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AERI - Aerie Pharmaceuticals to Discuss the RhopressaTM Phase 3 Efficacy Results from Rocket 1

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PRESENTATION

Operator

Good afternoon, ladies and gentlemen. Thank you for standing by and welcome to the Aerie Pharmaceuticals Rhopressa Rocket 1 Efficacy Results Conference Call. At this time, all participants are in a listen-only mode. Later, we will conduct a question and answer session and instructions will follow at that time.

(Operator Instructions)

Today's conference call will be recorded. It is now my pleasure to turn the floor over to Aerie's Chief Financial Officer, Rich Rubino. Please go ahead sir.

Richard Rubino - *Aerie Pharmaceuticals - CFO*

Thank you, Roland. Good afternoon and thank you for joining us today. With me today are Vicent Anido, our Chairman and Chief Executive Officer; Tom Mitro, our President and Chief Operating Officer; Brian Levy, our Chief Medical Officer and Casey Kopczynski, our Chief Scientific Officer.

Today's call is also being webcast live at our Web site, investors.aeriepharma.com and it will be available for replay as indicated in our press release. The purpose of today's call is to discuss the 90-day efficacy results of the initial Phase 3 efficacy trial known as Rocket 1 for Aerie's triple-action drug Rhopressa being developed for the treatment of glaucoma and ocular hypertension.

Before I turn the call over to Vince, I will address forward-looking statements. On this call, we will be making certain forward-looking statements including statements regarding the success, timing and cost of our clinical trials, the clinical effectiveness, commercial launch and potential future sales of our product candidates as well as other statements related to future events.

These statements are based on the beliefs and expectations of management as of today. Our actual results may differ materially from our expectations. Investors should read carefully the risk and uncertainties described in our press release as well as the risk factors included in our filings with the SEC.

We assume no obligation to revise or update forward-looking statements whether as a result of new information, future events or otherwise. Please note that the press release and associated slides that Vince will be discussing are available on our Web site.

With that, I will turn the call over to Vince.

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Thanks Rich and good afternoon everybody and thanks for joining us today. Obviously, I apologize for the short fuse. We got this data about 36 hours ago but we wanted to make sure that everybody had it on a timely basis and obviously as quickly as we can possibly do it.

What I like to do is just simply start with some of the highlights as you saw in the press release. Our Rocket 1 Phase 3 trial did not achieve a non-inferiority to timolol that we were expecting and what's interesting is that we had the original Phase 2b trial for Rhopressa did well and then we did the Rhopressa arm and the Roclatan trials and it did even better and then here it just didn't quite what we expected it to do.

And so obviously, we're very, very disappointed with that. I'm going to share with you all of the data that I can share with you at this point and so many times we talked about 9-point studies. We'll have 9-data points to share with you and so if you have to refer back to slide decks, so you could actually look at the same things that I'm going to talking about here in just a second.

As we were looking at the data after we got past our disappointment on the -- on the per protocol assessment, we started looking at some of the secondary endpoints. One of those was a predefined one which was looking at data points or intraocular pressures below 24 millimeters and when we looked at that, we got results as you'll see here in just a second or basically like what we have described as our grand slam scenario.

We were not only non-inferior to timolol but we're also anywhere between roughly 0.3 and over 1 millimeter better in timolol at all 9-time points. And so we found that quite curious, so we asked the guys to go back and take a look at the data and see at what point did we flipped from being inferior which was less than 27 to becoming non-inferior and start showing some numbers where we were actually numerically superior.

And it turned out that if we simply drop the top end of the range, so instead of going from 20 all the way up to less than 27, we drop that less than 27 to less than 26 millimeters of mercury. We actually started achieving non-inferiority immediately and started seeing a trend for more and more of the data points going in favor and showing numerical superiority over timolol.

And so as background, I just want to point out that this Rhopressa trial Rocket 1 is one of three different trials that we're doing. The other one is called Rocket 2, same general protocol with an extra arm for a b.i.d. form of Rhopressa or the b.i.d. dosing of Rhopressa and we'll get an efficacy read out there in Q3 of this year.

