# Myeloma with The MMRF

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**Full Transcript:**

**Priya Menon :** Hello, everyone, and welcome to the Cure Panel Talk Show on myeloma. I am Priya Menon, Scientific Media Editor, at the Cure Panel's Cure Talk, joining you from India and I welcome all of you this evening to a discussion on multiple myeloma. This is our first show on myeloma in the new year and the 44th episode of the Cure Panel Talk Show. Going forward, we have some interesting shows featuring eminent experts lined up for you this year. Please visit curepanel.carefeed.nic for more information on our upcoming shows or you can always mail me priya@trialx.com. Our previous show on myeloma had Dr. Fritz van Rhee of UAMS Little Rock talk about total therapy in myeloma, and today we are discussing multiple myeloma with the Multiple Myeloma Research Foundation or MMRF. Towards the end of last year in 2013, MMRF rolled out three important cancer research initiatives – big data and genomic sequencing, open access by sharing research data, and empowering patients to find clinical trials that are best for them and trying to understand how MMRF hopes to achieve this and hence the myeloma community is the focus of today's discussion. My co-host for the day is Pat Killingsworth, multiple myeloma blogger, advocate, and author. Supporting cast on the panel are Gary Petersen, Editor of myelomasurvival.com; patient advocate, Cynthia Chmielewski; Matt Goldman; and Lizzy Smith. I welcome all of you to the show today. With that, I will hand over to Pat who will introduce us to our experts of the day and begin with the discussion. Pat, you are live on air.

**Pat Killingsworth :** Thank you, Priya, and wow, what a wonderful panel we have joining me this evening questioning – Gary, Cyn, Matt, and Lizzy. Doesn't get any better than that and what a great guest we have this evening! Anne with the MMRF is joining us. Anne, you there?

**Anne :** I am here.

**Pat Killingsworth :** How are you?

**Anne :** I am good. How are you?

**Pat Killingsworth :** I am great! Anytime you are a myeloma survivor and you can say you are great, that's a pretty good day, won't you say?

**Anne :** Absolutely.

**Pat Killingsworth :** Anne, could you just give us a little background about yourself and what you do at the MMRF and then we can get into the real discussion about all other important projects that the group is doing.

**Anne :** Sure. Actually, so, you know, thank you, Priya, and the rest of the Cure Talk team. It was an honor to speak last year and certainly we are very grateful for the opportunity to kick off or to be part of the new year as well and thank you, Pat, for those words as well. I am Vice President, Marketing, at the MMRF. I have been there almost 12 years. In that time, I have worn many different hats, but primarily I am responsible for marketing and communications around the MMRF as well as all of our educational initiatives for patients and caregivers and for healthcare professionals. Pat, do you want me to go directly into comments about the foundation as well or?

**Pat Killingsworth :** Sure unless you want me to translate and for our (laughter) listeners that basically means that Anne does the heavy lifting over there. (Laughter) I mean, you got to admit you do a lot that goes far beyond the job description you just read, but I don't know… I would think you as indispensable and I am sure your teammates feel that way too.

**Anne :** Thank you, Pat. No, you know its honestly a team effort and I was grateful for the opportunity to join the MMRF 12 years ago because I could see even at that time how the disease was about to change. I coincidentally had a friend who worked at Millennium and so I knew even prior to coming to the MMRF, I knew about Velcade and the potential for that to completely transform this disease that had had earned that, you know, not so much hope and, you know, the opportunity to work side by side with Katie Milewski who, you know, Pat, I know, you know, you met her and for those on the phone who know her, you know, she is a driven individual and coupled with, you know, her diagnosis of multiple myeloma, that drive and that urgency, it was contagious and I, you know, wanted to be a part of this and could see, you know, what was happening in the field and the company, the _____ Velcade and Lenalidomide and the field really starting to come together, companies getting behind the doctor, and then, you know, us trying to pull everyone, you know, all together. It was really motivating back then and, you know, 12 years later, wow!, the field has just changed so dramatically and, you know, patient experience today is vastly, vastly different. You know, I don't know if people like Jack Aiello or others are on the call, but certainly anyone who is around, you know, 10 to 12 years ago it was a very different place. So, you know, I will kind of use that as a safe way, you know, to speak a little bit about what we are doing. You know, Pat, you gave kind of a challenge or the statement that, you know, we think we could do a better job of really letting the patient community know about what we do and I think part of the challenge is we are a small team, about 30 to 35 people, based in Connecticut and we don't have people across _____we don't have people across the region and we are all very, you know, in a way very, very focused and excited by what's going on in myeloma research and really doing everything that we possibly can to accelerate new treatments for patients because we have seen the progress that the entire community has made working together in the last 10 or 12 years, but, you know, there are still challenges ahead. Its not cured; not every patient is living 10, 15, or more years. How can we make sure that, you know, we are bringing up the survival of every single patient and, you know, our activity span funding basic research, so we funded 150 centers worldwide, so anyone seen as a major academic center, here, Canada, Europe, we have probably provided funding there. We have done and I know there are some questions around this, so we can discuss in little more detail a lot in the field of genomic. Myeloma is a very heterogeneous disease, meaning I am sure everyone can see it, talking patient to patient helps. Everyone seems to have different symptoms and response treatments and that goes down to the molecular levels, not just kind of seen on the surface, but your disease really does differ from patient to patient. So, how do we better understand that so that we can get the right treatment, the right combination of the treatment, fit to patient as quickly as possible. Then, to our clinical network, we were working to accelerate early clinical trials and then on the education side, enrolling those trials and helping to educate the community, both patients and providers, about the treatments that are available. So, our research consortium is 16 centers and we have opened since we launched in 2006, 49 different trials with 24 different agents and what we are really proud of is not only the fact that Kyprolis and Pomalyst, some of those early trials, the trials that resulted in the FDA approval of those drugs were run through our clinical network. So, you know, we worked closely with the companies back before Onyx had _____worked with _____ in the very early days to, you know, come up with a plan to move that drug quickly and certainly we have had a longstanding relationship with Celgene dating back to lenalidomide and, you know, in addition to those two getting FDA approval, about 80% to 90% of those drugs that we are supporting in clinical trials are still being studied. So, you know, you may hear about how rich each drug development is, how many new drugs failed. We work so closely with our investigators that, you know, really some of the best in the world, to pick that portfolio, to pick those treatments that are most likely to benefit patients and we are very proud of that because at least a certain amount of efficiency so that for the most part, you know, you have seen MMRC trials, you know its been bettered by not only our internal team but some of the leading investigators in the world. We have also shown that our trials open and close, doctors, and some of the published benchmarks really, you know, underscoring our commitment _____We can talk, perhaps this will come up a little bit in some of the questions, but I did see that samples had questions about, you know, what's coming down the _____and you know we are focused on bringing forward new and better versions of, you know, the standard class

