



June 24, 2009

Welcome.

On behalf of the Multiple Myeloma Research Foundation (MMRF), we are pleased you are able to attend the **2009 MMRF Investors Summit – *Accelerating Drug Development: Results and Progress Toward a Cure.***

Hosted by the MMRF, this world-class program offers an unprecedented opportunity to learn more about the latest innovations in myeloma research and drug development in an intimate and engaging setting. Much of this research and progress is made possible by funding from investors of the MMRF and the Multiple Myeloma Research Consortium (MMRC).

World-renowned researchers who will be presenting and participating include:

- Kenneth C. Anderson, MD, from Dana-Farber Cancer Institute and Harvard Medical School
- Gregory A. Curt, MD, from AstraZeneca
- Rafael Fonseca, MD, from Mayo Clinic–Scottsdale
- Stacey Gabriel, PhD, from Broad Institute of MIT and Harvard
- Mohamad A. Hussein, MD, from Celgene Corporation
- Susan Molineaux, PhD, from Proteolix, Inc.
- Jasbir S. Seehra, PhD, from Acceleron Pharma, Inc.

This distinctive program includes presentations by the MMRF and the MMRC leadership team on the significant progress achieved this past year as a result of our organizations' efforts. MMRF-funded researchers will emphasize how their work is leading to new treatment options. This program's esteemed faculty will also provide an update on several important MMRC research and drug development efforts now underway, including the Genomics Initiative. Additionally, we will discuss future MMRC research efforts designed to advance promising myeloma therapies out of the lab and into early-phase clinical trials. The meeting's informal structure and social time will allow you the opportunity to meet with the MMRF, the MMRC, and the world's most renowned myeloma experts, all while interacting with other highly committed patients and caregivers.

Thank you for your continued support of the MMRF and for joining us today.

Most sincerely,

A handwritten signature in black ink that reads "Kathy Giusti". The signature is fluid and cursive, with the first name being more prominent.

Kathy Giusti  
*Founder and CEO*

A handwritten signature in black ink that reads "Scott T. Santarella". The signature is cursive and somewhat stylized, with the last name being the most prominent part.

Scott T. Santarella  
*Chief Operating Officer & Executive Director*



**2009 MMRF INVESTORS SUMMIT**  
**Accelerating Drug Development: Results and Progress Toward a Cure**  
June 23–24, 2009

**AGENDA**

**Tuesday, June 23, 2009**

- 6:00 PM            **Reception**
- 7:00 PM            **Dinner with Guest Speaker**  
Susan M. Molineaux, PhD  
*Proteolix, Inc.*

**Wednesday, June 24, 2009**

- 8:00 AM            **Light Breakfast and Registration**
- 9:00                **Welcome and Overview of the MMRF/MMRC Strategy**  
Kathy Giusti  
*Multiple Myeloma Research Foundation*  
*Multiple Myeloma Research Consortium*
- 9:15                **MMRF Research Investment Portfolio**  
Louise Perkins, PhD  
*Multiple Myeloma Research Foundation*
- 9:45                **MMRF Genomics Initiative and Personalized Medicine**  
Stacey Gabriel, PhD  
*Broad Institute of MIT and Harvard*
- 10:15              **Break**
- 10:30              **MMRC Tissue Bank**  
Rafael Fonseca, MD  
*Mayo Clinic – Scottsdale*
- 11:00 AM         **MMRF Biotech Investment Award**  
Jasbir S. Seehra, PhD  
*Acceleron Pharma, Inc.*

**2009 MMRF INVESTORS SUMMIT**



Accelerating Drug Development: Results and Progress Toward a Cure  
June 23–24, 2009

**AGENDA (CONT)**

**Wednesday, June 24, 2009**

- |          |   |
|----------|---|
| 11:45 AM | <b>Recap of Important Research Initiatives</b><br>Louise Perkins, PhD   |
| 12:00 PM | <b>Luncheon with Guest Speaker</b><br>Traver Hutchins<br>Patient Speaker  |
| 1:15     | <b>Perspectives of the MMRF/MMRC Model</b><br>Mohamad A. Hussein, MD<br><i>Celgene Corporation</i>  |
| 1:45     | <b>Novel and Combination Clinical Trials</b><br>Kenneth C. Anderson, MD<br><i>Dana-Farber Cancer Institute</i><br><i>Harvard Medical School</i> |
| 2:15     | <b>MMRF Research Investments (Donor Fund and Campaign)</b><br>Scott Santarella<br><i>Multiple Myeloma Research Foundation</i>                   |
| 2:25     | <b>Break</b>  |
| 2:45     | <b>Novel Partnerships</b><br>Gregory A. Curt, MD<br><i>AstraZeneca</i>  |
| 3:15     | <b>Question-and-Answer Session</b>  |
| 3:45 PM  | <b>Closeout and Thank You</b><br>Scott Santarella   |



