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CORPORATE PARTICIPANTS

David Connolly *Rhythm Pharmaceuticals, Inc. - Head of IR & Corporate Communications*

David P. Meeker *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Hunter C. Smith *Rhythm Pharmaceuticals, Inc. - CFO, Treasurer & Secretary*

Murray W. Stewart *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

CONFERENCE CALL PARTICIPANTS

Alan Carr *Needham & Company, LLC, Research Division - Senior Analyst*

David Neil Lebowitz *Morgan Stanley, Research Division - VP*

Derek Christian Archila *Stifel, Nicolaus & Company, Incorporated, Research Division - Director & Senior Analyst*

Graig Suvannavejh *Goldman Sachs Group, Inc., Research Division - Executive Director & Senior Equity Research Analyst*

Michael John Higgins *Ladenburg Thalmann & Co. Inc., Research Division - MD & Senior Biopharmaceuticals Equity Research Analyst*

Philip M. Nadeau *Cowen and Company, LLC, Research Division - MD & Senior Research Analyst*

Tazeen Ahmad *BofA Merrill Lynch, Research Division - VP*

PRESENTATION

Operator

Ladies and gentlemen, thank you for standing by, and welcome to Rhythm Pharmaceuticals conference call to discuss the Phase III data for setmelanotide in Bardet-Biedl and Alström syndromes. (Operator Instructions) Please be advised that today's conference is being recorded. (Operator Instructions) I would now like to hand the conference over to your speaker today, David Connolly, IR and Corporate Communications at Rhythm.

David Connolly - *Rhythm Pharmaceuticals, Inc. - Head of IR & Corporate Communications*

Thank you. Please go ahead, sir. Thank you, and thank you to everyone for joining us this morning as we discuss the positive top line results from our pivotal Phase III clinical trial evaluating setmelanotide in patients with Bardet-Biedl and Alström syndromes. Please note the press release issued earlier today and presentation we're using for this conference call are available online in the investors and media section of our website at rhythmtx.com. Before we begin, I'd like to remind everybody that there will be forward-looking statements made on this call. Actual events or results could differ materially from those expressed or implied by any forward-looking statements, such as a result of various risks uncertainties and other factors, including those set forth in the Risk Factors section of our Forms 10-K or 10-Q or any other filings that we make with the SEC in the future.

In addition, any forward-looking statements made on this call represent our views only as of today and should not be relied upon as representing our views as of any subsequent date. We specifically disclaim any obligation to update or revise any forward-looking statements.

Turning to Slide 3. On today's call are Dr. David Meeker, Chair, CEO and President of Rhythm Pharmaceuticals; and Dr. Murray Stewart, our Chief Medical Officer; and Hunter Smith, our Chief Financial Officer is with us and available during the Q&A section.

With that, I'll turn the call over to David.

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Thank you, Dave. Thank you all for joining us just a few days before the holiday break. So today, we're pleased to announce the top line data from our pivotal Phase III trial evaluating setmelanotide to treat early onset severe obesity and hyperphagia in people with Bardet-Biedl and Alström syndromes.

We know just how important this study is for the families living with these syndromic diseases. We know from patients, caregivers and healthcare professionals, how they struggle with the tremendous physical and emotional burden associated with early onset severe obesity and hyperphagia. Despite this, there are no approved therapies that specifically address the underlying genetic cause of these conditions. So before we jump into the details of the trial, however, I want thank the Rhythm team, our investigators and the clinical staff at sites around the world for their dedication and hard work in making sure this trial was executed well and on time, especially during a very challenging year. COVID-19 has exerted a far-reaching impact throughout the world, causing tremendous pain and loss for so many, and it has changed how all of us go about our lives.

We are particularly grateful to the healthcare professionals who persevered and remain steadfast in their commitment to our study despite the many demands made on their time this year. Finally and most importantly, thank you to the patients and families who participated in and continue to participate in our clinical trials. You remain our most important partner in our mission of changing the care and treatment for people with rare genetic diseases of obesity.

In this study, setmelanotide delivered statistically significant and clinically meaningful weight loss and hunger reduction, but as we will detail when going through the data, we saw a clear and robust response among participants with Bardet-Biedl syndrome, but no weight loss in the 3 patients with Alström syndrome who were part of our primary endpoint analysis. That said, there were hunger responses. And 1 of the 2 patients younger than age 12 is losing weight.

So we have more to learn and need to understand the full dataset before drawing conclusions about Alström. There's clearly a signal here.

So moving to Slide 5. For today's news, let's start here. This is a slide many of you are familiar with, which outlines what we are trying to do at Rhythm and the journey that we are on. As a company, we are focused on rare genetic diseases, which manifest with early onset obesity and hyperphagia, these diseases, including Bardet-Biedl and Alström are distinct from general obesity.

As we said many times, this is not a drug for the generally obese. Specifically, we are targeting genes where data shows that loss of function in that gene results in a defect in the Milano-Cortin 4 pathway. Setmelanotide, in a highly precise way, has the potential to restore function in that pathway, decreasing the insatiable hunger and enabling weight loss. The journey we are on is to help the healthcare system recognize that obesity is a disease; a highly complex disease with multiple potential contributing factors and that in a small percentage of patients, their obesity may be driven by a genetic disruption in this MC4 pathway. And as we have shown with policy, RevPAR and PCSK1 deficiencies. And now with today's data, adding potentially BBS and Alström's, there is a possible treatment. Making a diagnosis does matter because you might change your treatment plan.

So on this slide, we have our 3 areas of focus and 3 significant milestones that we are pursuing. And today's data shows, we are making great progress. So last month, just after Thanksgiving, we announced that setmelanotide, IMCIVREE, was approved by the FDA with a branded name IMCIVREE for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to POMC, PCSK1 or LEPR deficiency. Making IMCIVREE, the first ever FDA-approved therapy for these rare genetic diseases of obesity.

IMCIVREE is a first-in-class precision medicine that specifically addresses the obesity associated with 3 genes tightly linked to the MC4 pathway. With today's news, we hit our second milestone and paved the way for Rhythm to bring setmelanotide to many patients with Bardet-Biedl in an already well-characterized patient community, and we expect to deliver on our third milestone soon as well.

In the first quarter, we will provide data from our ongoing basket trial and outline our growth strategy, including opportunities for setmelanotide in many more genes associated with this pathway.

So turning to Phase 6, let's move to the data -- to Slide 6. So overall, 34.5% or 11 of 31 patients redeemed responders as they achieved in 52 weeks on therapy, weight loss of greater than 10% with a p-value of 0.0024. I would point out that 10% weight loss is a high bar that Arbitral defined, and this illustrates the outsized effects that setmelanotide has where the MC4 pathway is impaired. That said, I would remind you that a 5% weight loss is considered a clinically meaningful reduction in weight in an individual with obesity. Mean weight reduction in this trial was 6.2%.