proteasome inhibitors and MM. As some of you may know, there are four versions of proteasome inhibitors. Millennium has one that is in phase 3 that, you know, in the next couple of years could be widely available, which, you know, would mean no weekly trips to the cancer center. You could have an essentially all-oral regimen. And, Onyx has one, that's a little bit earlier in development as well. And then, you know, when you look at the new classes, there are a ton of new classes. You know what, I think we are excited about, what I think a lot of patient's doctors are excited about are some are of these antibodies. And, elotuzumab which, you know, is in phase 3 trials, it could be available in a couple of years, is the first one coming and then when you look earlier, the daratumumab and anti-CD38 antibody and then Sanofi also has an anti-CD38 antibody called (laughter) SAR650984, just remember SAR. Hopefully, these will get better names soon, but you know what's exciting about both of these is they have shown to work on their own, which is very unusual in this disease. And, ultimately, that will be combined with other treatments and it remains to be seen, you know, what combination will work best, but the fact that they can work alone in patients who have failed, you know, Velcade and Revlimid and perhaps even Kyprolis _____hugely exciting for us and, you know, where we have actively partnered with Sanofi and then, you know, doing all that we can on daratumumab as well which is more in the, you know, _____enrollment part of trial conduct, but you know potentially looking at bringing that into the consortium in the future as well. We open every year between about six and eight trials. We will have, you know, some involving antibodies and then grade new classes as well and some of the ones that we are excited about, you may have read about agglutinin which is a BTK inhibitor and that's oral, so any time we can bring an oral agent, certainly effectiveness is most important, but any time with an oral agent, you know, we get particularly excited about that. We are also looking at doing some trials in very specific patient population, so you know, for example, patients who have deletion of chromosome 17p. Those patients, you know, are at higher risk for disease progression, so we are looking at some very specific combinations both in newly diagnosed patients as well as those who are relapsing/refractory. In parallel to all of these efforts, we are continuing to characterize the disease at genomic level and that goes back to my earlier point that the disease is highly heterogeneous and we are finding out even just two weeks ago a publication from Genomics Initiative that we started back in 2005, where, you know, at the time we were pioneering in this effort. There were discussions that the NIH too starts a profile at a very deep level. Other cancers or myeloma were not even discussed. So, we thought you know what, we were just going to take this on, emulate what's being done in these other cancers but, you know, not rely and build our own collaboration to move this forward and so technology changed dramatically. The profile they were looking at back then, you know, is I get very, very different terms, the whole genome sequencing that's possible today and just two weeks ago in Cancer Cell, we published on 203 samples and it was just building on the original 38 that were published back in 2011. Then, a lot of the same findings were confirmed, but the one thing that was different when I was re-looking at the publication today in preparation for the call _____its the heterogeneity within the individual, so an individual patient had on average four or five different types of myeloma cells. So, you know, its clear that for _____of single drug is not going to do it, two drugs might not do it. So, how do you figure out, you know, what the right combinations are and I did see some postings about people saying, well this heterogeneity appears later in the disease. What this confirms is that's not true. Of the 203 samples, 100 were patients who had never received any treatment. So, you are looking at, you know, the disease being very complicated even at diagnosis. It changes over time, but what tends to happen is certain of the myeloma clones, if you will, are controlled and then, you know, by certain therapies and then others crop up and its not just the combination of treatment that anyone had but what does the sequence look like and I hope (laughter)…

