
# Sarepta Therapeutics

*Sarepta Therapeutics presentation delivered at the 33rd Annual J.P. Morgan Healthcare Conference on 01/15/2015.*

SPEAKER 1: Good afternoon, everyone. My name is Brittany and I'm on the JP Morgan Biotech Equity Research Team. I'm pleased to introduce our next company, Sarepta Therapeutics. And with us today is CEO Chris Garabedian. And just as a reminder, the breakout room is in the Victorian Room, which is around the hallway in a U shape.

SPEAKER 2: Thank you, Brittany. It's great to be here. Thanks to J.P. Morgan for the invitation. I'm going to stand over here to highlight some of the slides. Again, Sarepta Therapeutics, our lead program, we have RNA technology that we're advancing in a variety of areas, but most notably in our lead program for Duchenne Muscular Dystrophy. So, I'm going to talk a little bit today about a recent update of 168 week data that we shared. I'll be making some forward looking statements. So please refer to our SEC documents for filings associated with the risk factors of the company. Sarepta Therapeutics is based in Cambridge, Massachusetts. We also have facilities in Corvallis, Oregon. We're a late stage company focused on the RNA technology applications across rare and infectious diseases. We do have active research labs in both Cambridge, Massachusetts and Corvallis, Oregon that's churning out research on our chemistries and new applications. And we have five DMD clinical trials underway currently. We have more than ten new research programs underway. And we have two chemistries, our PMO for Duchenne. But PMO Plus for antiviral applications influenza, Marburg, and Ebola have been in the clinic and tested in humans. And we're well capitalized, with over 200 million at the end of this year in cash. But I'm going to talk primarily today about our lead program for Duchenne Muscular Dystrophy. It's a devastating muscular dystrophy that affects mostly boys, about 1 in 3500. Our lead program targets Exon 51. It's a highly fragmented population. And the Exon 51 population represents about 13% of the Duchenne boys around the globe or about 1,800 in the U.S. if you use the CDC incidence figures of 1 out of 3,500. What our technology is doing, is it's taking a mutation in the dystrophin gene, this is the essential protein in muscle, and the Duchenne patients have an out of frame deletion that renders them unable to produce this essential protein. There's also a genotype and phenotype that exists called Becker Muscular Dystrophy and they are able to produce a dystrophin protein. It's truncated, but it's functional. And what it is, it leads to a very different progression of disease and natural history. So you see Becker here highlighted and you can see how there's an advance. If you see these bars here that's the Duchenne

phenotype. So they, for Duchenne, they typically lose ambulation in the 10 to 12 year period. Sometimes a little bit later. Where Becker Muscular Dystrophy you see often times they can continue walking beyond 15 years of age sometimes into their adult lives. What we hope to do is start to get closer to the Becker phenotype. Now it's important to note that Becker patients continue to progress, we see declines in Becker patients. And compared to our study, these Becker patients had a nine and a half year head start of producing truncated dystrophin. That's important to know when we go over our clinical data. We've made advances in our clinical program and the progress toward the regulatory filing. We are still planning to submit an NDA by midyear. We're going to go over the 168 week data that we just released on Monday. But we're also moving forward with our clinical studies and we're making good progress for all of the requests that the FDA had that would go in our NDA based on the guidance we received in October. So we're moving forward with the safety data and newly exposed patients. They required us to have at least three months and at least 12 to 24 patients. I can tell you today, we are already dosing that range of patients as I speak here today. So we have no problem meeting that safety update for the NDA by mid-year. Results from the fourth biopsy, are expected for a sub set of patients. We'll be pleased if we get half of the boys to agree to a fourth biopsy. I'm happy to say that the scheduling of those biopsies are already under way with specific dates that are being scheduled on the calendar. We know families have been contacted about the fourth biopsy. So we expect those to happen and, again, still have that data in time for a mid-year NDA. The dystrophin rescore was also something that the FDA requested to have us get three independent pathologists review the original primary end point of dystrophin-positive fibers. That's underway and we should have that in time for that mid-year NDA. They also requested us to get as much natural history data. We've reached out to all the sites to be collecting that data and compiling that. And then the MRI was another one they urged us to do. It wasn't a requirement. But we've already contacted that site and have data, some of the data in-hand, and we're starting to compile that. We also had a recent update with the EMA. This was a scientific advice meeting, non-binding. The initial feedback was they would like to see additional data to consider a conditional approval. But they did say continue the dialogue so that as more data emerges, we will go back to them and continue this conversation of what would be enough to consider conditional approval. We also shared with them our eteplirsen programs. Specifically, the confirmatory study and explained to them the untreated cohort. The end points that we're going to be gathering and the long-term follow-up we expect to have with eteplirsen. And the general feedback was positive for that study. So we feel that that study could satisfy any additional requests for the EMA. But we also hope to meet with them later this year to get more guidance of what type of data would they need to see additionally to consider a conditional approval. So again, right now we have three eteplirsen studies dosing. Our ongoing extension study, Study 202, which we have 168 week data I'll share with you. We are already dosing our ambulatory

