Bikash Verma, Celyad

One of the most promising and scientifically sophisticated therapies for blood cancers is the Chimeric Antigen Receptor T cell (CAR-T) therapy. It has demonstrated phenomenal response rates for Acute lymphoblastic leukemia (ALL) and B cell lymphomas. CAR-T therapy is a complex combination of technologies from oncology, immunology and gene therapy. However, even though being very successful in lymphoid malignancies, the classic CAR-T approach has been largely unsuccessful in myeloid malignancies. Celyad has developed a novel CAR-T platform by using receptors from NK cells which has helped overcome the limitations of classic CAR-T constructs. Our recent data has demonstrated impressive results including complete response among AML patients - and with far less toxicity. This presentation will discuss clinical development of NKG2D based CAR-T therapy and its recent successes in AML.

ADCs in AML: GO and Beyond
Patrick A. Zweidler-McKay, ImmunoGen

With the re-approval of gemtuzumab ozogamicin (GO), the impact of antibody drug conjugates (ADC) for AML patients has been established. With the ability to delivery
chemotherapeutic payloads with increased specificity and decreased toxicity, ADCs have the potential to enhance the efficacy of existing chemotherapy and novel inhibitor strategies, or provide an alternative to systemic chemotherapy entirely. Challenges include exploring the choice of targets, delivering effective payloads, mitigating potential toxicities and optimizing combination strategies for safety and efficacy.

**Novel Targeting of AML and T-ALL**
John F. DiPersio, Washington University School of Medicine

T cell malignancies represent a class of devastating hematologic cancers with high rates of relapse and mortality in both children and adults for which there are currently no effective or targeted therapies. Despite intensive multi-agent chemotherapy regimens, fewer than 50% of adults and 75% of children with T-ALL survive beyond five years. For those who relapse after initial therapy, salvage chemotherapy regimens induce remissions in 20-30% of cases. Allogeneic stem cell transplant, with its associated risks and toxicities, is the only curative therapy.

Targeted therapy against T cell malignancies represents a significant unmet medical need. Such targeted therapies have shown great potential for inducing both remissions and even long-term relapse-free survival in patients with B cell leukemia and lymphoma. Engineered T cells that express a chimeric antigen receptor (CAR) directed against T cell malignancies are limited by several significant obstacles. First, the shared expression of target antigens between T effector cells and T cell malignancies results in fratricide, or self-killing, of CAR-T cells. Second, harvesting adequate numbers of autologous T cells, without contamination by malignant cells is, at best, technically challenging and prohibitively expensive. Third, the use of genetically modified CAR-T cells from allogeneic donors may result in life-threatening graft-vs.-host disease (GvHD) when infused into immune-compromised HLA-matched or mismatched recipients. We hypothesized that deletion of CD7 and the T cell receptor alpha chain (TRAC) using CRISPR/Cas9 in CAR-T targeting CD7 (UCART7) would result in the efficient targeting and killing of malignant T cells without significant effector T cell fratricide or induction of GvHD.

**FDA Work to Expedite the Development of Products to Address Serious and Life-Threatening Conditions**
Peter Marks, CBER/US FDA

Traditionally, the role of FDA has been to ensure the safety and efficacy of medical products. Increasingly, the agency has been charged with expediting the development and availability of products that address serious and life-threatening conditions. Toward this end, Congress has provided the agency with the authority for several expedited development programs, including breakthrough therapy and regenerative medicine advanced therapy designation, which were enacted during the past several years. As FDA moves forward to expedite the development of advanced therapies for patients in need, the agency sees its role as contributing across the spectrum of product development, from fostering the development and implementation of improved manufacturing technologies, to helping to establish standards for product development, to facilitating the optimal design of innovative clinical trials for product evaluation, to streamlining the regulatory approval process to the greatest extent possible, while still maintaining our standards for safety and effectiveness.