**Pat Killingsworth :** Anne, let me jump in here so (Ahh..) you can take a breath. Anne, there are multiple other tangents we could go up on here, I think. Two things jump out of me, the first is that, you know, we talk about messaging in politics_____and its very clear, it should be clear to anyone listening that the MMRF is involved in a wide array of very technical and diverse types of programs, all designed to help promote research and ultimately help us as patients and you know the message, I think, is lost, we have talked about this. The message gets lost because its complicated stuff and it doesn't create a sound byte. You know you hear about this in politics all the time, so I am not asking so much for your comment on that. That's just an observation that I think should be clear after listening to you talk about all of these complex, different types of things. And, the second thing is this has got to be expensive, (laughter) I mean you have physicians and researchers on staff, did you know?

**Anne :** We do. Well, yeah. So, we have two PACs right now and we are in the process of trying to hire _____and that's the board, you know, our Board of Directors _____and they feel rightly so, that you know we need, you know, an oncologist on staff as well.

**Pat Killingsworth :** Sure, so what… Could you just tell me and then let's get to the panel. Could you just tell me how much money was raised and/or donated to the MMRF in 2013? What was your budget?

**Anne :** So, we are not completely through with the audit process because we just closed the end of December but in the…

**Pat Killingsworth :** Oh, and your fiscal year may be different than the calendar year. What's your fiscal year?

**Anne :** No, its the same. They are consistent. We are just in the process of, I think the books are officially closed, but let's say in the high 20s, so you know close to 30 million dollars.

**Pat Killingsworth :** Okay. So, close to 30 million dollars. That's a lot of money.

**Anne :** It is.

**Pat Killingsworth :** And its not enough.

**Anne :** Its not. Yeah, and its not easy. The one thing if I can ……two more minutes before we go to the panel, and this is why I said we are dirty. I can talk about what we do in myeloma and myeloma research for hours (laughter) and hours, but you know what we saw in Genomics Initiative, what we did was we took samples from our MMRC site. So, if there are folks on the phone who are seen at one of our 16 centers and, you know, have been seeing, you know, were seeing four 6 years ago, you may have had samples that weren't involved in that. But, it was a snapshot in time. So, we learned that to really understand this disease at each level, we needed to follow patients over time. So, the CoMMpass studies that some of you may have heard about will follow a thousand patients from diagnosis part to any treatment and then do the sequencing work prior to treatment at best response and then at each relapse, so that we can see with many, many more patients, you know not only understand with an individual patient but start to kind of group patients into these different, what we call, subtypes and come up with hypotheses for what treatments could be best for them and what's really neat about CoMMpass is that all of the data goes into the public domain, so you know typically what happens in research, and this is not unique to myeloma or cancer, this is across the board. You know researchers hold on to data, companies hold on to data and once its published, you know its out there, but it can take years and you know with our commitment to speed, we saw that as a barrier to making progress in the disease. I mean I have to recognize so many of the partners that we have, you know, 75 sites worldwide now. We have four different pharmaceutical companies backing us. There can be no IP coming from this and all of the data goes into the public domain. And its exciting because that means we can, you know, get researchers for myeloma, from outside myeloma, maybe from completely different field, looking at this data and, you know, what we are doing this year because in 2013, we had 200 patients sequenced, so we are screening the critical mapped data and coming up with hypotheses that will be moved into our clinical trials. So, you know, that's going to be a big focus. Last year was very much okay, let's get CoMMpass really rolling and we are completing enrollment this year. We can talk about the community gateway during the panel, but the researcher gateway which has all the CoMMpass data and then the gateway for patients, let's get those up and running and come back in this year, 2014, focus on analyzing that data and starting clinical trials so its all out there.

**Pat Killingsworth :** Okay. Yeah. (Laughter) Thank you. That's fascinating! Gary, are you with us?

**Gary Petersen :** Sure, I am, Pat. How are you doing?

**Pat Killingsworth :** Take it away.

**Gary Petersen :** Okay, will do. You know one of the things and I was really stumped when I came up here during your discussion and that was the funding for multiple myeloma and yeah, you think 30 million dollars, that seems like a lot of money; however, the National Cancer Institute has a budget of 5 billion dollars of which I think the top 10 on their list doesn't even include myeloma and the funding for the 10th one is 18 million and so we must be down there some place in the single digits in millions. So, without the funding from the MMRF, my assessment is there would be much less done in our disease and for that I'll say that its great that you guys are showing me the money.