confirmatory study on our Study 301. And we are already dosing our Study 204, this is the non-ambulant study or advanced disease population that enrolls patients up to 21 years of age. And we will begin dosing this quarter in a younger population, ages four to six year olds, who are amenable eteplirsen. I'm also happy to report we put a press release out this week that we've dosed our first patient with the next exon-skipping drug for Duchenne targeting Exon 53. So we are pursuing this program. We believe in the technology, we believe in the utility across our DMD platform, and we're moving forward with that. And also, I provided update last year that we have received feedback from the FDA on our master protocol for a placebo-controlled study targeting Exon 45 and 53 and we are in the process of getting that study up and running so that we can have first patient enrolled by mid-year. This is our overall DMD pipeline. Just wanted to highlight we've made a lot of progress. We've already started dosing and enrolling our confirmatory study. But we have 39 infusion sites which is the ultimate target. This is a hub and spoke model. We have two of the two surgical sites already initiated and enrolling. 11 of 14 hub sites. These are the sites that do the clinical outcome measures and so we make progress every week to get more sites up and running. And 18 of the overall 39, which makes it easier for the families to go to a more local institution or clinic to get infusions. They would need to find a way to get to the hub sites every 12 weeks for the clinical evaluations and updates. You can see our other studies. We're targeting four or more sites for our advanced non-ambulatory study. Four sites for our younger patient study in Europe. And seven sites for our younger pa, I'm sorry, our younger patient study in the U.S. seven sites, four sites are enrolling our European study with Exon 53. Just this highlights the unique properties of eteplirsen based on our morphalino backbone that you see here on the right. Importantly, we have now approximately 50 patient years of safety and dosing at the 30 mg/kg weekly dose that we're administering in a clinic with our confirmatory study and our target for Exon 53 and 45. So again, we think we have a unique differentiated chemistry and I'll talk a little bit more about that later. So I want to go over the 168 week data. This is the schema of our Phase IIB design. It started as a placebo-controlled Study 201 for 24 weeks. We rolled all the patients over to open label eteplirsen, at week 25 continued to follow them.

This is the baseline characteristics. We enrolled a older population than you typically see in controlled trials looking at DMD ambulatory boys. And our, again, our average six minute walk here was about 370 across the 12 boys based on the mean of two measures taken at baseline. Earlier this week there was a presentation that made some cross-study comparisons to our competitor data of a small study that they did open label to our study that I just described. So I wanted to highlight and clarify some of the points that were raised. And you know I was approached after that presentation by researchers who felt it was inappropriate and that this is not done to make sure that we hold you know an appropriate forum to have scientific dialogue and exchange. I was approached by people in the community who were confused about the