Murray will walk you through some specifics related to each syndrome, and how they impacted the analysis. On hunger, we saw a very robust reduction across the board. The mean reduction in hunger score was 30.8% and overall, 60.2% of participants achieved a reduction in their hunger scores greater than 25%. And for each of these readings, the p-value was highly, highly statistically significant.

So we have a clear, robust response among the 28 Bardet-Biedl patients and the primary endpoint analysis set, and the totality of the evidence here clearly supports our regulatory plans, both in the U.S. and Europe. In Alström's, I will remind you that we have 1 of 4 patients with a very robust response in our Phase II and clear signs of activity in this trial, which needs to be fully understood prior to defining next steps. So as you listen to Murray's presentation, I'd like you to keep 3 points in mind: First, if we hit the primary in all 3 key secondary endpoints and a trial run in the background of COVID, which has had a well-documented negative impact on obesity. To be honest with you, I hadn't fully appreciated the challenges that we were facing until we unblinded the data; second, the trial included a much higher number of adolescents who are still growing, confounding the fewer weight loss analysis; and third, we included the 3 Alström patients who showed no weight response in our primary efficacy analysis, and thus had a delusional effect on the DBS results.

So with that, I'll turn the call over to Murray for some more detail and color on the data, the trial design and Bardet-Biedl and Alström syndromes. Murray?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Thank you, David. I too want to thank everyone at Rhythm and our investigators and the clinical staff at our trial sites. It's been a difficult year with COVID-19 for many businesses across every walk of life. Interestingly and perhaps unsurprisingly, we see research point to weight gain and reduced physical activity due to COVID. And the paper published in October in the Journal of Obesity, research has spanned more than 1/3 of the responders who were overweight or obese at the beginning of the pandemic reported gaining more weight. Our patients suffering from Bardet-Biedl or Alström syndrome are no different, although it may even suggest it's a bit more difficult for them. They thrive in routine. And when that's disrupted, it can have a significant impact.

In another study, adolescents aged 6 to 18 report a significant increase in unhealthy food consumption, screen time and less sleep during the pandemic. This unusual environment of isolation, social distancing and disrupted routine, in my opinion, make the results we're announcing today even more remarkable.

And as I start to say, that's why I'm so thankful and even impressed with our Rhythm team, our investigators and the patients and families participating in this trial responded to these challenging circumstances. We quickly transitioned and leveraged properly calibrated to scales and IPAs to collect regular weight values and hunger scores remotely and monitor patient compliance with minimal disruption.

For the 52-week visit, all were conducted in person. Certainly, looking back on just how much changed in the last year since we completed enrollment in this trial, I'm grateful for everyone's commitment to the patients in this trial, I'm very proud of how we accomplished the completion of this trial.

With that, let's move to Slide 8. By now many of you are familiar with the MC4 pathway and how setmelanotide is designed to work in these patients. But for those who are not, let's take a look. MC4R pathway is an hypothalamus to the brain. When working is intended, there is a neuronal cascade of activity that results in the MC4 expressing neurons sequences entirety, feeling of fullness and reduced hunger sensation after we eat. When MC4R neurons are not fully expressed, there is the insatiable hunger or hyperphagia and drive to keep eating. And for people with rare genetic disease of obesity caused by an impaired pathway, they're drifted to overeat. And as a consequence, they develop severe obesity at an early age.

So what's happening with BBS, so this genetic defect lies within the pathway, and we believe the silia dysfunction, present in patients with Bardet-Biedl syndrome diminishes intracellular signaling within the pathway. For BBS with loss of function proteins, will see a disruption to let

receptor transport traffic into cell membrane. This, we believe, produces downstream signaling, resulting in increased hunger or hyperphagia. I'll point out here that Alström syndrome is also celiopathy, and that coupled with similarities in the clinical presentation link it to the Bardet-Biedl syndrome.

However, the genetic variance underlying Alström syndrome is a defect in almost one gene. This is less well-established as part of the pathway compared to the genetic variants and the Bardet-Biedl genes underlined by the Bardet-Biedl syndrome.

Trial 9 -- Slide 9. As shown on Slide 9, the trial is designed to buy setmelanotide for the treatment of insatiable hunger in severity state and individuals living with Bardet-Biedl or Alström after 52 weeks of active therapy. We enrolled 32 patients with Bardet-Biedl syndrome and 6 patients with Alström syndrome given a total of 38 patients at the start of the study. These patients were randomized 1:1 in the first phase of the trial. The 14 weeks of the first phase is a double-blind placebo-controlled portion of the trial. This period included the titration period so the patients stopped from 2 milligrams and then went up to 3 milligrams of setmelanotide.

Importantly, this upfront placebo period is designed to provide a controlled comparison in the beginning of the study. To show differences in weight and hunger. It also enabled us to eventually put all patients on to active therapy. Now the primary endpoint is the proportion of patients who are 12 years of age who achieved at least 10% reduction in body weight from baseline to 52 weeks of active therapy. It's important to note that our statistical analysis plan called for this primary analysis to be deducted for all patients reached 52 weeks of active therapy. And of the 31 patients, older than 12 enrolled in the study, 24 had reached 52 active therapy by December 2, 2020, when we lock the data.

Slide 10 shows us the demographics. Here is an overview of the baseline demographics of 31 patients who were evaluable for the primary endpoint. So how did we get to 31? We started with 38, enrolled the trial, 5 of them are younger than 12 and 2 of the patients withdrew from the trial who were on placebo, so in fact they never received that (inaudible). So 38 minus 5 is 33; 2 withdrawing placebo, that's how we arrive at 31. I'd like to point out that the mean age for these participants with just about 21 years age. And 14 of them were adolescents. The starting weight is 117 kilograms, nearly 280 pounds, with a mean BMI of 43, clearly severely obese patients.

I'd also like to note that 15 of these patients had cognitive impairment. This patient population faces many challenges in trying to manage their hunger and weight gain, given the age and cognitive capabilities, never mind speaking changes due to the routine brought about by the pandemic.

So what about the data on Slide 11? So I'm glad to say we met the primary endpoint with 34.1% proportion of participants, achieving 10% weight loss from active baseline to 52 weeks of active therapy. This was most statistically significant with a p-value of 0.0024 and clinically meaningful.

This represented altogether less responders, all of which were in BBS patients. The first pre-secondary endpoint, the percentage change of mean weight was for all 31 subjects randomized a baseline to active therapy. This included dropouts, the reduction was 6.2% and with an absolute change in weight from 117 to 109 kilograms, which is clinically and statistically significant with a p-value of less than 0.0001.