**Anne :** Yeah and you know _____the pharmaceutical companies are investing a lot, a lot, and its much more than NCI in this disease, so certainly you know developing a drug is not cheap. Their overall estimate is one billion dollars. I think, you know, a small disease like myeloma, you know, its not like cardiovascular disease where you have thousands of patients but suffice to say its still in the hundred of millions of dollars. So, if you think about that and then think about, you know, our 30 million, its kind of a drop in the bucket, but its expensive to develop drugs and what we are hearing now is that if we start to break the disease down, so myeloma is not one disease, its, you know, 8 or 10 different diseases. Some of the companies are saying, wait a minute. There wasn't a very big market before and you know there are all these really great drugs. I am not going to pay for a trial. We are not going to pay for a trial in this small population by ourselves, so more and more _____global, you know, multi-billion dollar companies saying, "You know what, you are going to have to help us pay for the trials," so you know, we really do need if we are going to get this done and get these more, you know, tailored therapies moving forward, we absolutely need to be able to, you know, raise the money to pay for those trials.

**Gary Petersen :** Another, you know, one of the things obviously is money and focus that you guys seem to provide, you know, and excellent focus on those that have the greatest possibility, but one of the things that I read is that only 3% of the population participate in clinical trials, of the myeloma population, and as a result, you know, we are really limited by that resource as well, not just the money, but also in finding people to be part of the clinical trial, so have you found that to be an issue and if so, what kinds of things are you doing to expand participation in clinical trials?

**Anne :** So, that's a fantastic question and you know a lot of the phase 3 trials, you know, for myeloma are largely ruled out _____because the companies can't enroll enough relapse patients quickly enough. We have done, you know, some educational programs. We have, you know, related to Cure Talk, a searchable database of trials where, you know, you can click and literally connect right to the center if you think you might be eligible. You know, through our consortium some of the sites refer, you know, 50% of their patients to trials, but I think what it comes down to and this is a problem that was a challenge 10 years ago, is that, you know, if your doctor doesn't suggest that to you or kind of back your decision, it is difficult for patients to push that and you know, what we are trying to do is help patients understand, be more proactive in telling patients about trials specifically for them. So, through our community gateway, which is you know, kind of a companion to the gateway that has the CoMMpass data, we are asking patients to share information about themselves so that we can connect them with other patients who may, you know, it could be as simple as someone who is your age, someone who, you know, lives in your area, or it could be someone who, you know, shares the same molecular profile and so not only we can match them, you could be matched to groups, and we have expert-led interest groups and then next phase which is coming, you know, probably by the end of the first quarter, telling patients about trials that are right for them and then, you know, potentially following up with a nurse from our call center to say, "Hey, you know, it looks like you could qualify for these trials. Do you want me to place a call to the center?" Even I am, you know, learning more and more about barriers that exist and I think some patients also may be under the impression that, you know, their center, especially if they are seen in the main center, has all the trials and the truth is a lot of centers, you know, the management at some of these cancer centers is pretty strict so you don't take on more trials than you can enroll, so they won't take on competing trials. Companies will say to them, "You know what, you already have a trial. Looking at a competitor, you know, we are not even going to approach you for this trial." So, its important for patients to know to look beyond their center because their center doesn't have everything and we are trying to make it as easy as possible through the gateway to let patients know, reach out to patients and say, "Hey, you know, maybe you should consider this specific clinical trial based on your profile."

**Gary Petersen :** I wonder sometimes, you know, because having talked to a number of people that, you know, perhaps, I don't know, 80%, I don't know what the number is, go to local oncologist or local clinics and somebody there treats them and they don't know further than that and they, you know, I am not sure that this is the case, but you know if we count all the skilled myeloma professionals and look at how many people they treat, you are going to come up with maybe 10%, 15%, 20% of the total population, so the other 80% are probably not even hearing that there is such a thing as a clinical trial only because that local oncologist has no, you know, iron in that fire. You know, there is nothing there for him, you know he loses a patient if he suggests that they go to one of these better facilities that have access to clinical trials, so I wonder how much of that is an issue.

**Anne :** Yeah, I think it may be, its hopefully becoming less an issue. You know the good thing is that with, you know, drugs like Velcade, Revlimid, Pomalyst, Kyprolis, you know, local, you know, community _____can really successfully manage patients. You know 10 years ago, we were really, 15 years ago, encouraged patients to get to major centers, but now, you know, there are really good drugs in the first couple of, you know, stages of disease and more and more _____say, "Hey, my doctor wants to participate in the daratumumab phase 3. Could you, you know, pass this information along to the company?" So, you know, we are happy to do that as well, to help facilitate some of these larger practices potentially participating in trials. So, that's changing as well and bringing the trials to the community, which, you know, everyone wins because you know, as you pointed out, few patients participate in trials and if we can, you know, disperse trials throughout as many practices as possible, certainly the phase 1 technically usually has to be done in a major center, but those are, you know, 20 or 40 patients. The larger phase 3s can be done in a lot of these practices. So, I think its becoming less of an issue and I think even where it becomes an issue, a lot of the major centers are very collaborative and are very used to dealing with, you know, a patient's local doctor and they are not trying to poach, you know they really aren't trying to poach anyone. They will work closely with the doctor and then the patient, you know, goes back to the doctor, the first doctor, and I think its about having an open dialog with your doctor, I mean its a difficult thing to do, but many, many doctors are receptive to it.