conclusions that were being drawn across these studies. And while I understand that it's a competitive space we realize that live in an ecosystem where the DMD community is out there looking at this, right? Researchers, it's not just the investor community. And so, we thought it was important to highlight and clarify some of the things so people don't come to the wrong conclusions about how to interpret our study results vis-a-vis our competitor. So first, a few notable facts about eteplirsen in the Study 201/202. Study 201 was a randomized, double-blind, placebo controlled trial over 24 weeks. Patients were not recruited into an open label single arm study. There we no dose adjustments, treatment interruptions that occurred during the study. A stable steroid dose was required. This was a very highly controlled study at entry and again randomized double blind placebo controlled at the start. Study 201's primary endpoint was dystrophin-positive fibers. It was described prospectively. We met our endpoint, showed a statistically significant increase the ITT population, including the twins over 24 weeks. That data was presented at AAN, the American Academy of Neurology in the spring of 2012, and at that time we were accepted as a late breaker abstract. We started to describe the clinical results that came out of that study. We explained at that point that we were going to be excluding two twins who were in a non-ambulant state. They could not do the six-minute walk test at week 24. And we described a MITT population at the 24 week timeframe that we said this is how we're going to look at our data from here on. Three years later, we're still reporting that data the exact same way that we did at 24 weeks. We showed an 18-meter difference between the eteplirsen-treated group and the placebo group, excluding these two boys at 24 weeks that continued to separate until we had dystrophin confirmed in the placebo folks, who then stabilized. Why did we exclude the two twins? We felt we had a good rationale. First of all, they were identical twins with the same genotype. They had the lowest scores on the six-minute walk test at baseline. They were rapidly progressing. They already were below 250 meters by week four, the first measure we took after they qualified at baseline to get into the study. And subsequently, we've seen MRI images, our Chief Medical Officer Ed Kaye looked at these images. And saw two that stood out as markedly different than all the other boys in our study. And they looked like they were duplicates, like there was a mistake. It turned out they weren't duplicates, they were the non-ambulatory twins we had in our study. And clearly, they had lost significantly more muscle in their quadriceps. And explained why they even restoring dystrophin to not much muscle in the legs, couldn't necessarily stop them from losing ambulation. The twins continue to be treated, safely, they did have dystrophin in their upper arm extremity muscles. They continue to demonstrate strong lung function, heart function, and use of their upper extremities three-plus years after enrollment in the study. Second point is the differences in the patient population and the difficulty of drawing cross-study comparisons. Study 201 was designed to enroll a DMD population that would likely show a decline on the six-minute walk. We had limited drug supply. We could only do this size study at the time. It was going to take us a year just to produce enough drug to continue these boys on

treatment. It was going to take several years to be able to raise the money to be able to build out more manufacturing capacity and do a larger study, which we're doing this year. So we had to be very measured and careful in our patient selection. So we excluded boys who were younger than seven, okay? Because they are known to show improvements on the six minute walk tests. We excluded boys who were too healthy, who were over 400 plus or minus 10%, or over 440 at baseline. And again, this contrast to the drisapersen study which was started as a dose escalation phase in which all boys received drisapersen and the subsequent ten boy extension phase. At baseline of the initial dose escalation phase when these boys were selected for enrollment, one boy was non-ambulant and only five of the remaining 11 boys, would have qualified for the study 201. Of those five boys that would have qualified for study 201, three became non-ambulant after drisapersen treatment. Two who became non-ambulant during the extension phase. In some of the eight boys currently reported to be ambulant, only two of those would've qualified for our study 201 entry criteria. The last point I want to make is that we are committed to transparency. In all of our clinical trial results and that's what we've done with this study from the beginning to the 168 week data. We understood the importance of doing that, so I talked about how we had, from the beginning, described the MITT population. Sarepta has provided biopsy results from study 201 and 202 across all patients. Even at the individual level. Only a small portion of the more than 400 biopsies taken across all of the drisapersen studies have been publicly disclosed. Sarepta has provided regular ongoing clinical data results. From study 201/202 beyond the six minute walk including pulmonary function tests, any loss of function in other measures forced their rise from supine which includes the non-ambulant twins. And lastly, Sarepta has regularly reported complete 201/202 safety data on all patients. No safety information or comparison was present in BioMarin's Monday presentation. And we think if we did do a side by side apples to oranges comparison, it deserves to see how does the dystrophin data stack up? How does the safety data stack up? So I wanted to clarify that, because we had a lot of people very confused and upset about the characterization of this data set. So let's talk about the 168 week data. First, I want to highlight, we did enroll an advanced population. One to two years older than most of the controlled studies that have been done in DMD, as you can see here. And a six minute walk test that was approximate or even more progressed than the other controlled studies and we followed these boys out now 3.2 years. We know from natural history these boys who are over seven decline on a linear fashion over year over year over year. So this presentation by Payne, Mercuri is the most recent natural history that's been shared, the most longitudinal data. And you see a 150 meter decline over that three year period. And interestingly, the boy started almost exactly where our boys started at 375 meters or so at baseline. This is our data over more than three years. We have shown that the placebo patients who were only delayed 24 weeks before starting eteplirsen had a profound effect on their outcome on six-minute walk. Just that 24 week delay, which we talked about, started to see the separation then. Before