**MMRF**  
Investors Circle

## Participants

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**MMRF**  
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## Abstract

### **Susan M. Molineaux, PhD**

*Proteolix, Inc.*

Despite the significant advances that have occurred in the last decade with the development of new and better drugs, multiple myeloma (MM) remains an uncured disease. The Multiple Myeloma Research Foundation (MMRF) is unique among patient advocacy organizations because it so strongly supports and promotes the scientific efforts of the academic community, the clinicians, and the biotech and pharmaceutical companies in their quest to find new treatments for MM. The MMRF, and Kathy Giusti, have a deep understanding of the drug development process, and based on this knowledge, they have pioneered an innovative program that brings clinicians and drug companies together to identify new potential targets for therapy, to support academic labs and drug companies in the development of new experimental drugs, and to help organize the clinical trials necessary to test those experimental drugs. This organization, the Multiple Myeloma Research Consortium (MMRC), focuses on streamlining the process to allow for the rapid discovery, development, and approval of new drugs.

Proteolix, Inc., is a private biotech company devoted to developing new proteasome inhibitors for the treatment of MM and other cancers. Our lead product candidate, carfilzomib, was discovered at Proteolix and is a highly selective next-generation proteasome inhibitor. We have been working with the MMRC from the inception of our clinical program in 2005. Our two Phase I studies were conducted at the clinical sites in the MMRC network. The MMRC introduced us to clinicians, and worked with us and the clinical sites to get trials started and patients enrolled as quickly as possible. After our initial Phase I trials showed that carfilzomib had promising activity in myeloma patients, we were excited to be able to continue our collaboration. In 2007, the MMRC and Proteolix embarked on a series of Phase II studies to test carfilzomib in different types of myeloma patients. These were the first Phase II studies that the MMRC did in conjunction with a company, and the trials again showed promising results for carfilzomib. In 2008, the MMRC and Proteolix started a large (250 patient) Phase II trial that, if the results are successful, will allow Proteolix to file for an accelerated approval of carfilzomib in the United States for the treatment of myeloma patients who have failed currently approved therapies. This is just one example of how the partnerships that the MMRC forges with biotech and pharmaceutical companies are transforming and streamlining the process of getting new treatments to myeloma patients.



## **Abstracts**

### **MMRF Genomics Initiative and Personalized Medicine**

**Stacey Gabriel, PhD**

*Broad Institute of MIT and Harvard*

Cancer is a disease of the genome – caused by germ-line susceptibility and various acquired somatic alterations. Knowledge of these alterations will inform our knowledge of cancer etiology and will increasingly allow prediction of response to therapy, guided development of new therapies, and improvement in cancer diagnosis. The revolution in genome technology, driven by the development of next-generation sequencing technology, is now transforming systematic cancer genome characterization. We will present data on the first comprehensive whole genome sequencing of multiple myeloma including analysis of single base changes and genome-wide view of structural rearrangements.



## **Abstracts** (cont)

### **MMRC Tissue Bank**

**Rafael Fonseca, MD**

*Mayo Clinic – Scottsdale*

The MMRC Tissue Bank (TB) was created in 2004 as a way of supporting basic, translational, and clinical discoveries that would require utilization of peripheral blood (PB) and bone marrow (BM) samples collected from myeloma (MM) patients. This represented a unique opportunity, but certain challenges existed including the submission of samples from multiple institutions. To establish a practice of collection of these samples under the most rigorous conditions, we decided to execute all operations of the MMRC TB under the rubric of good laboratory practices (GLP). The GLP environment assures investigators that all samples provided by the MMRC TB meet a minimum set of specifications for quality. Intrinsic to this process, we have a commitment to continuous quality improvement. As part of the GLP operations, we hold regular internal and external audits that provide assessment of variance in samples submitted to the MMRC. The MMRC TB currently supports a number of Phase I and Phase II clinical trials for MM. It also has served as the bio-repository source for the MMRC Genomics Initiative project (a joint project between the MMRC/TGEN/Broad). This is a unique genome cataloging exercise that positions MM as one of the human diseases where there will be the greatest knowledge regarding the genetic aberrations leading to disease pathogenesis. As of June 2009, the MMRC has processed a total of 2421 BM samples and 2055 PB samples. We currently receive samples from 14 different institutions. In 2008, we accrued 698 samples consisting of 667 BM samples and 553 PB samples. We have extracted DNA/RNA from BM samples supporting the aforementioned genomics project (GEP/aCGH) including 250 pairs of RNA and DNA, as well as an additional 100 DNA paired samples (MM cells and PB WBC) to Broad for whole genome sequencing. We have stored in the TB approximately the following derivatives: 58,104 slides (@ 24/BM), 4842 BM plasma vials (@ 2 x 2mL aliquots), 4110 PB plasma (@ 2 x 2mL aliquots), 2421 white blood cell aliquots from the BM, 1853 vials of 138+ cells (MM cells), and 5941 vials of other BM elements. We have stored a total of 3171 vials of PB cells from patients with MM.