**Pat Killingsworth :** Thanks, Gary.

**Gary Petersen :** You are welcome.

**Pat Killingsworth :** Could we move on to Cindy here and give her a shot? Cindy, I have seen your list of questions and you have some phenomenal (laughter) questions, you have got a dozen of them here, could you maybe pick your top, the best of Cindy's three questions and ask Anne?

**Cynthia Chmielewski :** I think I will do that. Thanks so much, Anne, for what you have told us so far. Actually lot of the questions I had were answered by your introduction. I guess one question I have is we keep on talking about different things, in the beginning genome and things like that. Can you just tell us a little bit about how that's done and what they find out once they have the sequence? What is sequencing, gene and genome all about?

**Anne :** Okay. Could you cut out a little bit _____? I think I heard the question and talking about mapping the human genome and why its important? Is that what?

**Cynthia Chmielewski :** Right and how do you do it?

**Anne :** Okay. So, you know, one thing to make sure that everyone understands is that, you know, the DNA of your normal cell is different from DNA of your myeloma cell. So, you know, you take Kathy Giusti as an example. She has an identical twin. You know, they are identical except for myeloma cells. Karen has nothing like her myeloma cells. Those have a completely different, you know, cell DNA. So, the human genome because there really has been limited work and limited evidence as to what's wrong, you know, familial, you know being inherited, you know the human genome I think it may become more in value, but its really the myeloma genome. So, looking at your myeloma cells and understanding where there are

differences between your normal cells. So, what the researchers did in the Genomics Initiative and we are doing in CoMMpass is patients have myeloma cells taken out of their marrow as well as, you know, regular blood so that they can compare what are the differences, you know, what does this person's normal DNA look like versus, you know, what does their normal genome look like versus their myeloma genome and that's where you can start to understand, you know, the different genetic mutations that appear and you know, when you look at, you know, for the first 38 that we did during the Genomics Initiative and I think is… Cindy, I got a list of your questions, while I may be answering _____answer one of your questions in this one. One thing that we felt a very specific mutation in a gene called BRAF and it had never been seen in myeloma before. Its common in melanoma and there is a drug called vemurafenib given to melanoma patients, about 50% of them who have this very specific mutation and you know it was seen in about 4% of the sample, and interestingly that has been consistently seen in the larger set, the 203 and then in CoMMpass as well. So, you know, because of the heterogeneity, certainly mutations that are more common like p53 which is, you know, deletion of 17p that's seen in, you know 15 or so percent of patients, but when you are looking at ones that are 4% or 5%, you need a lot of different samples and even going back to genomics, I think there were seven that had these other mutation that appeared in the second set, what was seen in the first 38. So, its important to have, you know what we are trying to do is now build these collaborations because other, especially in Europe, there are other centers doing this kind of work. So, we have our thousand, imagine pulling that together with many other centers, you know, hundreds of samples and really making sense of this disease. Does that answer your question?

**Cynthia Chmielewski :** It does. So that's where this and I am trying to make sense of this whole initiative too. So, that's where this big data something, like all this information is being entered into some type of computer program? Is that what is happening?

**Anne :** Yeah and quite honestly the big data is exactly that. Its a huge amount of any kind of data, in the sense its genomic data. I mean its like truly ends of line of you know sequencing down to, you know, at the deepest level that you could look at these genes and this is all of the genes. There is difference, whole genome versus whole exome. Whole exome sequencing is those that are expressed and that may be all that's needed. Looking at everything, you know, may not provide value, but we want to make sure that we are looking at the full landscape before we narrow down and even, you know, when I said the data goes into the public domain, its not the raw data, its analyzed at a certain level because, you know, we couldn't put all the raw data on to the gateway that we developed, which is really kind of more for translational researchers or clinicians because its almost like Amazon where you _____you know women who are over 65 who were treated first time with Velcade and have a translocational 4:14 and then you will, you know, sit back to what those patients look like, but the raw file, I can tell you because we are sending them to some of the sponsors, its literally hundreds of thousands of dollars to pull that data and just create the file, to be able to transfer that data to them and in Genomics Initiative where we had some information going through a public portal cloud, the sequence data we have to put out through a different program to the government because of the shear size of it.

**Cynthia Chmielewski :** Oh, yes. When you were saying public domain, its for everyone to look at, doctors, for people, the members of the MMRC?

**Anne :** Absolutely, so on the Genomics Initiative, that was those 200 that we are just talking about, that is a public portal _____and you need to register just so they can see who is on there and, you know, we have like 1400 or 1500 people who have registered to look at that data and the same with CoMMpass. You do need to register and you are supposed to be a non-profit and be an academic research institution, but yeah, anyone can access it. Really for both, there is a short time where the partners get access to it and then after that, you know, if it _____during that time. Its just, you know, to, you know, put your publication for example, but if your publication is not done in time, the data is out there in the public domain, you have lost your opportunity.

**Cynthia Chmielewski :** Yeah. The community gateway for the myeloma population, myeloma patients can communicate with each other through that community gateway and will be able to search other patients like

you. Well, I am thinking from what you said that maybe researchers, nurses, physicians will start searching that data and then reaching out to some patients who they might think are good for clinical trials. Is that what I am hearing you say?