So what about the hunger data on Slide 12. setmelanotide's results in hunger scores were clear and robust, with 60% of participants seeing a reduction in most hunger scores of 25% or greater. And the change in hunger score from baseline was a reduction of more than 30%. Recall for this endpoint, on a daily basis, we ask patients to rank their most hunger, or call it worse hunger, over the preceding 24 hours on a scale of 1 to 10 with 10 being the most hungry.

Interpreting hunger in clinical trials is challenging in general. Importantly, we used a different method for patients with cognitive impairment, which is not part of this analysis for the primary and key secondary end points. That's why the end here is only 16 as we used a different assessment tool for the remaining 15, adding up to 31. That said, the reduction in hunger was quite remarkable here and results are particularly gratifying.

So let's have a look at the 2 populations. So next Slide 13. As David said, we're disappointing the data related to patients with Alström syndrome that this positive outcome is always going to be a bigger challenge than BBS. We did see 1 out to 4 Alström syndrome respond in a Phase II trial, and we hope for the better results here. We have completely further analysis all these data in the coming months before we make a final decision on Alström syndrome.

It's clear that having no Alström syndrome responders in the primary endpoint diluted our results in BBS, especially given that one of those patients withdrew, another 2 actually gained weight. It's important to note that one of the patients, younger than 12 has lost nearly 8% of the body weight, and we've observed reduction in hunger scores between 20% and 30% in the Alström patients.

This coupled with the results of our Phase II, give us reason to believe that there is a path forward for Alström syndrome, and we'll need to analyze the data. Additionally, I'd point out that we're now using an internal gene prioritization methodology based on NIH Finjan network framework is our new strategy of interrogating a selective pathway genes. What this framework is designed to do is to find genes and categories as weak, moderate or strong or very strong in their effect on the loss of pathway function.

All the genes we select for basket, and the agility to intend to study as well as Palm Clear and Bardet-Biedl are classified as strong or very strong. The OMS1 gene, however, will be classified as moderate under the scoring system. So it may not be surprising that this trial did not show the same robust results in Alström patients than we saw on the BBS. Going forward, we're going to focus on strong and very strong category genes.

Slide 14 is a closer look at patients with BBS. We're clearly pleased with the data, as it relates to BBS patients and it does, to some degree, mirror our Phase II data. In that trial, all the responders were adults and the 1 addressing patients the BBS enrolled in that trial did not meet the responder criteria. So when we look at the 11 BBS patients in this Phase II trial, who did achieve percentage weight loss, 8 of them were adults.

And when we look at the data and the responders, the mean percentage weight loss was 14.7%, and the absolute weight loss for these responders with 17.2 kilograms or nearly 38 pounds in 1 year. We also saw weight loss between 5% and 9% in 5 BBS patients, 3 adults and 2 adolescent.

So when we step back and just look at the BBS adults alone, 11 out of 15 or 73% had greater than 5% weight loss. And 8 out of 15 or 53% had greater than 10% weight loss. We have to do more work on adolescent patients.

As we look at the BMIZ scores, which takes into the account the height and expected growth as children, this will provide a better assessment and more full assessment of the effect in adolescent patients on their weight related to their height.

So what about the safety profile in the study? Let's look at Slide 15. So the safety profile is very consistent with what we've seen in our other studies. With the main adverse events being mild injection site reactions, hyperpigmentation, nausea and infrequent vomiting. There were 3 serious adverse events in 2 patients. One patient had an SAE of blindness and later on SAE of suicidal ideas, neither of which were thought to be drug related, and the patient continued in the second (inaudible) study.

It's important to note here that blindness is a part of the Bardet-Biedl syndrome. One patient had an SAE of anaphylactic, which initially was thought to be regulated by the PI. When we unblinded the ascertainment, we found out the patient was actually on placebo treatment. 5 patients had treatment-related AEs that led to discontinuation, there were no treatment-related cardiovascular events and no death. Overall, a good safety profile.

I'd now like to hand back to David.

David Connolly - *Rhythm Pharmaceuticals, Inc. - Head of IR & Corporate Communications*

Okay. Thank you, Murray. And I hope it's clear for all of you why we are extremely excited about the Bardet-Biedl results and obviously, recognizing we have more to learn in Alström's. So in summary, Bardet-Biedl syndrome specifically is a -- moving to Slide 17, is a serious ultra-rare disease with no approved therapies. Clinical features of Bardet-Biedl may include cognitive impairment, polydactyly, renal dysfunction, hypogonadism and visual impairment.

Based on published data and our internal epidemiology work, we estimate that Bardet-Biedl affects approximately 1,500 to 2,500 people in the United States, and we project a similarly sized population in Europe. And we know between 70% and 80% of people with these diseases are affected by hyperphagia and early onset severe obesity. There remains much work ahead of us for BBS as this syndrome -- as with any rare disease, is greatly

underdiagnosed and relatively unknown outside of a few experts in both the U.S. and Europe. Thankfully that is changing due to leading KOLs like Dr. Bob Haus at the Marshfield Clinic in Wisconsin and established patient advocacy groups like Bardet-Biedl Syndrome Foundation.

So on Slide 18, we capture some of the emotional and psychological challenges through these quotes. I think while the physical signs of BBS may be appreciated, what is less well understood is this emotional and psychologic burden of living with BBS or caring for an individual with Bardet-Biedl.

We know full well from our work with patients and families how incredibly difficult it is to deal with the food-seeking behaviors of infants and toddlers especially when you have no idea, there is an underlying genetic disease. And we understand that over the course of these patients' lives, hyperphagia and rapid weight gain can be 2 of the most difficult and debilitating symptoms to manage. And early work out of Dr. Haus' team has highlighted the fact that this onset, these symptoms of hyperphagia and weight gain happen early, as early as between ages of 2 and 5 and then progress from there. We've heard stories of babies crying nonstop until they receive another bottle in instances shown here, but instances of a baby going from 10 pounds to 20 pounds in a month.

As the children with BBS get older, parents are forced to lock up refrigerators and cabinets. Physicians, too, from our market research are eagerly awaiting a therapy that treats this hyperphagia obesity and the many comorbidities that come with it.

So today, we believe, marks a turning point in the journey to address these needs of the patient's families and healthcare providers.

So on Slide 19, we outline our path forward. So we expect to complete this trial and collect 52-week data points on the few remaining patients around the end of the first quarter of 2021. As Murray said, we'll look further at the data from each of these disease states analysis on BMIZ score for our adolescent population, which is extremely important to correct for their underlying growth and data from the 14-week double-blind, placebo-controlled period will be available at that point. From there, we plan to submit a supplemental NDA with the FDA and submit an MAA to the European Medicines Authority for BBS in the second half of this year. We'll continue, as I said, and we have said, to evaluate the strategy for Alström syndrome and believe there may be a path forward there as well.