**TriLeukeVax: A “Next Generation” Autologous Immunotherapy for Leukemia**
Karin Gaensler, UCSF

There is an unmet need for novel therapies for high-risk acute myelogenous leukemia (AML), as most patients relapse after chemotherapy-induced remission. Compelling evidence for the efficacy of immunotherapy in eliminating minimal residual disease (MRD) in AML is provided by the superior outcomes of allogeneic
hematopoietic stem cell transplants (HSCT) that provide graft vs leukemia (GVL) effects mediated by donor T cells. However, many patients, such as those >60 years old, are ineligible for allo-HSCT, and overall survival is less than 15%. Thus effective, novel approaches are needed to increase post-remission survival. Autologous tumor vaccines have advantages for stimulating AML-specific immunity because responses are directed to multiple AML-associated and minor histocompatibility antigens, some unique to the patient. This reduces the risk of escape mutants that can occur with immunotherapies targeting single antigens. Previous studies with autologous AML vaccine studies (GVAX trial), in which UCSF participated, have shown promise; however, inefficient antigen presentation due to down-regulation of the critical co-stimulator CD80 on AML, may limit reliable induction of effective anti-leukemic immunity.

We have now generated novel autologous AML cell vaccines that simultaneously express the co-stimulatory protein CD80, missing on AML cells, and the heterodimeric protein IL-15/IL-15Ra. IL-15 is a cytokine uniquely suited to stimulating anti-tumor immunity. It shares with IL-2 the ability to stimulate NK and CD8+ memory T cells. However, in contrast to IL-2, IL-15 shows less T regulatory cell (Treg) stimulation, protects immune effectors from Treg suppression, and improves memory CD8+ T cell expansion. Co-expression of IL-15 with the IL-15 receptor alpha subunit (IL-15Ra) is required for trans-presentation to responding cells, and greatly increases both the half-life and activity of IL-15. To rigorously test this novel immune-stimulatory combination, we used the 32Dp210 murine leukemia model because this tumor reproduces the profound tumor-mediated immunosuppressive effects seen in human AML. Our studies show that 32Dp210 leukemic cells exhibit early homing to bone marrow, with stimulation of inhibitory immune effectors and up-regulation of the immune-regulatory molecules PD-1 on T cells and PD-L1 on tumor cells. We generated 32Dp210 leukemia cells expressing IL-15 and IL-15Ra, or CD80, or IL-15/IL-15Ra/CD80, and administered these as irradiated vaccines intradermally. Without vaccine treatment, leukemic mice had an overall survival of less than 10 weeks, as did mice injected with leukemia and then vaccinated with irradiated, parental 32Dp210 cells. Overall survival after treatment with either CD80 or IL-15/IL-15Ra-expressing 32Dp210 cell vaccines was 40-60%, whereas 80% of leukemia-bearing animals treated with 32Dp210-IL-15/IL-15Ra/CD80 vaccines survived. Anti-leukemic immunity was durable, as surviving mice rejected leukemia when re-challenged with unmodified tumor. In vivo antibody depletion studies demonstrated that CD3+CD8+ T cells, but not CD3+CD4+ T cells, were required for vaccine mediated anti-leukemic effects. Our studies establish the potent immune-stimulatory effects of IL-15/IL-15Ra/CD80-expressing AML cell vaccines and provide a universally applicable approach for generating personalized leukemia vaccines with the potential to better control MRD. Ongoing studies are examining the effects of engineered human AML in stimulating leukemia specific cytolytic responses.
BIOGRAPHIES

**Yi-Bin Chen, MD**, Massachusetts General Hospital: Dr. Yi-Bin Chen is the Director of the Blood and Marrow Transplant Program at Massachusetts General Hospital. He completed his undergraduate studies at Yale University and medical school at Harvard. He conducted his residency at Massachusetts General Hospital and fellowship at the Dana-Farber Harvard combined program before joining the faculty at MGH in 2008. His clinical interests are improving outcomes for patients undergoing both autologous and allogeneic hematopoietic stem cell transplantation. His research interests have most recently focused on novel therapies to prevent and treat acute graft-vs-host disease as well as the introduction of maintenance therapies after allogeneic transplantation to prevent disease relapse. He lives in Needham, MA with his wife and 2 children.

**Naval Daver, MD**, MD Anderson Cancer Center: Dr. Naval Daver is an Associate Professor in the Department of Leukemia at MD Anderson Cancer Center. He completed his medical school from Grant Medical College and Sir J J group of Hospitals, Mumbai followed by a residency and fellowship in hematology-oncology from Baylor College of Medicine. He is a clinical investigator with a focus on molecular and immune therapies in AML and Myelofibrosis and is principal investigator on >25 ongoing institutional, national and international clinical trials in these diseases. These trials focus on developing a personalized therapy approach by targeting specific mutations or immune pathways expressed by patients with AML, evaluating novel combinations of targeted, immune and cytotoxic agents, and identifying and overcoming mechanism of resistance. He is especially interested in developing monoclonal and bispecific antibodies, immune checkpoint and vaccine based approaches in AML, MDS, and myelofibrosis and is leading a number of these trials at MDACC. Dr. Daver has published >150 peer-reviewed manuscripts and is on the editorial board of numerous hematology specific journals. He has also authored numerous abstracts at national and international conferences.

