



MULTIPLE MYELOMA  
Research Foundation

# MMRF INVESTOR IMPACT REPORT 2018

“WE ENVISION  
A WORLD  
WHERE EVERY  
PATIENT HAS  
PRECISELY WHAT  
THEY NEED TO  
PREVENT OR  
DEFEAT CANCER.”

**Kathy Giusti**

Founder and Chief Mission Officer  
Multiple Myeloma Research Foundation

# WE SEE THE CHALLENGES, AND WE DRIVE THE SOLUTIONS.

Over the past year, we have not slowed our pace. We continue to make unprecedented advances in accelerating precision medicine for all patients.

Our MMRF CoMMpass Study<sup>SM</sup> continues to drive our progress. The insights we are gaining from CoMMpass are advancing myeloma science in many ways — from analyzing why some patients have a better response to standard treatments to understanding the right treatment path for patients with even the rarest of subtypes. Every piece of data is invaluable.

Because of these successes, we've committed to strengthening the CoMMpass data set by using it in new and innovative ways. To that end, we have launched new groundbreaking initiatives that leverage our massive data set:

## **The MMRF Immunotherapy**

**Initiative** is investing \$15 million to speed the ever-expanding role of immunotherapy as a treatment for myeloma.

## **The MMRF Answer Fund**

uses CoMMpass data combined with other data sets to answer clinical questions posed by myeloma researchers as well as the patient community.

## **The MMRF Prevention Project**

is the first-ever research effort dedicated to using our data for early detection and prevention of multiple myeloma.

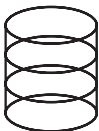
All of this work only has meaning if it positively impacts patients. By pursuing groundbreaking new treatments, focusing on early detection and prevention, and going directly to the community for their help in framing the most critical research questions, we are assured that our work is accomplishing what patients need.

By working together — patients, physicians,  
and scientists — we will unlock the key to a cure  
for every patient.

# OUR MODEL

With your help, we will make cures a reality. What the MMRF has built for patients does not exist without your continued support. Our unique model removes barriers to cancer breakthroughs and is the only end-to-end solution in cancer research. Your investment enables its extraordinary success.

## The Patient Data Bank



Generating and aggregating data to find the keys to the cure within each patient.

- MMRF CoMMpass Study<sup>SM</sup>
- MMRF CureCloud

## The Learning Network



Bringing world-class experts together to speed discovery.

- MMRF Researcher Gateway
- MMRF Answer Fund

## The Clinic



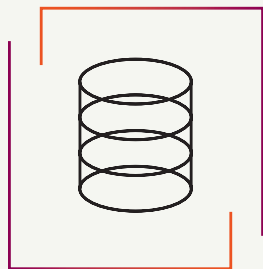
Delivering new therapies to the people who need them.

- Multiple Myeloma Research Consortium (MMRC)
- MMRF MyDRUG

Getting patients the right treatment at the right time puts the promise of a cure within reach.

# THE PATIENT DATA BANK

At the MMRF, our precision medicine model is built on data. Only by collecting and aggregating a meaningful data set will we have the information we need to find a treatment based on each individual patient's genomic and immunologic characteristics. We generate and store this data in our Patient Data Bank — the largest cancer genomic data set in the world.



## THE MMRF COMPASS STUDY<sup>SM</sup> UPDATE

The landmark MMRF CoMMpass Study has revolutionized how myeloma research is done. Since 2011, CoMMpass has significantly sped up the pace of myeloma research and development of new therapies.

Data from the CoMMpass Study continues to deliver information of significant value to myeloma researchers, as evidenced by the latest insights at the December 2017 American Society of Hematology (ASH) Annual Meeting and Exposition. Some of the key findings communicated at ASH 2017 include:

- New targets and pathways that can be driven rapidly to the clinic
- Rationales for investigating additional potential targets
- MMRF's collaboration with Gene Network Science (GNS) using GNS proprietary causal machine learning algorithms proved robust when applied to another large dataset and re-affirmed the importance of stem cell transplant in improving outcomes



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The MMRF has been instrumental in accelerating the development of novel therapies in multiple myeloma. Their early support of Selinexor was critical in moving it through clinical trials. Once FDA approved, it will be an important new therapy for patients.”