As a reminder, we have orphan drug designation for setmelanotide for BBS in both the United States and the EU and in the U.S., we have FDA breakthrough Therapy designation and in the EMEA prime designation, both of which provide us more access and on continued dialogue with both regulatory agencies.

So moving to Slide 20, we'll end where we started here. We're pleased that we're able to follow-up when the FDA's first approval of IMCIVREE for chronic weight management in adult and pediatric patients 6 years of age and older with obesity to POMC, PCSK1 and LEPR deficiencies with today's news in Bardet-Biedl syndrome and Alström syndrome.

Other than POMC, where the impairment of the MC4R pathway is at the most significant as we explore additional genetic impairments on that pathway in diseases like Bardet-Biedl, Alstrom's and others, we see more variability in response. But one data point remains absolutely clear when setmelanotide works, it works. As Murray said in the BBS patients who responded, they saw on average, a 14.7% reduction in weight at 52 weeks. And we know this effect goes beyond these initial indications. And early in the first quarter next year, we'll highlight our progress toward this third milestone with an update on our exploratory Phase II basket study and genetic sequencing efforts.

This update will include new data from individuals living with heterozygote obesity due to a loss of function variant and 1 of 2 deals on the POMC, PCSK 1 or LEPR genes as well as data from SRC1 and SH2B1 deficiency obesities. The update will also include data from our sequencing efforts, which now include samples from more than 37,500 individuals with severe obesity.

And so in closing, we're excited to continue this momentum from a challenging 2020 into 2021. And as we push forward on our mission to transform the treatment for people living with rare genetic diseases of obesity. With that, I'll turn it over to the operator for questions.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question comes from Phil Nadeau with Cowen & Company.

Philip M. Nadeau - *Cowen and Company, LLC, Research Division - MD & Senior Research Analyst*

Congratulations on the data. I'm sure this is a great day for patients and their families. First, one clarifying question. You mentioned the complexities of evaluating weight in adolescent patients with BBS. Do you have the figures for specifically the adult BBS patients. So what was the average percent reduction overall adult BBS patients? And can you remind us of the percent of BBS adults who actually responded to therapy?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Yes. Thanks, Phil. Murray?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. So first of all, the numbers that responded to the 10% weight loss. So with 11 BBS patients got 10% weight loss. And out of those 11, 8 were adults. And so we've not done the calculation of those 8 individuals that clearly, with all 11, we got 14%. And with the 8 adults, we will get more than that when we do the analysis. We've also looked at the BBS in all the adults for the mean weight loss. The mean weight loss was 6.2% if we looked at the BBS adults, we get up to 8% mean weight loss.

Philip M. Nadeau - *Cowen and Company, LLC, Research Division - MD & Senior Research Analyst*

Perfect. That is helpful. And then a second question. You mentioned 5 AEs leading to discontinuation. Could you tell us what specifically those AEs were?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. So it's important to note that these are called very early in treatment. So there were to individuals who, after day 3, complained of nausea and discontinued, and they were younger children. There was one nausea and vomiting. One of the withdrawals was the case of anaphylaxis, that was placebo. So that's 3 nausea and vomiting, 1 anaphylaxis, and there was an individual who had skin and injection sites and complaints [classified].

Philip M. Nadeau - *Cowen and Company, LLC, Research Division - MD & Senior Research Analyst*

And then last question from us. Can you remind us of the respective patient populations in Bardet-Biedl and Alstrom based on current estimates?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Oh in terms of size of population...

Philip M. Nadeau - *Cowen and Company, LLC, Research Division - MD & Senior Research Analyst*

Yes. In terms of size?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Yes. So in the U.S., so we project that they're on the order of 1,500, 2,500 Bardet-Biedl and again, the questions come up. I'm sure it will come up. How many have you identified, we'll answer that question by saying, in the hundreds have been identified, reminding people that -- where we are in the POMC and LEPR, much more rare in the sense and less well characterized, we're in the 10s. So on the 100s, we are working toward those numbers. There's clearly, again, because it's well characterized, and we have a better insight. There's comparable numbers on the 1,500 to 2,500 in Europe for that.

Alström is up to 500, clearly more challenging. I mean, the whole challenge of recruiting this trial, it was much easier for the Bardet-Biedl group, much more challenging to get the 6 patients in the Alström and so again, further evidence that, that is a more there and less well-characterized and diagnosed disease.

Philip M. Nadeau - *Cowen and Company, LLC, Research Division - MD & Senior Research Analyst*

Perfect. Congratulations again on the data.

Operator

Our next question comes from Derek Archila with Stifel.

Derek Christian Archila - *Stifel, Nicolaus & Company, Incorporated, Research Division - Director & Senior Analyst*

It's Derek from Stifel. Just a couple of questions and congrats on the data guys. Just maybe first on Bardet-Biedl. Can you just remind us on the natural course of the disease, is this similar to POMC, POMC disease. Patients gain weight every year? And I don't know if you have an estimate to how much they gain. And then another question, do you think that the results and the efficacy that you've seen with Alström's, is that -- is there any read-through to the basket indications that you guys are examining in the Basket trial? And then lastly, I don't know if you said this in the presentation or the prepared remarks, but what percent of the patients were adolescents in the Phase II. Can you just remind us?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Yes. So let me just the offer introductory comment, and then I'll turn it back to Murray. So in terms of weight loss, I think one of the things that's most remarkable about this therapy and the the way we're intervening, right? Unlike the general obese, where you have a multifactorial cause, you may have some underlying genetics contributing to your obesity, but obviously, behavior and calorie intake and the like are important contributors there and attempts to treat it often result in initial weight loss and then rebound.

Here with the obesity and the hungers being driven by the defect in the pathway, and to the extent that we can correct that, and it seems to restore the physiology in such a way that this weight is sustainable. So again, we're looking at weight loss at a year, not at the shorter time frame. It's out at a year. So this degree of weight loss sum is sustainable. The way loss that we are seeing, for example, in the populations we've treated for a longer period of time, POMC and LEPR they have continued to lose weight with some of the POMC patients getting back to a range of normal BMI. That's not to say (inaudible) get back to "a normal weight", but I think there is a reasonable expectation that once we correct this pathway, you have a shot at getting back to what would be your otherwise normal baseline weight maybe on the high end of the normal distribution, but whatever your set point is, we give you a shot in getting back to that.

And so we don't have, I think, long-term data here, and Murray will correct me, but I think there's a reasonable expectation that this Bardet-Biedl population in those Alström patients who are responding, can continue to go on and lose additional rate over time. Your second question there. The third was your percent of patients with Alströms -- sorry, the adolescents in the Phase II. Murray, do you want to take that? And then you have to remind me, Derek of the second question.