**Anne :** Yeah, that can happen or even, you know, its self reported data, so its a little bit different, although part of our vision is to be for those, you know, patients who have access to their electronic medical records and then, you know, for example I have seen at a center where, you know, you log on to a portal and you have everything. You know our vision is in the not too distant future be able to, you know, dump that into the community gateway as well and so, you know, researchers or nurses could also come up with hypotheses because, you know, there could be, you know, side effects that, you know, for whatever reasons have been under reported or, you know, not seen in the same way that they are when patients are self reporting them in this kind of situation, so there may be that kind of analysis done and who knows there could even be hypotheses or trials coming out of the community gateway as well.

**Cynthia Chmielewski :** All right. Will there be some updates on the community gateway because I know I have been trying to enter some data and I am just kind of fighting with the system sometimes because I guess when I was trying to enter some of my numbers, since I don't get my IgA or IgM tested, they would not let me enter something then or will there be like updates _____?

**Anne :** Yes and you have been, I mean I just _____ few people who have been tremendously helpful and you have been one of them and I know that Jenni has really appreciated your feedback. (Laughter) You know our goal is to have, you know, optimized by the end of the first quarter. You know right now, patients don't even have the ability to enter all _____ data, so the goal is for that to be fixed in the, you know, March-April time frame, but certainly I encourage anyone and everyone who is listening, if you have feedback, whether its what you think is a tiny glitch or something that you think is glaringly, you know, missing or not right on the gateway, please, please, please reach out to us because we just launched, you know, four months ago. This is, you know, certainly a work in progress and while we are trying to have a site that is kind of, the 1.0 complete by the end of March. You know we are evolving to, you know, again, you know, have a lot of patients to bring in, you know, clinical data and test results and all that and be able to, you know, conduct surveys and perhaps analyses of some of the self reported data and we want, you know, everyone to be engaged as well with findings. If you have, you know, something unusual about your myeloma and have never really found someone who had that experience, we want to enable that here so that, you know, you have a sounding board, you have someone to connect to and share information.

**Pat Killingsworth :** Ladies, I know that Matt has a couple of questions about the community gateway and I want to get him in here while he still has questions to ask (laughter) because so many things get covered from the time of the last question. Matt, are you there?

**Matt Goldman :** Yeah, I am here. Thanks, Pat.

**Pat Killingsworth :** Sure, sure. Hey, you have got the floor as long as you want, buddy.

**Matt Goldman :** Okay. (Laughter) Thanks. Anne, thanks for doing this and Pat, thanks for setting it up. I think this can probably be about a four-hour talk and we still have things to ask. I was just thinking that I was listening and I am going to go past my list of questions..

**Pat Killingsworth :** Sure.

**Matt Goldman :** To ask something else about what the MMRF does. You know you mentioned Kathy and her twin sister and I am wondering _____do you guys look at some of the factors that can lead to that sort of switch in a person's body that myeloma kicks in. You look at environmental factors and instead of the Genomics, do you see what the Genomics is serving is more as helping the treatment or its something more preventative or a little of both?

**Anne :** So, just to clarify your second question, I am not sure I quite follow the Genomics, can it be prevented or it helps guide treatment?

**Matt Goldman :** Is the danger that's coming out of the Genomics, you know you are taking all these different researchers and institutions, is the data being used more towards coming up with more effective treatments or can it be also used to try and figure out how to actually prevent people from getting myeloma?

**Anne :** Okay. So, I will tackle the first question. We haven't directly done work in terms of, you know, hereditary, I know there are some researchers, I think the name is escaping me, at Creighton University,……We are asking as part of CoMMpass, do you have, you know, with any cancer, even a first-degree relative with any cancer and certainly myeloma is one of those. I don't think in the last interim analysis which is a couple hundred patients, we hadn't seen anyone with first-degree relative. Interestingly, Kathy Giusti's grandfather had multiple myeloma. So, you know, its more epidemiological at this point. I don't think that there has been anything seen comparing, you know, the normal DNA of Kathy and Karen versus the myeloma, anything that seems apparent, but you know perhaps what we and others are doing, there may be hereditary factors that appear and then, you know, related along your second question, you know, the prevention piece also goes back to a hereditary factor, so that would be something that would appear in your, you know, normal genomes; however, you know, delaying, I guess, if we can identify, you know, MGUS or smoldering patients miss the entire community effort. Patients who are more likely to convert to active myeloma, now that some of these antibodies are emerging and the antibodies have, you know, especially these anti-CD38 antibodies are effective and don't have the same level of toxicity that some of the older treatments do, it may make sense to treat patients earlier and prevent that progression, especially those patients who can be identified at high risk. I think all of this is the early days and who knows maybe once we have a critical map of not just our own but, you know, worldwide data chart, there might be genes identified that lead to hereditary myeloma.