**Michael Kauffman**

CEO

Karyopharm Therapeutics, Inc.

## THE MMRF MOLECULAR PROFILING INITIATIVE

In 2016 we launched the Molecular Profiling Protocol, a precision medicine study seeking to sequence the DNA of 500 myeloma patients with the goal of finding genetic changes to target with new therapies. To date, we've enrolled 466 patients at 20 MMRC sites.

- A first analysis confirmed the existence of “actionable” alterations in 76% of relapsed myeloma patients.

These results validate our belief that precision medicine approaches hold great power for treating multiple myeloma. To leverage this knowledge, the MMRF has launched clinical trials for patients with specific mutations. We are also planning more efficient multi-arm clinical trial designs, like the MMRF MyDRUG, that will test more than one treatment simultaneously. This format will move promising new treatments through trials more quickly and get them to patients faster.

## MMRF IMMUNE NETWORKS OF EXCELLENCE

In 2017 we launched a three-year, \$15 million Immunotherapy Initiative, aimed at identifying which myeloma patients might respond to immunotherapy treatments.

The Initiative is centered around the creation of Networks of Excellence, which will bring together top researchers from different institutions for collaborative work in three areas:

- Creating new tests to identify patients likely to respond to immunotherapy
- Identifying mechanisms of resistance to immunotherapeutic treatments
- Establishing clinical trials of new immunotherapy treatments for myeloma

All these efforts will contribute valuable immune data to our Patient Data Bank and will move us closer to more precision medicine solutions for myeloma.

# OUR NETWORKS OF EXCELLENCE INCLUDE:

## **Combined Chimeric Antigen Receptor Therapy (CAR-T) and Active Immunization**

PRINCIPAL INVESTIGATOR:

**David Avigan, MD**

Beth Israel Deaconess Medical Center

## **Dissecting Immune Regulation and Dysfunction Within the Bone Marrow Micro-environment**

PRINCIPAL INVESTIGATOR:

**Ivan Borrello, MD**

Johns Hopkins Kimmel Cancer Center

## **Defining Optimal Tumor and Host Signatures for Immunotherapy of Myeloma**

PRINCIPAL INVESTIGATOR:

**C. Ola Landgren, MD, PhD**

Memorial Sloan Kettering Cancer Center



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The MMRF, and all of the patients and patient families they serve, have become our second family. Driven by the urgency of a patient founder, they work with the best doctors and researchers and have had incredible success in bringing new treatments to myeloma patients. We are proud to support their efforts.”

**TANI AND ERIC GELBER**  
MMRF Supporters



# THE LEARNING NETWORK

We believe that data has the most value when it's shared. That is why all of the information we collect and generate in the Patient Data Bank is freely available to the research community around the world via our Learning Network.



## THE MMRF ANSWER FUND

In 2017, the MMRF launched the Answer Fund, a multimillion-dollar effort to address important questions facing members of the multiple myeloma community and to help advance precision medicine.

The first question is how to define and treat high-risk patients. We asked top researchers to submit proposals that would use CoMMpass and other data to identify markers for high-risk myeloma. Two teams are working on this question:

**Constantine Mitsiades, MD, PhD and a team at Dana-Farber Cancer Institute, University of Florida Health Cancer Center and TGen** will use CRISPR gene-editing technology to understand the function of genes associated with high-risk myeloma and whether these genes might be good targets for drug therapies.

**Lawrence Boise, PhD, and a team from Emory University** leads a project that will study a high-risk gene pattern seen in some patients who relapse within 12–18 months of treatment to determine whether this pattern could be a target for the treatment of high-risk disease.

The next phase of the Answer Fund will identify the biggest challenges facing hematologists and oncologists who treat myeloma patients and find a way to solve those challenges.