Yes, sorry, I -- let me go on a -- sorry, Derek. The read through. I'll take that one. The read through -- actually, what's really encouraging about this is that back to Murray's explanation of how we are picking genes so earlier on in the program, again, without as much of an understanding as I think we have now, Bardet-Biedl and Alström were grouped together. They're both celial defects. We know they won't touch the pathway, but we didn't have a strong sense of 1 being stronger than the other necessarily, but a celial dysfunction, if it worked in one, maybe it work in the other.

I think what we understand now in using this Clinigen scoring system, which incorporates all available data, literature based mostly, but it includes an understanding if you have animal models through knocking out a gene, if you have biochemical data that gives you some information in the pathway, if you have epidemiologic data that shows that, that genetic defect is associated with a higher frequency of obesity.

When you pool all of that data, it allows you to rank these genes and attach to them, as Murray said, a categorization of very strong, strong, moderate or weak. And so everything that has scored strongly for us has been in the very strong and strong. Alstrom's was moderate and it's ranking. And so perhaps we -- there was a heads up there in terms of the results that we saw today. All the disease we are proposing to study going forward, including, as you know, some of the 36 genes we've talked to some of you about is being potential candidates for future investigation, all are in the strong and very strong category. So Murray, I don't know if you want to add anything and then the number?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. Yes. Maybe just a couple of things. So I think you ask for the sort of what naturally expected in BBS. So first of all, 80% of BBS patients are obese, they often present with their obesities from age of 5 upwards with a gaining weight. And the reason we've seen significant results is on diet and exercise from the (inaudible) rate data, you're not expected to get these BBS patients to lose weight.

So if there was a placebo, which we'll get more data on later out for the 52 weeks. You'd expect that D1 patient to get to 10% 1 or 2. So I haven't got 11 there, that's a clearly strong treatment effect because the natural history of Bardet-Biedl would not suggest these people would lose weight. Regarding adolescence, in Phase II, we just had 1 adolescent, and they didn't respond. So what we're really commenting on here is we've got a large number, 50% of our patients are adolescents and the reason we put them in, they have a high unmet need for their hunger, which disrupts a lot to the family.

And I'm really encouraged that we saw a reduction in hunger we're going to get quality of data later. And hopefully, that's when they would show improvement in quality of life from just hunger. But what we're seeing is we may not have seen so much weight loss in the adolescents for 2 reasons: One, if they are not changing the family eating habits, they're not going to have less calories, but I think the more fundamental thing for adolescents is the fact they're prepubertal. They haven't had -- they're either just having their growth spurts, and that's underestimating the effect on weight.

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Thanks, Derek. I mean, I think that's a really key point, right? When we're saying we didn't have 3 adolescents responding -- it's not that adolescents aren't responding. The point is, is that our ability to read through purely on weight and conclude they're responding is compromised by the fact they should be gaining weight. And so we need to correct with that.

Operator

Our next question comes from Alan Carr with Needham & Company.

Alan Carr - *Needham & Company, LLC, Research Division - Senior Analyst*

Following up on that, can you remind me the contribution, the number of adolescents you had in the Phase III for POMC and LEPR? And then, can you talk about what's gating to NDA or SNDA and MAA submission for Bardet-Biedl? Why is that second half of '21?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Yes. Murray, both of those for you. So the combination of adolescents and our POMC and LEPR trails?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. So in the POMC, there were 2 individuals under 12 out of the 10. And in the LEPR, only when we got supplemental, did we get 1 under 12, that was 8. And then we've got -- in the LEPR, we've got 1 to be 4 patients who are adolescents, 13- to 15-year olds. And in the POMC, we've got another 4 patients.

So there were adolescent patients in the LEPR and POMC, but interestingly, in the BBS, and we're actually seeing a lot greater proportion of 12 and 13 years old. So they're probably prepubertal first in the POMC, they were slightly older adolescents.

Alan Carr - *Needham & Company, LLC, Research Division - Senior Analyst*

So Murray, you had a fair number of adolescents in the POMC and LEPR Phase III trials, but you think -- but I guess you're implying that maybe there's a portion that were 12% to 13% is greater in the BBS, is that what you mean?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. So out of the 13 adolescents in the BBS, 8 of them at age 12 to 13 and what we've got to do is calculate their pubertal status. So part of the change in weight that comes when you go through puberty. So you can actually put on considerable amount of weight when you suddenly go through puberty.

So what may be happening is these individuals are going through puberty and they're gaining height. And therefore, it looks like the weight may be stable, whereas actually that's a good thing because without the drug, they may put on 20 or 30 pounds.

So we need to evaluate that. And the difference in the LEPR and POMC, many of them were slightly older and had gone through puberty.

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Okay. And I think Alan's second question was just on the timing of the SNDA and why second half?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. So as we pointed out, this is the top line data, and there are patients who initially started on placebo are still going through. So we'll complete the study at the end of the first quarter. And then we hope to file for the SNDA second half of 2021.

Operator

Our next question comes from David Lebowitz with Morgan Stanley.

David Neil Lebowitz - *Morgan Stanley, Research Division - VP*

When you look at what you have for Alström thus far, and you do talk about -- there is clearly some activity there. The data right now might not be sufficient. How do you look at presenting this to the agency, and how do you see a potential path forward, I guess, in this indication, #1? But also for other indications that might have similar profiles?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Yes. Maybe 1 comment, and then I'll turn it over to Murray. As Murray highlighted, we had one very clear responder in the Phase II trial. So 1 out of 4, losing more than 20% weight, good hunger response, clearly benefiting. And we have, and again, a little more to understand because we haven't been able to do the full dive yet, but that one child who has lost 8% weight. And again, I think, clearly responding.

So arguably, 2 out of 10 responders, 20% there. And I think what I'd remind you and what I am fully and we, at Rhythm, are fully expecting here is this is obesity, given the complexities that it has, we're going to get variabilities so expecting that we're going to see plus or minus 40%, 50% responses for these genes. And one of the questions that's been asked me is what's too low. What's the frequency that's not of interest? And the way I would think about this, if you had 1 in 10 patients responding and clearly responding, would that be of interest? And the answer is, "well, if I'm the patient, that's clearly of interest." And as a company, if we have a good way of getting at those patients, and I think what we're proposing is this 3-step process, which is: you present with the problem, the phenotype; you have a positive genetic test for 1 of the genes of interest; and you have a demonstrated response on a trial period on the drug.