And then long-term safety will come out of that study and that will be towards the end of the calendar year. We're also conducting a study in Canada for safety and that simply is meant to supplement what we're able to do with the safety component of Rocket 2.

Now turning back to the Rocket 1 results and so what I'm going to do is I'm going to try to remember to show you or to refer to which slides that I'm working on. So if you go to the slide deck, I'll be starting off with slide 3. This basically again just gives you a background of three different trials that we're doing. Rocket 1 was basically looking at the hypertensive efficacy of Rhopressa q.d. versus timolol b.i.d. on a non-inferiority basis. We're also looking at some safety.

Rocket -- I'm sorry slide 4, you could see the actual trial design. We actually randomized 411 patients over 36 sites of which 37 - 370 subjects were analyzed per protocols, those were randomized 1:1. As a reminder, we looked at efficacy, our primary endpoint was a mean intraocular pressure at the end of week 2, end of week 6 and on the 90th day. And we also looked at 8:00 a.m., 10:00 a.m. and 4:00 p.m. time points. This is on slide 5.

And then we're also showing you here the secondary efficacy endpoints that we were looking at. The one that was most interesting to us obviously was the assessment of looking at below 24 millimeters of mercury, so it was a pre-specified endpoint. Now on the trial conduct of the 411 patients, as I mentioned we had a number of early terminations. We had 44 of those -- a little over 30 in the Rhopressa arm, 13 in timolol and you could see the lump sum reasons for those early terminations.

And again as a reminder on slide 7, the per protocol population which is a baseline of below 27, we did not meet the criteria for non-inferiority to timolol. In some cases, we're actually a little bit better than timolol and in other cases, we're worse than timolol. Just something to point out here when we talk about a minus number, for Rhopressa that's actually a positive which means that we beat timolol by that amount as opposed to the plus number which means timolol beat us. What was interesting as we looked at the data was the inferiority that we saw was really driven by a very small subset of patients, Rhopressa patients without losing some efficacy over time about 20% of the patients in the population that we looked at which is below 27 millimeters.

And slide 8, this is the first one of several of these kinds of charts that I'm going to show you, what we're looking at the actual 9 data points and you could see a baseline at the 8:00 a.m., 10:00 a.m. and 4:00 p.m. where the patient started. We had 182 patients on Rhopressa, 188 on the timolol side and you could see that we started out pretty well and then starting with 8:00 a.m. on day 43 and then at 8:00 a.m. and 10:00 a.m. on day 90, we were not able to achieve the non-inferiority metric for Rhopressa over timolol.

Obviously, this is a bit of a surprise given that we had seen in all of our clinical trials at below 26 millimeters of mercury. The 26 and below we were equivalent to latanoprost and that latanoprost is typically about a millimeter or so better than timolol. I'm going to show you these slides and they're up on the slide deck where we actually do it graphical form. I'm not going to be referring to those. It's just more for illustrative purposes that you and other audiences can take a look at that.

One of the interesting things again as we took a look at the data and again we've only had it for a couple of days now, a little less than that and what we wanted to do is understand sort of why we lose this efficacy and so what's commonly called the drifting. And in all patients that were assessed, the 370 that we looked at and then obviously the 182 for Rhopressa, we had 36 drifters at pressures of 27 and below.

What's interesting is when you drop by 1 millimeter and you look at below 26, we knock out half of the patients who drifted. We're down to 18, below 26, meaning when you go to the pre-specified endpoint which -- secondary endpoint which is below 24, it all dropped all the way down to five drifters.

So, the point here is that for timolol we also saw roughly about a 5% drift, patients drifted, so that's basically what we're considering to be the noise level. So by the time we got down to 24, we were down to again what we will consider the noise level.