**Matt Goldman :** Uhhh hmm… And then with the community gateway, to be honest, I got myself into the system initially when I first heard about it and then it was sort of out of sight, out of mind and I never really thought about it again until actually it was called and set up. Is there a way that you guys are looking at sort of promoting it a little bit more, I mean because it seems like it serves a great purpose.

**Anne :** Yeah. You know, its, and I know Cindy has had, you know, based on conversations with Jenni who is, you know, our Project Manager and the project has had some great ideas. You know we have been hesitant it would be too much marketing until the site is optimized because there are, one, there are still some bugs and, two, its just not where we want it. You know, we don't have everything up and running. You know, we wanted to launch it last year and you know get some folks on there and having experience of such. We have been a little bit quiet about it until we have everything where we want it to be for the end of phase 1 and then, you know, at that point, I know that Jenni will be looking for kind of a team of advisers, you know, a small team of advisers in terms of not, you know, what is publicized but just the marketing aspect of it and trying to understand how much outreach is appropriate, you know its getting a daily _____before we launched _____ and I signed up for this diabetes site and literally I get in, you know, every singe day. Is that overkill due to the weekly visits, you know are there certain triggers to allow people to sign up for how frequently they want to be notified about updates, so all of that needs to be developed and certainly if you have, you know, ideas or would like to become more of a, you know, again kind of an adviser to us, we would be happy to have you.

**Matt Goldman :** Okay. Thanks. Ummm… One more question if that's okay. Going back to, you have started taking data from different investigators and research centers across the country and kind of putting it all together, could you sort of give a little overview on how you do that? How do you take different data or different centers that might have different approaches or even different periods? How do you put it all together and come up with something very sort of have a little more cohesiveness?

**Anne :** So, well, CoMMpass is a protocol. Its not an interventional study. So, you know, patients involved in CoMMPass, all they need, they have to require treatment and then they can be with a proteasome inhibitor

and/or IMid, so its not, you know, like a clinical trial where you are trying _____investigational treatments, but there is, you know, a protocol that the doctors have to follow, so you know, they have the same informed consent and they fill out the same case report form for patients and, you know, submit the data that way. You know when it comes to having others, you know, add their data to the research gateway, I can tell you for the first portal that we developed for the Genomics Initiative, there are data on there from Arkansas, from Millennium, from Mayo, from Dana-Farber. You know, they waited until they published, you know, fair enough that's how your new event _____emails, but at least they were still willing to put the data in there and we have had discussions not just with, you know, US-based companies or researchers, but excitingly, as I mentioned earlier, a lot of its work is going on in Europe as well and they are very kind of excited to, you know, join this effort and add their data so that, you know, I think the details will be about, you know, matching fields and what not, but its been done to a smaller set before, so I think we are hopeful that we can do it to the research gateway as well.

**Matt Goldman :** Okay. Thanks very much.

**Anne :** Oh, thank you.

**Pat Killingsworth :** Thanks, Matt, and that's great. Let's rotate back, Mr. Gary Petersen, follow up.

**Gary Petersen :** Oh, my God! Lizzy, Lizzy, isn't she on?

**Pat Killingsworth :** I am sorry. I didn't mean to… Sure. Apparently, Lizzy was detained, something came up, so in her questions, I have several other questions that have been covered, so we are good to go up there. I didn't mean to throw you off there. Anything else you would like to suggest?

**Gary Petersen :** Yeah, yeah, sure, definitely and thank you so much for all your time, all your efforts, and all your energy, and all of the folks at the MMRF. One of the things that I saw at ASH and I was a little disappointed and maybe its because I just didn't see it, but I didn't see that there were any clinical trials you had or any focus on putting together, you know, the new good therapy which is Revlimid, Velcade, dex, you know, which is kind of the current standard of care for high risk and for a lot of people and including either daratumumab or ARRY-520. The reason I ask that is because I noticed that there was an in vitro analysis not too long ago that showed that that combination of Revlimid, Velcade, dex, and daratumumab was significantly head and shoulders above just RVD in effectiveness and I was thinking, you know given that, you know, wouldn't that be something that there would be more focus on, either a RVDD or a RVDA for ARRY-520, so are there plans for trials in the near future for this combination? Just one more thing, just like you said before, it looks as though, you know, you give it one drug and it knocks a chunk and then there is another chunk that's resistant to that and you give it another drug and it knocks that chunk and it sounds like, you know, these four knock out a lot of chunks and maybe that would be the one that might be our home run.