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When Kent was first diagnosed, I did a lot of research and came to the conclusion that if I really wanted answers the MMRF was the best source. Working for a firm that advocates for scientific research, I know how important it is, and the MMRF was in line with that approach.”

**DEBBIE AND KENT WELLS**  
Multiple Myeloma Patient  
and Supporters

## THE MMRF PREVENTION PROJECT

Last year, the MMRF launched the first-ever research program dedicated to the early detection and prevention of multiple myeloma. A multimillion-dollar gift from the Perelman Family Foundation established the Perelman Family Foundation Early Disease Translational Research Program as part of the MMRF Prevention Project. This program seeks to speed efforts toward early detection, delayed disease progression, and prevention of this incurable disease. Through partnerships with six leading researchers, we will focus on:

- Better understanding of genomic determinants of early disease progression
- Impact of microenvironmental factors on early disease progression
- Enhancing tumor immunity in MGUS/SMM
- Building out the smoldering myeloma data set and trials

## OUR PREVENTION PROJECT RESEARCH PARTNERS:

### **Kivanc Birsoy, PhD**

Rockefeller University

To use metabolic profiling to study how myeloma cells change their metabolism and apply that knowledge to create novel anti-myeloma therapies.

### **Madhav Dhodapkar, MBBS**

Winship Center for Cancer Immunology

To identify the signals that regulate the relationship between the immune system and gut-related inflammation and determine whether modifying the triggers that disrupt that immune balance will prevent cancers such as myeloma.

### **Elizabeth Manasanch, MD & Robert Orlowski, MD**

MD Anderson Cancer Center

To understand the role of immunotherapy in delaying or preventing progression of SMM to multiple myeloma.

### **C. Ola Landgren, MD, PhD**

Memorial Sloan Kettering Cancer Center

To find DNA markers of stable monoclonal gammopathy of unknown significance and smoldering multiple myeloma (MGUS/SMM) versus markers of progressive disease. Dr. Landgren's lab has developed a DNA sequencing assay called myTYPE that identifies the genetic changes that cause this progression.

### **Irene Ghobrial, MD**

Dana Farber Cancer Institute

To develop a highly sensitive method for detecting MGUS and SMM for use as a screening and monitoring patients.

## RESEARCH FELLOW AWARDS

These awards help prepare and support the next generation of young investigators at the forefront of research into myeloma research. The MMRF Research Fellows are investigators at the postdoctoral, medical fellow, or junior faculty levels working under the supervision or guidance of a research mentor.

### IN MAY 2018 – WE ANNOUNCED FIVE \$75,000 AWARDS:

**1 | Histologic and Molecular Predictors of Renal Outcome in AL Amyloidosis**

Cindy Varga, MD  
Tufts Medical Center, Boston MA

**2 | Characterization of Genetic Vulnerabilities in Multiple Myeloma**

Nicholas Banovich, PhD  
The Translational Genomics Research Institute (TGen), Phoenix, AZ

**3 | Nanoparticle for Early Detection and Minimal Residual Disease (MRD) Disease in Multiple Myeloma**

Alexandre Detappe, PhD  
Dana-Farber Cancer Institute, Boston, MA

**4 | New Generation CD138 Chimeric Antigen Receptor Targeting Multiple Myeloma**

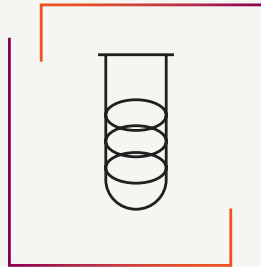
Chuang Sun, PhD  
University of North Carolina at Chapel Hill's Lineberger Comprehensive Cancer Center, Chapel Hill, NC

**5 | Patient-Specific Mutation-Derived Tumor Neo-Antigens (MTA) as Targets for Cancer Immunotherapy in Smoldering Multiple Myeloma (SMM)**

Donna Edwards, PhD  
The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY

# THE CLINIC

The Clinic is the critical endpoint of the MMRF Precision Medicine Model – all of the work of the Patient Data Bank and the Learning Network is aimed at delivering new treatments to patients.