## **Abstracts** (cont)

### **MMRF Biotech Investment Award**

**Jasbir S. Sehra, PhD**  
*Accelaron Pharma, Inc.*

The MMRF selected Accelaron Pharma, Inc., as a recipient of its 2007 Biotech Investment Award, providing a total of \$1 million in milestone-driven funding to propel the development of ACE-011 forward in multiple myeloma (MM). A broad development partnership between Celgene and Accelaron to further advance the drug was subsequently announced.

Accelaron is a biotechnology company developing protein therapeutics that affect tissues, including bone, skeletal muscle, vascular, adipose and erythropoietic tissues. Activin, a member of the TGF- $\beta$  superfamily of genes, regulates bone and red blood cell growth. ACE-011 is a protein therapeutic that blocks activin signaling resulting in increased bone density and red blood cell levels and is being developed for bone loss and anemia associated with cancer.

In MM, the growth of tumor cells in the bone marrow increases the activity of bone resorbing cells while decreasing the number of bone forming cells, resulting in very fragile bones subject to nonimpact fractures. ACE-011 has a novel mechanism of action in that it increases the number of bone forming cells that are then able to replace lost bone. In animal models, treatment with ACE-011 prevents bone loss and additionally is able to increase survival by inhibiting the growth of tumor cells. ACE-011 also decreases the anemia (increases red blood cells) often encountered in patients with MM due to the growth of the tumor in the red blood cell producing bone marrow environment or due to the effects of chemotherapy on red blood cell production. These data indicate that ACE-011 represents a novel multipronged therapeutic approach to treating MM.

ACE-011 has been studied in Phase I clinical studies in healthy volunteers and was shown to have a long serum half life of 24–31 days allowing for infrequent dosing of once per month or less. Once monthly treatment with ACE-011 increased bone mineral density in healthy volunteers. Moreover, within one month's time, ACE-011 increased hemoglobin (an indicator of total number of red blood cells in circulation) by 3 g/dL, which is equivalent to transfusing three units of blood. ACE-011 is being evaluated in Phase II studies for effects on anemia and bone loss in patients with MM and in patients with breast cancer.



## **Abstracts** (cont)

### **Perspectives of the MMRF/MMRC Model**

**Mohamad A. Hussein, MD**  
*Celgene Corporation*

The advances in the therapy of any disease rely on understanding the cause and the mechanism of the illness. To develop therapy, a partnership between patients, treating institutions, and pharmaceutical industry is key. The development of the MMRF, and later the MMRC, has fostered the link between the three entities fostering scientific collaborations and facilitating timely logistical execution of contracts to initiate clinical trials evaluating new combinations and agents.

The better understanding of plasma cell dyscrasias and hematologic malignancies, in general, has allowed Celgene, in collaboration with different groups, to develop different classes of new molecules for the therapy of hematologic malignancies, in general, and multiple myeloma (MM), in particular. The major classes of agents are the immune modulators (IMiDs), hypomethylating agents as represented by Vidaza<sup>®</sup> (azacitidine), a new class of anthracyclines that combine the traditional anthracycline activities, as well as topoisomerase 2 activity, phosphodiesterase 4 inhibitors, and last, but not least, activin receptor 2A inhibitor.

In the IMiDs class, two compounds are in different phases of development; Revlimid<sup>®</sup> (lenalidomide), which has gained recent approval for the treatment of relapsed/refractory MM (June 2006) and is currently being developed for management of earlier disease stages as well as in combination with other agents, especially monoclonal antibodies directed at different targets on the MM malignant cell or its microenvironment. More recently, pomalidomide, a more potent immune modulator, is in early clinical trials to determine the dose and schedule, as well as the patient population that will benefit the most from the agent. One of the two studies evaluating the agent is being conducted by the MMRC. This agent has shown significant activity in patients who are refractory to Velcade<sup>®</sup> (bortezomib) (60% of such patients responded) and lenalidomide (50% of those patients responded).