Clearly, you're responding your pathways or confirming that it's impaired and that 1 in 10 patient would be of interest. So I think the path forward for Alström's here is to: one, confirm the weight results I'm just describing; two, continue, we'll have long-term follow-up data on some of these patients as well, totality, the evidence is important; three, the other elements right, hunger scores, quality of life scores and the like.

So all of those things, I think will be -- what we will be looking at, and I think they do potentially offer us a way forward. And to your question about reading through to the others, yes, we're going to see variability, but I absolutely believe that we will have an ability to file on genes with variable responses as long as we have a way to identify the responders. Murray?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

A couple of comments around that. So the study wasn't proud to show benefit in Alström's. We've clearly shown statistical significance in the total and in Bardet-Biedl. The numbers are small with Alström's. And I agree with Dave, there may well be a way forward. And I don't think we should just be looking at weight. I think the remarkable effect on hunger and the decrease quality of life in patients continuing show that both the patients and the physician treating his patients see value, and we need to describe that value to the agency.

Alan Carr - *Needham & Company, LLC, Research Division - Senior Analyst*

One additional question. I know that traditionally, in the past with a lot of other types of diet drugs. The response tends to weigh in at one point and then patients actually start regaining weight.

And so naturally, one question would be with patients on this drug. What happens towards the end of the period with patients on this drug, what types of trends continue and what types of trends, I guess, after the period for patients that have preceded at that point, what types of trends going forward? Have you seen with these patients?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. So I'm very encouraged actually what seems to be very different about this compared to other obesity drugs. A lot of other obesity drugs just affect calorie intake and you decrease your calories. What's happening here is we're actually correcting a defect in the pathway that seems to affect energy expenditure as well.

So what we've seen consistently in all our populations is a downward trend that continues over a year until many patients get to a normal BMI. And I think the fact that this is doing well shows the fact that patients are continuing on therapy in the long term.

And we've got long-term BBS and Alström. We've got long-term patients in POMC and LEPR, who are continuing to get their weight down. And when they get down towards a normal body mass index, that seems to be maintained.

Operator

Our next question comes from Michael Higgins with Ladenburg.

Michael John Higgins - *Ladenburg Thalmann & Co. Inc., Research Division - MD & Senior Biopharmaceuticals Equity Research Analyst*

I want to go back to comments you made in the Phase III LEPR results. You had noted the -- in the conference call that it's possible the patients dosed -- dosing was not high enough in the LEPR patients. So I want to ask that same question here with the BBS, Alström results. How do you feel about the dosing in the trial? And 1 follow-up then on the Alström patients.

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Yes. Murray, dosing?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. So I think the 8-week had a bit fix dose, peak over on 2 and 3 milligrams. We've not analyzed to see whether there is a difference in dosing across the response rate, although I must say, I'm -- I won't think increased dosing would necessarily get a better response.

We've explored the higher dose in healthy test up to 5, and we'll continue to keep an open mind about whether we increase the dose in patients, but I think the remarkable response rate tells me it's probably not a dose of PK issue.

It's whether they've got an abnormality in the system because when we do see in that, people really do respond. So I'm not ruling out the need for the higher dose of some individuals, but I don't think the answer to the lack of response is necessary dose related.

Michael John Higgins - *Ladenburg Thalmann & Co. Inc., Research Division - MD & Senior Biopharmaceuticals Equity Research Analyst*

Okay. That's very helpful. And then 1 question back on the Alström set. Did you see a correlation with the hunger scores and the weight loss. It's just a handful of patients, but just looking for some insights there?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. So what's interesting, and that's why we think we need to keep the door open for the Alstrsöm's.

So in the 2 of the patients who actually gained weight, they were showing a reduction in hunger. So one of the things happening is they're feeling less hungry, but if their eating habits aren't changing.

So if the parents are putting the same food in front of them. And unfortunately, all they eaten for not necessarily hungry, just to have it in behavior.

So what we need to look at is effect on behavior because certainly, what we've seen is a reduction in hunger. It doesn't always translate to weight loss in the Alström's. And there may be reasons for that in terms of eating behavior and patterns.

Michael John Higgins - *Ladenburg Thalmann & Co. Inc., Research Division - MD & Senior Biopharmaceuticals Equity Research Analyst*

And then just a follow-up in hearing that in the basket study, our adolescents enrolled. And given what you've said, any potential for change in the protocol or impact on the families?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. So what is important is the analysis we do. So I think we -- a drug we didn't decide to do a sensitive analysis on children under 18.

So as we move ahead, I think we'll analyze people above 18 separately from adolescents given this problem of growth.

Michael John Higgins - *Ladenburg Thalmann & Co. Inc., Research Division - MD & Senior Biopharmaceuticals Equity Research Analyst*

Would that require a protocol or any kind of an amendment in the conduct of the study or do you have that flexibility as it's set at the FDA now?

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

We have that flexibility in the basket. And as to say, we actually put it into 1 of the sensitivity analysis in the Bardet-Biedl stuff anyway.

Operator

Next question comes from Tazeen Ahmad with Bank of America.

Tazeen Ahmad - *BofA Merrill Lynch, Research Division - VP*

Congratulations from the progress. I just wanted to get a sense of how you're thinking about, ultimately, what would be the ideal age to start treatment?

You talked about adults and you talked about adolescents, what is your goal with the adolescent population?

And then a second question after that is, how would you talk about your view about what compliance in a real-world setting would be -- I don't know if this is the right comment to be making, but for example, the growth hormone deficiency market is one which also has daily injection frequency and people talk about compliance rates for that population.

Would it be appropriate to think of this population is similar to that rare disease population?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Yes. Good questions, Tazeen. So let me go first, Murray will add in. It's a genetic disease, and it presents early in life.

And so like many diseases, the earlier you can intervene, not only would you -- the earlier you reduce those symptoms, but also the long-term complications.

I think it's reasonable to expect those are also going to be less if you can intervene early. So we want to intervene as early as it appears as a problem, which means in the Bardet-Biedl, the work suggests between the ages of 2 and 5, it's already starting to present.

So we have right now in our POMC LEPR label down to age 6, Murray's got plans in place to go down and look at patients between the ages of 2 and 5.

So that, for sure, would be the goal. The second is what is the goal in the adolescents? And I think I just -- it's so important that everybody understand this.

We've been spending a lot of time highlighting the fact that the adolescents, in a sense, have reduced our ability to see the full effect here and the like.

I think that's not the message. The message here is that we're not seeing a weight loss, pure weight loss in the adolescents, but that's not to say we're not seeing the benefit.

And what Murray was explaining there with the concentration of individuals in the pubertal period where we might expect a disproportionate growth spur.

They likely are getting to more normal BMIs, and this is what we'll find out when we do the BMIs analysis, which will correct, as you know, for that height and the growth and give a correction factor, if you will, to their benefit.