Now we've been taking a look at why did we have 80% of the patients do extremely well and yet only -- and looking at the total number of patients 20% of them had this drifting occur and we think there's a couple of different explanations as we take a look at some of the patients who are going to do so over the next month or so. We think that one likely explanation is that some of these patients with the higher IOPs could actually have had glaucoma for quite a while.

And so if they were on for example latanoprost or any other prostaglandin where a lot of the [acreage humor] was being shunted away from a trabecular meshwork that may have led to further fibrosis occurring at the trabecular meshwork to the point where a drug like ours that works primarily on the Rho-kinase inhibition and increasing the outflow through trabecular meshwork, if it's basically extremely fibrotic or drug may not work, so -- and probably most like won't work, so that could be a possible explanation.

We did some patients where their IOP spiked tremendously. In fact, back up to non-medicated levels and so it makes you wonder whether we had quite a few inches -- or quite a few patients where, yes, for whatever reasons that they just were not particularly compliant but they stayed on in the study, and so therefore, we got a calculation -- calculated into the results. Obviously, concomitant meds can also influence we'd say. And we'll continue looking for the right -- or what the answers or the possibilities could be but given the actual period of time, those are the best possible explanations that we have in terms of why some patients actually drifted but yet the majority did not.

Now turning to the lower baseline intraocular pressures, again as I mentioned earlier we could -- we had pre-specified in our statistical plan looking at below 24 millimeters of mercury and so when we start looking at that, and again we hit our grand slam scenario. We had not only hit non-inferiority versus timolol but we were numerically better than timolol at each and every time point and I'll walk you through what that looks like here in just a second and so that's when, after we saw that, we went back and had the guys take a look at the dropping of -- from below 27 to then below 26 and below 25 to try to see at what point we flip from being inferior to non-inferior, and it turned out that it was at 1 millimeter below the top end.

So when we got to below 26 millimeters of mercury, we became non-inferior to timolol and we started hitting or actually beating them numerically at the majority of the time points.

You could see on slide 12 the actual results for below 26. Remember this was not pre-specified, this is our own analysis of the data. So, I want to make sure everybody is clear about that but you could see that we had a pretty good IOP drop pretty much across the board. You could also see that the reflection there of continuing drifting a little bit that was caused by, as I mentioned, now 18 patients instead of 36 in a total cohort.

But, we also started seeing that we were numerically better than timolol at quite a few of the time points and again it was four clear ones and one that -- one marginal one. So as a former marketing guy, we still conclude that's a positive one for us.

On slide 14, you can actually see what happens in a pre-specified endpoint of below 24. Now this just to be really clear, this is what we expected at below 27 millimeters of mercury data to look like based on our original assumptions. We assume that we would drop pressures and drop them well. We also -- and we were able to achieve non-inferiority against timolol at all 9 time points.

And then the numbers in green, that's what we expected to see. Somewhere -- I think we told just about everybody that we talked to that we would see somewhere between a half a millimeter at a millimeter of numerical advantage to Rhopressa over timolol at every time point. So here, as you could see we had anywhere from 0.3 to 1.4 millimeters of improvement. So, this is what we're expecting to see, so again -- but we missed it as far as the primary endpoint is concerned.

Now from safety and tolerability point of view, we didn't see any drug-related serious adverse events. The most common adverse event we did see was conjunctival hyperemia which occurred in about a third of the patients and 80% of that was pretty mild and so again no major surprises. We saw some usual adverse events associated with eye drops and again no major surprises here, relative to what we've been reporting for the Phase 2 trials.

So just to summarize here from a next steps point of view, as we look at Rocket 1, we continue to do quite a bit of work and make sure that we understand all the data, make sure that we continue to - we won't get the final data sets here for another week or two. We'll take a look an awful lot of those until we see what's going on.