The class of hypomethylating agents as represented by Vidaza has been shown to reverse resistance to Revlimid by modulating the local chemical environment around the malignant myeloma cell. Currently, studies evaluating dose and schedule, as well as effects of these compounds in combination are underway.

In summary, development of therapy for diseases is a collaboration between patients, academic institutions, industry, and government agencies. When all are synchronized, therapeutic development is significantly enhanced.



## **Abstracts** (cont)

### **Novel and Combination Clinical Trials**

#### *The End of Novel Therapies*

**Kenneth C. Anderson, MD**

*Dana-Farber Cancer Institute*

*Harvard Medical School*

Bortezomib, lenalidomide, and thalidomide all target the multiple myeloma (MM) cell in the bone marrow (BM) to overcome conventional drug resistance in laboratory and animal models; all treat advanced MM and newly diagnosed MM. There have been six FDA approvals in the last five years, and median survival has been extended from three to seven years. Current goals include: improving classification and developing personalized therapy; validating novel agents targeting MM and the BM; evaluating the role of stem cell transplantation; and developing novel immune therapies. First, personalized medicine optimizes response by selection of the right medicine for the right patient at the right time. Genes (DNA and RNA), mechanisms regulating genes (microRNA), and gene products (proteins) all show promise to allow for identifying individualized therapies. Second, novel agents target the MM cell surface (HuLuc 63 antibody), cytokines in the BM (antibody to B-cell activating factor), and mechanisms needed for tumor cell growth and survival (new proteasome inhibitors carfilzomib and NPI-0052; and immunomodulatory agent pomalidomide). Clinical trials in the Multiple Myeloma Research Consortium (MMRC) already look promising. Third, rational multiagent combination therapies such as lenalidomide, bortezomib, and dexamethasone achieve synergistic MM cell death in preclinical studies; and remarkably achieve 100% response, with 71% very good partial or complete response, in newly diagnosed MM. In an attempt to improve outcome, pegylated liposomal doxorubicin has been added to this combination in an ongoing MMRC clinical trial; moreover, a clinical trial will now evaluate the role of high-dose therapy in the context of this high extent and frequency of response to combined novel therapies. The addition of heat shock protein inhibitor tanespimicin, Akt inhibitor perifosine, or histone deacetylase inhibitor vorinostat to bortezomib can sensitize or overcome resistance to bortezomib; Phase III international clinical trials are evaluating these combinations for FDA approval. Finally, novel strategies can create designer vaccines and/or educate patient immune cells to recognize and kill their own MM cells. These four trends assure that MM will soon be a chronic illness in most patients, with sustained complete response in a significant fraction. The MMRC represents a novel collaborative model to assure the rapid translation of these innovative strategies from the bench to the bedside to achieve this goal.



## Abstracts

### Novel Partnerships

#### *The AstraZeneca Clinical Partnership Program*

**Gregory A. Curt, MD**

*AstraZeneca*

New opportunities are possible when AstraZeneca (AZ) works in partnership with selected external groups. AZ brings both a broad portfolio of novel oncology drugs and expertise in scientific and regulatory-driven development programs to such relationships. The partnering group adds scientific, clinical and operational expertise, resource, reputation, new ideas, and importantly, access to patients. By providing early access to its development portfolio, studies that might not otherwise be done can take place at reduced or no costs. In addition, the safe harbor of the partnership might facilitate negotiations for combination studies with agents from other companies. To add value to the relationship, AZ will also allow access to an annual MTA catalog of AZ compounds including probes, discontinued clinical candidates, clinical candidates, and discovery compounds. The Clinical Partnership Program is not the preferred delivery for prioritized (critical path, decision-making) trials, but they do enable a larger developmental footprint at relatively little additional cost. Already, there are several examples of activity signals with specific agents that would have been lost without the engagement of AZ with an external partner. The Multiple Myeloma Research Foundation (MMRF) and the Multiple Myeloma Research Consortium (MMRC) are both well known for innovation in the biology and treatment of this disease. It is the first foundation to be approached by AZ with a specific agent, in this case the Aurora-B inhibitor, AZD1152, as a possible new treatment for patients with refractory myeloma. It is hoped that this will be the beginning of sharing highly selective targeted agents more broadly with selected segments of the research community.