**John F. DiPersio, MD, PhD**, Washington University School of Medicine: Dr. John F. DiPersio, Deputy Director, Alvin J. Siteman Cancer Center and Chief of the Division of Oncology at Washington University School of Medicine in St. Louis and the Virginia E. and Samuel J. Golman Professor of Medicine.

Dr. DiPersio's research focuses on fundamental and translational aspects of leukemia and stem cell biology. These studies include identification of genetic abnormalities in human leukemias, understanding processes involving stem cell and leukemia cell trafficking, and clinical and translational programs in both leukemia/myelodysplastic syndrome and stem cell transplantation.

Dr. DiPersio is President of American Society of Blood and Marrow Transplantation, a member of the Board of Scientific Counselors (Clinical Science and Epidemiology) of the National Cancer Institute, an elected member of American Society for Clinical Investigation and American Academy of Physicians (AAP), previously Chair of the American Society of Hematology (ASH) Scientific Committee on Hematopoiesis and the 2013 recipient of the Daniel P. Schuster Distinguished Translational Investigator Award from Washington University, the 19th Annual AACR Joseph H. Burchenal Memorial Award for Outstanding Achievement in Clinical Cancer Research in 2014 and the 2014 recipient of the American Society of Hematology Mentor Award for Clinical Investigations. He has authored or co-authored more than 300 publications and over 60 invited reviews and book chapters.
Dr. DiPersio received his M.D. and Ph.D. from the University of Rochester and his B.A. in Biology from Williams College. He completed an internship and residency at Parkland Memorial Hospital and The University of Texas Southwestern Medical Center in Dallas. After serving as chief resident at Parkland Memorial Hospital, Dr. DiPersio completed a fellowship in the Division of Hematology/Oncology at the University of California, Los Angeles (UCLA) where he stayed on as an Assistant Professor before moving to the University of Rochester and then four years later to Washington University.

Terry J. Fry, MD, Center for Cancer Research, National Cancer Institute: Dr. Fry received a B.A. from Colgate University in 1988 and an M.D. from Georgetown University in 1992. After completing a pediatric residency at Georgetown in 1995, he served as Chief Pediatric Resident. From 1996-1999, Dr. Fry undertook fellowship training in pediatric hematology and oncology at Johns Hopkins University. After postdoctoral training in the laboratory of Dr. Crystal Mackall, Dr. Fry established a research program focused on the immunology of stem cell transplantation as a platform for cancer immunotherapy. Dr. Fry became Chief of the Division of Blood and Marrow Transplantation at Children’s National Medical Center in 2007, a position he held until 2010 when he returned to the Pediatric Oncology Branch as Head of the Hematologic Malignancies Section. He is a member of multiple societies including the American Society of Hematology, the American Association of Immunology and the American Society of Blood and Marrow Transplantation and was elected into the American Society of Clinical Investigation. He also serves in leadership positions in the Oncology Strategy Group in the Pediatric Blood and Marrow Transplant Consortium and the Cellular Therapy Committee in the Children’s Oncology Group.

Karin Gaensler, MD, UCSF: Dr. Karin Gaensler is a member of the Hematological Malignancies and Bone Marrow/Stem Cell Transplantation program at UCSF. She earned her medical degree from Harvard Medical School and then went on to complete her residency in internal medicine and a fellowship in hematology-oncology at the University of California, San Francisco. She holds the Krishnamurthi Endowed Chair in Hematological Malignancies. Studies in the Gaensler laboratory have focused on mechanisms of gene regulation during ontogeny, and on the development of gene transfer and stem cell transplantation approaches for the treatment of hematologic disorders. More recently, Dr. Gaensler has developed a collaborative research program in immunotherapeutic approaches for the treatment of acute myelogenous leukemia at UCSF and with the Department of Hematological Medicine at King’s College, London, where she holds an honorary Visiting Professorship.