So it's not that we expect that they're benefiting less. It's just not presenting as clearly with weight loss alone.

And then your third one, the view of compliance, it's an interesting one these. And so again, we'll have to learn.

One thing that's been interesting is that in the trial so far, we don't have the data specifically on this trial, but patients seem to have been pretty compliant.

And I'm going to give you 1 anecdote. The LEPR patients, I will remind you, when we presented the LEPR data, we had 5 out of 11 patients, 45% who had responded in losing 10% or more weight loss.

3 of those individuals who did not respond during the trial period had actually stopped the drug because there was a placebo period and they thought the drug wasn't working.

And so they came off drug. Then they realized that actually, it was working, ended up going back on drug. And so where we are with the LEPR patients now is, we had 11 patients in the trial. We added 4 supplemental patients, so a total of 15 LEPR patients have been treated in our trials to date.

12 of those 11 -- of those 15 are in the long-term extension, and they're there because they're continuing to benefit. So this is a disease where the hunger comes right back.

If you think about it, a pain, you stop taking your pain meds, the pain comes right back. Unlike growth hormone, you'll have a daily reminder or every 2 day in low, but it's quick that the hunger is back and you need to take your med.

So I don't know if growth hormone is the right one, but we won't have 100% compliance for sure, but it may be higher than growth hormone.

Tazeen Ahmad - *BofA Merrill Lynch, Research Division - VP*

Okay. Just based on what your expectations are maybe for additional weight loss over longer periods of time.

Is it possible that if a patient has been on therapy for a few years, in the meantime, they can develop better control of eating and what they're eating, and they end up in a place where they don't necessarily need to be on therapy, let's say, every day, is that something that's possible?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

That is absolutely possible. But here's why -- I mean, I think for all of us, of course, I mean, obesity is a function of how many calories we take in and how much energy we expend.

So to the extent that people do a better job of managing their caloric intake. And there's variability. So I think for sure, that will happen with some.

I think, again, we're not fixing the underlying genetic defect permanently, right? It's not like a gene therapy. So when the drug comes off, that pathway is still impaired. So although I think what you describe is possible for some percentage, I don't know.

But I think it's less likely. I think the majority is you've got this defect, you live with it for life. And then as long as you're not taking this corrective factor, you're going to be at risk for gaining weight.

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. I think it's been unlikely they'll be able to go back to no -- because it's not like, oh, we're now introducing a new behavior.

The drive to eat when you stop the drug comes back and people thought, ohh well a (inaudible) drug quality, but the weight goes up and the weight goes up, not because they're not trying, it's because that insatiable drive to eat, the hyperphagia that is a genetic abnormality.

So I think it's very unlikely that they'll be able to adapt and be okay. I think, unfortunately, this means do we need to stay on the drug.

Tazeen Ahmad - *BofA Merrill Lynch, Research Division - VP*

Okay. And then the last question is on financials. Can you just give us an update on your current cash balance, and how far out do you think that takes you?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Yes, Hunter's on the call.

Hunter C. Smith - *Rhythm Pharmaceuticals, Inc. - CFO, Treasurer & Secretary*

Sorry, Tazeen, I was on mute. We had about $200 million in cash at our last quarter in reporting, and we expect that to get us into 2022. I would also mention that we received the PRV as part of our approvals back earlier this year, and we have the ability to monetize that as well.

Operator

(Operator Instructions) Our next question comes from Graig Suvannavejh with Goldman Sachs.

Graig Suvannavejh - *Goldman Sachs Group, Inc., Research Division - Executive Director & Senior Equity Research Analyst*

Congrats team on the data. Just a few questions, if I could. One, just wanted to get a sense of the commercialization strategy here. I know with LEPR and POMC, there wasn't going to be a sales force.

I'm just wondering if that's going to be a similar approach here. And just wondering on the assumption of an approval how we should expect kind of the market uptake of the drug should be realizing that it's a different patient population versus POMC and LEPR?

And I have a few follow-ups as well.

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Yes. Yes. So for the commercial approach here, I think what -- the way I would ask you to think about this is there's a set of activities, which serve every population we're going after here.

This rare genetic disease population as a group. And the most important activity there is sequencing the testing.

And so we are for example, as we pursue this next round of Phase III trials, looking at the basket genes, we will be doing sequencing as part of that.

Each of these gene panels include all of the genes, including the Bardet-Biedl gene and so that activity itself will drive a very significant level of screening for Bardet-Biedl patients as well.

Genetics are only 1 part of the diagnosis. It's a clinical diagnosis, but that will raise a flag, perhaps for people to start thinking about Bardet-Biedl.

So that will help, number one. Number two is this clinical trial effort, again, which will be a larger effort on identifying what's sees a round number of 50 sites, 25 to 50 sites in the U.S. and some number outside the U.S.

Those sites become potential treater sites for all of the rare genetic diseases, obesity, not just that Basket trial, right?

We're educating people are getting familiar with the drug, we're thinking about testing. So all of that work again, lays the groundwork for everything, including a Bardet-Biedl and Alstrsöm's effort.

Third, the skill set that's most useful at this point on a commercial lot is the medical affairs, again, what rare diseases struggle with is lack of disease awareness.

And so there's already, we have a medical -- there's a workforce on the ground in the U.S. and in Europe today. So again, serving all efforts, including Bardet-Biedl.

And then as we get closer to the Bardet-Biedl launch, we will put a commercial sales force, technically, again, I never think so much that this is a drug that you need to sell in a situation where you've got a rare disease and an unmet need and only one solution, but they will have their own role that salesforce in terms of supporting the transfer access, helping patients get access to the drug.

And, of course, additional disease awareness. So I don't know if that helps, but it will not be -- we will take a more concerted effort in the sense of the sales force than we have in the POMC and LEPR groups.

And then the approval, we will have unlike POMC and LEPR, which is I'm absolutely convinced, we will get to the larger patient numbers that we see as the full potential of this drug over time, out of the gate slow.

As I said, in the 10s. Bardet-Biedl, we'll have a much steeper ramp. And it will have a much steeper ramp because we have just better characterized patient population because they have other manifestations, they're more quickly diagnosed than the work we have to do in the other rare genetic diseases of obesity. And so we'll start with larger numbers, and they will move to therapy more quickly.

Graig Suvannavejh - *Goldman Sachs Group, Inc., Research Division - Executive Director & Senior Equity Research Analyst*

Okay. I just wanted to get back to the data. So you've got about a 35% response rate. And I'm wondering, is there an ability to optimize kind of being able to predict which patients will be better able to respond to treatment.