And then obviously, start turning our attention to the expected unblinding of the results for Rocket 2 which is expected to be in Q3 of this year. Just as a reminder in Rocket 2, we do have an extra arm which is the b.i.d. dosing of Rhopressa in addition to the q.d. and then timolol twice a day. And in there we also have the same endpoint i.e. where we have above 20 millimeters of mercury and below 27 was the entry criteria. And in addition to that, we had to be -- it's a non-inferiority trial to timolol at all 9 time points.

We also have the secondary endpoint, the same one that we have in the Rocket 1 trial which is the -- above and below 24 millimeters of mercury. And so you can imagine that we're going to be spending some time here from a regulatory point of view assessing whether it makes sense for us to go start talking to the agency about taking a look at switching the end points here and using a secondary endpoint as our primary one because again all we've reported so far is that we completed enrollment of that clinical trial. We have not locked the database and so we haven't see any of the data at this point. So certainly if we're going to make some changes, we'll do so before all those things happen and we'll do that in concert with the FDA.

Now we're planning ahead, so we try to figure out sort of Okay, so we missed on this first one but we had some pretty good data just below i.e. 1 millimeter lower at the top end of the range. Once you assessed that, it will look pretty good. So obviously we're taking a look at what would be required to move forward with getting approval for Rhopressa, that we do think we have an efficacious drug here.

And obviously, looking at doing another clinical trial at a lower range i.e. maybe dropping the upper end down to roughly 25 or so and maybe dropping the lower end below 20 certainly would make all the sense in the world. So as we assess flipping the endpoints for Rocket 2, we'll also in parallel be looking at the start of another trial just because if we don't see Rocket 2 data until Q3, then we may not be able to start another trial until after that.

We may want to go at risk and go ahead and start another Rocket -- this would be Rocket 4 trial which should be replicated of Rocket 1 in terms of the protocol just for efficacy. So, it's a 90-day trial, so we may choose to start that early. And so again, a lot of it would be decided over the next month or so.

Now relating to Roclatan obviously we do have an awful lot of plans to move forward with that program and certainly to start that program because again now we do believe that Rhopressa is moving towards what we believe is an efficacious drug and we think we just need to highlight and maybe change the endpoints or the entry criteria for the next trial and move towards approval there. So, we're assessing whether we want to start one or more of those Roclatan trials prior to releasing the data for Rhopressa but -- for the Rhopressa's Rocket 2 and then -- but again we'll make those assessments as we go through and have further discussions with the FDA.

And so again, that's the clinical plans as we go forward at some of the regulatory plan and some of our thinking as we move forward and one of the things that I do want to point out is that thanks to the support that we got from many of the investors during the IPO and obviously the other financing that we did in the fall of last year with Deerfield and then we actually hit our stock, it was moving pretty good over the last quarter or two.

We activated a portion of our shelf, the at-the-market, the ATM component and raised -- and we're able to secure an incremental 30-plus million in financing. So as -- as of today we have almost $180 million in the banks, so in our current burn rate of about 60 million. And we have quite a few years left of cash where we can actually execute on this strategy -- on the current strategies for Rhopressa and also Roclatan certainly withstand the incremental trial that we think we'll have to do with Rhopressa. But at the same time, continue our efforts to build out the pipeline.

So before I turn it over to the operator for questions, I do want to thank everybody here in the company for a job incredibly well done. As you can imagine, the last couple of days have not been a lot of fun for the guys and we do have a lot of the employees on the call. And so, this has been an awful lot of hard work to get to this point and while we're disappointed that we missed the primary endpoint, we are pleased with some of the other information we were able to pick up and the fact that it was a not much of a miss, it was still a miss.

I don't want to downplay that but the fact that we were able to get to the numbers we were looking for efficacy by just simply dropping the upper end of the range by a millimeter. It's just -- that's awfully close where we have about a 0.5 millimeter difference and just in IOP reading that we get. So again, I want to thank them for a job incredibly well done and I do want to point out from a commercialization point of view that as we look at this, even as we look at these lower -- or lower IOP ranges from a commercialization point of view, let's not forget that 80% of the patients who have glaucoma in the United States have pressures that are under 26 millimeters of mercury.