## INNOVATIVE TRIALS

The Multiple Myeloma Master Protocol, called MyDRUG, is a unique trial design focused on dramatically accelerating clinical development and approval of therapies. MyDRUG will be a multicenter study of several different investigational agents and drug combinations in patients with relapsed myeloma. Patients will be assigned to treatments based on genomic tumor analysis.

## CLINICAL TRIAL HIGHLIGHTS

The Multiple Myeloma Research Consortium (MMRC), the MMRF clinical network of 25 centers in the United States and Canada, evaluates novel agents and combinations for their safety, efficacy, and feasibility in Phase I & II clinical trials. To date, the MMRF has conducted over 80 clinical trials and at any given time, has over 20 active trials ongoing.

### 2018 ACTIVE CLINICAL TRIALS

	NOVEL AGENTS/ MECHANISMS	ANTIBODIES & IMMUNE	PIS & IMIDS	MOLECULARLY TARGETED
RELAPSED OR R/R/RACE011	<ul style="list-style-type: none"> <li> ACE011</li> <li> Ibrutinib/ Kyprolis</li> <li> Venetoclax/ Ninlaro</li> <li> Selinexor/Dex</li> <li> Selinexor/ Kyprolis</li> </ul>	<ul style="list-style-type: none"> <li> Emlipiciti/ Pomalyst/ Dex</li> <li> Rev/Dex/ Emlipiciti +/- Cyclophos (Amyloidosis)</li> <li> Emlipiciti/ Pomalyst/ Velcade/Dex</li> <li> Isatuximab</li> <li> Isatuximab/ Kyprolis</li> </ul>	<ul style="list-style-type: none"> <li> Pomalyst/ Kyprolis/Dex</li> <li> Pomalyst/ Ninlaro/ EMD/PCL</li> </ul>	<ul style="list-style-type: none"> <li> Idasanutline/ Ixa 17p deleted</li> <li> PINR Biomarker- driven</li> <li> Dabrafenib/ Trametinib</li> <li> JNJ- 42756493</li> </ul>
NEW DX/ TRANSPLANT	<ul style="list-style-type: none"> <li> Emlipiciti/Rev/ Velcade/Dex</li> </ul>	<ul style="list-style-type: none"> <li> Emlipiciti/ Kyprolis/ Rev/Dex</li> </ul>	<ul style="list-style-type: none"> <li> Ixazomib/ Revlimid/ Dexransplant*</li> </ul>	
SMM		<ul style="list-style-type: none"> <li> Emlipiciti/ Rev/Dex</li> </ul>		

KEY

 Phase 1

 Phase 1/2

 Phase 2



## RODNEY GILMORE JOINS THE MMRF AS DIRECTOR

The MMRF is pleased to announce the addition of ESPN college football analyst and attorney Rodney Gilmore to our board of directors. For Mr. Gilmore, this role is personal — he first connected with the MMRF after his own myeloma diagnosis. Mr. Gilmore lives in the Bay Area with his wife, Marie, and has two adult children, Anthony and Nicole.

# FINANCIAL INTEGRITY

We raise at least \$50 million per year to accelerate precision medicine and fuel a pipeline of potentially life-extending treatments. Almost 90 percent of the funds we raise go directly to research. This commitment to meaningful spending and prudent financial planning has consistently earned us a 4-star rating (the highest possible) from Charity Navigator. The MMRF has also received a “Best in America” Seal of Excellence from the Independent Charities of America and an “A+” rating from the American Institute of Philanthropy.

As a patient-founded organization, we know how urgent our work is. We also know we can’t do this work alone. Philanthropic giving fuels the creative, innovative science that leads tomorrow’s cures. With your support, we can continue to make scientific discoveries that lead to major breakthroughs for the myeloma community.





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