Coleman Lindsley, MD, PhD, Dana Farber Cancer Institute: Dr. Lindsley is an Assistant Professor of Medicine at Dana-Farber Cancer Institute and Harvard Medical School. He received his BA in music from Swarthmore College, and his M.D. and Ph.D. in Immunology from Washington University School of Medicine, then completed a residency in internal medicine at Brigham and Women’s Hospital and a fellowship in oncology at the Dana-Farber Cancer Institute. The primary focus of his laboratory is the biology and treatment of myeloid malignancies. His genetic studies have led to new genomic models of leukemia classification and MDS outcome after stem cell transplantation.

Peter Marks, MD, PhD, Center for Biologics Evaluation and Research, FDA: Dr. Peter Marks received his graduate degree in cell and molecular biology and his medical degree at New York University. Following this, he completed an Internal Medicine residency and Hematology/Medical Oncology fellowship at Brigham and Women’s Hospital in Boston, where he subsequently joined the attending staff as a clinician-scientist and eventually served as Clinical Director of Hematology. He then moved on to work for several years in the pharmaceutical industry on the clinical development of hematologic and oncology products prior to returning to academic medicine at Yale University where he led the Adult Leukemia Service and
served as Chief Clinical Officer of Smilow Cancer Hospital. He joined the FDA in 2012 as Deputy Center Director for CBER and became Center Director in January 2016. Dr. Marks is board certified in internal medicine, hematology and medical oncology, and is a Fellow of the American College of Physicians.

**Gwen Nichols, MD, The Leukemia & Lymphoma Society:** Gwen Nichols received her BA from Williams College. Dr. Nichols received her MD with Honors from the State University of New York. She trained in internal medicine at the University of Chicago, and did her hematology-oncology fellowship at Memorial Sloan-Kettering Cancer Center where she served as Chief Fellow. She did post-doctoral research and was a Leukemia Service attending at MSKCC before being recruited to Columbia University as Director of the Hematologic Malignancies Program. At Columbia she was a PI on numerous clinical trials, ran an active translational research laboratory, and was an Advisory Dean of Students. Committee service included numerous grant review committees, the SWOG Leukemia Committee, the Education Committee of ASCO, and she continues to serve on the Scientific Advisory Board for the International Waldenstrom’s Macroglobulinemia Foundation. She was chosen “Physician of the Year” at Columbia, and received the Humanism in Medicine Award. Dr. Nichols joined Roche in 2007 and led the MDM2 franchise. In 2013 she became the Translational Medicine Group Head for Molecularly Targeted Therapeutics and Oncology Site Head for the Roche Innovation Center in New York. As of March 2017, Dr. Nichols joined the Leukemia and Lymphoma Society as their Chief Medical Officer, where she oversees the mission including research, patient access, education, public policy and advocacy.

**Bikash Verma, MD, DVM, Celyad:** Dr. Verma is the Head of Clinical Development and Medical Affairs at Celyad. As a physician-scientist, previously he worked in clinical development at Novartis and GSK. Prior to his clinical research in the industry, he worked in academic research at Harvard Medical School, and through CDC at Massachusetts Department of Public Health. He is specialized in immunology, immuno-oncology and preventive medicine which he accomplished through his post-doctoral, doctoral, and masters degrees and fellowships completed at University of Massachusetts and affiliated hospitals, University of Illinois, S Illinois University, Birsa University, International School of Medicine, Tufts University, among others. He serves on the board of Museum of Public Health and is the president of the International Health Organization (IHO).

**Patrick Zweidler-McKay, MD, PhD, ImmunoGen:** Dr. Zweidler-McKay is the Medical Director for Hematologic Malignancies at ImmunoGen, a biotechnology company that develops targeted cancer therapeutics using antibody-drug conjugate technology. He was previously the Deputy Department Chair for Pediatric Research at M. D. Anderson Cancer Center, Section Chief for Pediatric Leukemia and a physician-scientist focused on novel therapies for acute leukemias.
Thank you to all of our Organizers, Speakers, Sponsors and Delegates! Without your dedication, support and participation AML 2018 would not be possible. We greatly value your comments regarding AML 2018 as well as thoughts or suggestions for improving future conferences. Please take the time to fill out our survey when we send it to you next week.

Sincerely,

The Boston Society