So even by dropping this range, we don't think that's going to have any impact at all on our ability to commercialize and also one of the things that was a pleasant surprise was how quickly our investigators were able to enroll patients at lower ranges. And so as we think about doing a fourth Rocket trial, then we think that we should be able to achieve a pretty quick enrollment there and move forward for approval.

At this point, what I like to do is I turn it back over to the operator for Q&A.

QUESTIONS AND ANSWERS

Operator

Thank you. (Operator Instructions).

Our first question comes from the line of Adnan Butt with RBC Capital Markets. Your line is now open, your question please?

Adnan Butt - *RBC Capital Markets - Analyst*

I'm sorry on the -- on the outcome, so for Rocket 2 that's coming up next, is it possible to change the endpoints [part] on blinding to the lower baseline IOP?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Hey Adnan, how are you. Yes, we actually have talked to Marv Garrett, who runs our Regulatory and QA Group here in the company. As you know, he has worked with us in many years in both Allergan and ISTA and we actually have done that before. We had those discussions with the agency on a number of other drugs. And as long as you do it early enough and you haven't, quote, taken a peek at the data and things like that and haven't turned in the statistical, the final plan, you can certainly do that.

Obviously, we need to make sure we understand all the ramifications of that not only for Rhopressa's Rocket 2 trial but also he's got an extra arm in there, the b.i.d. arms. We want to make sure we're thoughtful about considering that and certainly need to consider whether in fact is -- whether the drifters that we saw were simply an aberration or whether this thing is real.

So -- but the direct answer to your question is yes. We think that it is a viable from a regulatory point of view as long as you haven't locked the database and looked at it to change the endpoints. And by the way, our rationale is pretty simple which is if we're running these clinical studies serially, we will certainly change the endpoints right now. So, let's see whether you can actually put a sense together that allows us to be logical when we have our discussions with the FDA.

Adnan Butt - *RBC Capital Markets - Analyst*

And then what's -- when would you be able to have those discussions about if you can or if you shouldn't change the criteria for Rocket 2?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

We'll take a look at over the next couple of weeks, we'll have the entire data analysis because right now all we have our top line tables and so we have the entire data analysis over the next couple of weeks. We'll have those discussions. We'll sit down with the FDA informally at first but formally if needed as we think about making those changes. So, it will be probably a month or two would be my guess.

Adnan Butt - *RBC Capital Markets - Analyst*

Okay. Second question and based upon what you're seen in Rocket 1, what would you not expect from Rocket 2, is it a - is it a dosing issue or is it refractory patient issue? Because, yes, you mentioned there is a b.i.d. arm in Rocket 2.

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

We don't think -- we don't think this drifting is fixed by simply dosing the drug b.i.d. We think that this drifting is either at least in our preliminary analysis that Casey and Brian have walked us through is that, it is due to in all likelihood the fact that the patients may have been diagnosed with glaucoma a long, long time.

We can't forget the latanoprost opens up a secondary drain which further diverts acreage humor away from the trabecular meshwork causing even more fibrotic damage. And so we think that it's really the person's trabecular meshwork is shot to the point where using a Rho-kinase inhibitor opens it up. There's nothing to open up and so we think that explain -- that would be our current best guess in terms of the -- the best explanation we have.

And then secondarily, I'm sure it really does look like there's some patients who just were not compliant, weren't staying on their meds because their pressures -- because we -- I mean they were so high after the first -- the day fifteen information that it just didn't seem like they were on a drug.

Adnan Butt - *RBC Capital Markets - Analyst*

One more question and then I'll get in line. In terms of -- in terms of going ahead with the Roclatan -- Roclatan program, again would you need to discuss and when might you be able to decide if you -- you can go ahead with that program?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Well, I think we had plenty of discussions both the FDA and European authorities and so we have a pretty good handle on it. It's purely a risk assessment for us at this point as to whether we want to move forward prior to unblinding Rocket 2.