dystrophin positive fibers were confirmed at week 48 as we expected, they continued to decline until week 36. They lost 68 meters and we generally stabilized them until more recent declines in the 2.5 to 3 year period. The early treatment group continued to be stable on treatment. Until again more recently we enrolled patients who we thought would be having this trajectory of decline at the start of the study much like we saw in the placebo control. So this underscores the point further. Both groups started in the high 390s. Okay? The delayed treatment group, 24 weeks on placebo, okay? And 12 weeks before dystrophin was present, they ended up declining to 327 meters. The treatment group, it has taken more than three years for them to decline to the same degree that we saw in the untreated 24 weeks off at week 36. We think this is remarkable and we've pushed out, right, that type of decline in the treated group significantly. This just shows we've sustained the treatment effect. We had a statistically significant difference in the modified intent to treat eteplirsen group versus placebo at week 32. We've maintained that now all the way through 168 weeks at each time point on the primary six-minute walk measure. And then this just shows you, we had it week 36, again the last time point before all of the boys confirmed dystrophin at 48 weeks positive fibers. We had five boys who were below 350. Now many in the DMD community have said okay boys below 350 or 330, one publication says, should not be enrolled in ambulatory trials because they progress too rapidly to a non-ambulatory state. In fact, Mercuri's paper says, by 18 months, you have a high risk of losing ambulation if you're below 330. So we have half of our boys at week 36 who started at 317 and here, more than two years later, they're still on their feet. And they've shown a trajectory of decline that has been generally stable through most of that period until recent. Again, a similar rate of decline on treatment, regardless of if you're below 350 or above 350. Oh, and I'll just highlight that the second bullet here, a publication came out by Craig McDonald saying if you were below 350 based on the ataluren placebo arm with Duchenne, you lose 107 meters in 48 weeks. We haven't lost that in these boys from week 36 through week 168. This just shows you the progressive nature of this disease and many of these DMD boys lose the ability to rise from supine and the ability to climb stairs first. So you can see here that even including the non-ambulant twins, who basically could not do any of these ambulate, climb stairs or rise from supine from week, you know 24 on they show that they were still able to, to maintain that. I'm sorry, the other boys were able to maintain this at a rate better than what natural history would suggest, even on glucocorticosteroids. So again, we think this is notable that we have half of the boys that are teenagers now. And this data would suggest only 10% of them would be able to rise from supine. Half of our boys who are teenagers are able to do this. Same thing on ability to climb stairs. A little more than 30% could do it in the teenage years and here we have more than 60%. Pulmonary function has also shown remarkable stability. We know we're getting in good to protein expression in the diaphragm. And we've shown good stability very different than what all the natural history studies would suggest on FVC percent predicted, MIP percent predicted and MEP percent predicted. And lastly the

safety profile has held up incredibly well over more than three years. In fact, we were reporting on proteinuria this just shows no clinically significant treatment related adverse events. No discontinuations or treatment interruptions. We had been reporting on proteinuria. This last 24 weeks we had no incidences of transient proteinuria. And in fact all of the proteinuria across this study have occurred at a lower rate than our placebo background rate in the first 24 weeks of the study. We see the same safety profile in the next two drugs that are entering the clinic and we continue to advance the research pipeline with morpholinos. And I'll just briefly talk about we've been busy. We've been hiring people in the research team. We've got senior level people in research at the VP level. Senior Director, Director level across biology, chemistry. We are moving forward, advancing the research programs in our company. And because we do believe we have a chemistry that can be best in class in the RNA space. This just highlights that the two drugs, which these are side by side comparisons in the same experiments show significantly better protein expressions with morpholino chemistry verses the 2-O-methylin drisapersen all things being controlled for. The sequences show a ten-fold greater activity than the drisapersen sequence. And the dose, because of the cytokine induction we see here, with drisapersen, we have a five to eightfold higher dose. I'm not suggesting that a tenfold higher, chemistry advantage times a tenfold higher sequence advantage, times a five to eightfold dose advantage translates to a 5 to 800 more efficacious drug. But I'm just highlighting that these drugs are markedly different and have different activity profiles. So we just highlighted recently that the research programs that we've identified across rare genetic disease neuromuscular anti-infectives include myostatin inhibition, progeria, adult onset Pompe disease, Lupus and graft versus host, with Toll-like receptors that we licensed last year. And also, drug resistant bacteria, largely gram negative resistant infections across as you can see here, burkholderia, Pseudomonas, klebsiella, acinetobacter and gonorrhea. And again, I'll briefly go through this because of time but you can see the slides on our website on these early promising research programs. Again, we have good share volume daily. This market cap is an error here. But we had over 200 million at the end of the year. And again, we thank you for your interest in Sarepta, and I look forward to the breakout room for Q and A. Thank you.

---