You mentioned that while the addressable patient population is about 1,500 to 2,500 in the U.S. You currently see it as you've identified 100s and not 10s versus POMC and LEPR, I'm just trying to get a sense of how you'll be able to kind of be better able to target the patients that might see a benefit?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Yes. No, Greg, thanks for that question because it's important to clarify. I'm going to ask Murray to walk you through. And Murray, if you can walk through from the 35% trial result, which includes both Bardet-Biedl and Alström's to the -- if we use the 5% in greater world to the 16.

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. All right. So I think the 34.5% obviously represented the total population. So if you just look at the BBS, you then get 11.

And look at adults alone, you get 11 out of 15, that's 73%. And then if you -- that includes the 5% weight loss. If you just got the 10%, you get 8 out of 15, which is 53%.

So 34% really is broad and included Alström's. So what we're seeing is that the data is stronger or more clear in responders when you look at BBS adults alone.

And also, the 10% is a high bar. So when you include people who are gaining clinical benefit above 5%, you clearly have 11 out of 15 and then it would be even higher if you actually choose the people who dropped out.

So with a couple of people who as you saw drop out with too early. So you're then getting 11 out of 13, if you do the adults who withdrew. So that clearly, again, is the higher percentage. So I think what we're seeing is we can identify people who responded based on excluding the AS in this population and looking BBS adults alone, but that is just one aspect. I think I do want to highlight that at adolescents, it's not that it's not working. It's just that weight alone is not the best assessment.

And one thing that hasn't come up as well as looking at the BMI's score, we probably want to look at their growth curves.

So what we've done in the LEPR and POMC when we filed is we looked at individual growth curves. And what people are, are there's 2 or 3 standard deviations from normal.

And then what will be good is if they get back on the normal curve, so what we'll be able to plot out is the change in their BMI based on their growth curves to show benefit.

So I wouldn't sort of say, "Oh, it only works in a few number of people." I would say, "it's more complex than just looking at the totality."

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Yes, Greg, let me give you one more shot at that as well because I think this is so incredibly important. In our Phase II trial, we had 6 out of 9, 67%, small data set.

As Murray said, and this is paradoxically, we often think about trial results as being better than what we might see in the real world. This is a case where I actually think the real-world results will be better than (inaudible) official primary endpoint trial results.

So that's where 11 met to 10%, 5 additional patients were between 5% and 9%, they're clearly going to stay on drug. They're clearly benefiting. Hunger scores are down. They're over 5%.

They're going to continue to lose weight over time is our expectation. So that 11 plus 5 equals 16 over a denominator of 28 patients is 57%.

So I don't think the results we're seeing today in this trial are at all different from what we saw in our Phase II.

There's more to learn about the adolescence, as Murray said, and we'll be able to update these with more precision. But that's -- part of the reason I'm thrilled with the BBS results is, I think, we confirmed what we saw in our Phase II.

Graig Suvannavejh - *Goldman Sachs Group, Inc., Research Division - Executive Director & Senior Equity Research Analyst*

Okay. That was very helpful. Help me to understand. Just 2 quick ones. Do you have an ability to measure the impact to any of the other comorbidities that these patients have with BBS?

And then my second last question is if you could provide color on your current comfort with where consensus estimates are for 2021 and 2022?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

I'm sorry, the last one of consensus, what was the last part? Sorry. Graig.

Graig Suvannavejh - *Goldman Sachs Group, Inc., Research Division - Executive Director & Senior Equity Research Analyst*

It was just comfort with where consensus sales or revenue are for the company for 2021 and 2022?

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Got it. Okay. Murray.

Murray W. Stewart - *Rhythm Pharmaceuticals, Inc. - Chief Medical Officer*

Yes. So maybe I can do the quality of life issues. So obviously, this is top line day-to-day where we're really presenting the weight and the hunger.

In our full analysis, we've got significant amount of additional data. So we've got SF36 rating scales. We've got pediatric quality of life data. And what this really will be able to demonstrate is effect on sleep behavior. So we will have a lot more data to come on quality of life that is key.

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

And Hunter?

Hunter C. Smith - *Rhythm Pharmaceuticals, Inc. - CFO, Treasurer & Secretary*

Graig,, this is Hunter. Just in your question about consensus, it has moved, I think, significantly there are 1 or 2 analysts who do include a PRV financing in their numbers.

So that needs to be taken into -- or sale of a PRV voucher in their consensus numbers, and that needs to be taken into account when examining consensus.

I still think the critical thing for analysts to think about is that we expect patients in the first couple of years in the 10s on -- from POMC and LEPR.

And that continues to be the case, and we'll continue to share that message with the analyst community.

Operator

And I'm currently showing no further questions at this time. I'd like to turn the call back over to David Meeker, Chief Executive Officer, Rhythm, for closing remarks.

David P. Meeker - *Rhythm Pharmaceuticals, Inc. - Chairman, President & CEO*

Great. Well, thanks, everybody, for joining today. And what is, again, another exciting day for Rhythm, as we said at the beginning, and this is an amazing journey that we're on.

And we started out focused on a very, very small number of patients with a genetic defect, tightly linked to this MC4R receptor in the POMC patient population.

And what's increasingly becoming clear is that there are many more, I think, many more genes, upstream, where we're not getting the full engagement of that MC4 receptor, and therefore, a drug like setmelanotide engaging that receptor directly can make a huge difference.

So I hope what you take away from today is that we've confirmed robust responses in our Bardet-Biedl population that there's clearly a signal in Alström, and your questions are appropriate, like we need a little more work to clarify the exact path forward, but the level of response there, I think, may well be one that will support approval as well.

If you respond to this drug, you respond, you do well. And so taking the 11 responders, you cleared 10%. On average, their weight loss was 15%.

And then I tried, as I said in my comments there, right at the end, I think it's important to look at the trial data, but it's also, I think, reasonable to project ahead to what's going to happen in the real world.

And I do think, I'll say it again that real-world use of this drug may -- it's going to be more significant than our high bar 10% threshold at 1 year, cutoff might suggest.

So the 39% of patients are the pure Bardet-Biedl patients who -- the 11 of 28, who met the threshold at the clinical trial definition. You add the 5 in, you get to 57%, 16 to 28.

Again, I'm thrilled with that result. And then more to come on adolescents. Don't take that as a negative. It's a genetic disease.

We want to intervene early and we will intervene early. So more to learn, but by no means do we think that's the wrong population.

In many ways, that is the best population. The earlier you intervene, the better you do. So with that, we'll sign off. And we look forward to updating you and talking to you again in January, presumably, our first quarter, but we're going to aim for January to update you on the Basket results and what I hope will be another exciting day for Rhythm and our journey here. So thanks again for tuning in. Goodbye.

Operator

Ladies and gentlemen, this concludes today's conference call. Thank you for participating. You may now disconnect.