**Anne :** A couple of things, you know, the ARRY-520 now has a name which is actually probably even more difficult to pronounce, filanesib, and daratumumab are both, you know, still in phase 2, so its still early days. I know on the daratumumab that the phase 3s are planted and likely to launch in the early part of this year or this year, but hopefully the first half, and I am not sure if ARRY-520 is quite there yet. You know I think it is more than a couple of challenges. You know, if its possible to give less, you know, fewer drugs than more and get the same kind of impact, then you spare the toxicity and then the cost. You know, I think that's one thing where, you know, we really haven't, you know, spoken with companies directly, but when you are looking at RVDA and RVDD, that's three-name brand of drugs, so I think, you know, first and foremost from a, you know, efficacy-toxicity, if you can get away with just having a dara with one of those and having something, you know, has quite a high response rate and, you know, the phase 3s are looking at, you know, the differences between an embedded proteasome inhibitor versus having all four, you know, I think start there and then, you know, before you jump to a phase 3, you would do, you know, a phase 1. I am sure many investigators have this idea, you know, to start with a phase 1, perhaps as you said, in a high risk, you know, like a deletion 17p population. If you can get, you know, high durable responses because the issue

there is not so much of response rate as the durability, then perhaps if you move into greater trials, but you know I think if we can get away with, you know, less is often more and then maybe, you know, figure out the right sequence because the other challenge could be if you use too much, you know, do you lose those options down the road when you may have another clone emerging that could be sensitive to one of those treatments. So, there's a lot to be figured out, but I am guessing you will at least see some kind of higher study with that combination down the road.

**Pat Killingsworth :** That would be good, the combination, Gary.

**Gary Petersen :** Oh, yeah, thanks, Pat. They did put together the combination of Revlimid, dexamethasone, and daratumumab and the initial results were stellar. In the in vitro study, you know, the four-drug combination was even better than that, at least that was my understanding.

**Pat Killingsworth :** Yeah. I mean with that, you know, you don't do what the toxicities look like, but I mean actually I think, you know, we will have to figure out ____ you know, maybe is worth, you know, a four-drug combination as we give, you know, patients four drugs…

**Gary Petersen :** (Laughter) You are talking to somebody who went to the UAMS with two other folks and so when you talk about four drugs, you know, we are the ones that had like six-drug combinations.

**Pat Killingsworth :** Sure. No, no, no…

**Pat Killingsworth :** You just laughed at four drugs (laughter).

**Gary Petersen :** Yeah, I laughed. You show me your four drugs and I will race you to six. (Laughter)

**Pat Killingsworth :** Anne and Gary, before through I cut this off because we have got to be about at the end of our time. I wanted to suggest to see what everybody thought. Anne, if you would be willing to come back sometime in the near future, I think I would like to try to focus some of this and maybe have one, two, or even three shows on specific types of things that the MMRF is doing. There's just so much to process and maybe if we focus a little bit, for example, maybe one of the gateways when you are ready to announce the gateway and maybe you come back and help patients work with that a little bit.

**Anne :** No, actually, and you know, (laughter) we are a small team, but you know others of my colleagues can come on as well, you know, if say there is a topic on immune therapy, you know one of my, either John or Daniel, I mean they are tremendously passionate about that area and same with, you know, precision and medicine in precision trials, you know, I think, you know, our vision is, you know, to be able to, you know, have these trials. We have different RMs, different patient profiles and, you know, I think having, you know, one of them on those topics could be phenomenal as well. They are scientists, but they love to talk. They love, love, love talking with patients and I think can talk at an appropriate level.

**Pat Killingsworth :** Oh, I have met them. They are wonderful, very, very enthusiastic and committed to what they do. So, we will coordinate things and try to come up with some topics. That's a great idea and the community gateway, I am glad you said that you are not really pushing it yet because at one point I got a couple notices saying, hey, you have got 14 people that want to, its not for your friend (laughter), what do you call it, (connection) connect and I don't think _____[01:02:30] anything for three weeks, so either I am suddenly friendless or I just figured you guys are working on stuff.

**Anne :** Yeah. No, its still there. I actually, you know, (laughter) _____, so you know if you need help, you know, if you forgot your user name, password or anything, but you should go _____ pending.

**Pat Killingsworth :** Done. Okay. Priya, are we set?

**Priya Menon :** Ah, yes. Thank you so much, Pat. Anne, it was great having you here and yes, I will get in

touch with you and it would be a wonderful opportunity to have you and your colleagues back on our show again and we can actually plan out couple of shows and topics and I will be in touch with you regarding that. Anne, thank you so much for being with us today. Pat, Gary, Cindy, and Matt, I think your contribution is irreplaceable. Thank you so very much. And, to the audience, we have quite a few people dialed in today. Please make sure you mark your calendar for the 26th of Feb. We are having Dr. Vincent Rajkumar of Mayo Clinic with us. Its at 5 p.m. and earlier than our usual show and we are going to discuss myeloma cure versus control. You can always access MMRF trial search tools on myeloma trials at myeloma.trialx.com/ask. For more details of upcoming shows, please visit curepanel.carefeed.nic and you can always mail me priya@trialx.com regarding anything with Cure Panel Talk Show. The link to this show will be shared via email to all participants. Thank you very much. It was a wonderful show today.

**Pat Killingsworth :** Thanks, everybody. I don't know how you keep it all very amazing.

**Anne :** Oh, no. Thank you. Honestly, its been such a pleasure. Like I said before, I could go on for two more hours (laughter), so thank you. I really appreciate the opportunity.

**Pat Killingsworth :** So, I am going to go and take you up on that. Thank you.

**Priya Menon :** Thanks, everybody. Okay. Thanks. Good night.

Thank you. Bye, bye.