All sorts of different ways of mitigating that obviously like we're thinking about with Rocket 4, I mean we can start t that now and pick up a little bit of time. We can also start one of the Roclatan trials quickly as soon as we can, do that at risk and sort of move that forward or we can wait but it's purely a -- I think we have all the data that we need. It's purely now a risk assessment on our part. So, we'll do that over the upcoming couple of months.

Adnan Butt - *RBC Capital Markets - Analyst*

Thanks.

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Yes.

Operator

Thank you. Our next question comes from the line of Annabel Samimy with Stifel. Your line is now open, you question please.

Annabel Samimy - *Stifel - Analyst*

Hi, thanks for taking my question and also sorry for the disappointment. I just want to make sure we understand something. The endpoints that you had which was 5 out of 9 have to be within 1 millimeter and the rest with a 1.5 millimeters. That was not for a mean point that was for the range it seems. I just want to clarify that point because if you're looking at the mean, all of them are within that 1.5.

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Yes, so when you did the confidence interval, you have the delta that you're looking at, has to be adjusted and so -- because you're really looking at the upper end of the confidence interval and so the delta that -- so anything above 0.7 millimeters became inferior. So it was not as -- so when you're doing the confidence interval you really have to take into account the upper end of the range.

Annabel Samimy - *Stifel - Analyst*

Okay. All right, so I also just want to clarify -- I mean it seems that it's highly unusual for just that 1 millimeter has such a dramatic effect on the results. So what -- what portion of the patients were in that 27 millimeter range and does that mean that a good number of the 28, 26 millimeter patients are also didn't really meet that non-inferiority somehow within that range or is that thinking about it incorrectly?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Let me try this, so if you take a look simply at the actual numbers we enrolled -- per protocol, so after the dropouts or the early terminations I'm sorry, we had 370 patients, right. So now that was at below 27, so when you look -- drop at 2 -- below 26, we had 277 patients. So, the difference between those two numbers are the ones that we're in that 1 millimeter that we're talking about.

Annabel Samimy - *Stifel - Analyst*

Okay.

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

At that level, we had 18 out of -- 18 drifters that were in those numbers and so it was 18 drifters that for just Rhopressa alone were between -- because I was giving you there the ends for the totals. But if you go back to the slides, you'll see that end for Rhopressa at below 27 was 182 and then the end for Rhopressa in the below 26 was 133, so roughly 49 patients.

So of those 49 patients, 18 were drifters, so you take those out and really the -- or bring it down to normal i.e. noise level of 5% we would have been fine. I'm not sure I'm answering your question though.

Annabel Samimy - *Stifel - Analyst*

Okay, maybe I'll just move on for a second. But I just want to understand also something about what you said on the duration. So, you mentioned several reasons for the duration was that some of these patients may have been, had much more severe trabecular meshwork damage, maybe it was a compliance issue, maybe it was -- I don't remember what the last point was but shouldn't that have that applied to all the patients? I mean shouldn't this -- did you check to see these patients why would there more damage in the Rhopressa patients than in the timolol patients, shouldn't it be pretty balance in that regard?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

So they worked -- so they worked differently, right. So, the Rhopressa works by the three mechanisms and so -- and you could see that playing it out because they had a normal trabecular meshwork and the combination of decreasing the amount of fluid being produced with increasing the outflow to trabecular meshwork especially at the lower ends as we look at 24 and below where the episcleral venous pressure becomes really critical, we did fine.

And so, it was really in that upper end of the patients and so if we can't use what we consider to be the primary mechanism at those upper ends which is the outflow via the trabecular meshwork. It does put a damper on the efficacy of our drugs. So whereas timolol doesn't require that you open up to meshwork and all it does is really begin shutting down the amount of fluid being produced.

Annabel Samimy - *Stifel - Analyst*

Is that not a mechanism that Rhopressa had as well though?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Yes, but that not to the same level as timolol does.

Annabel Samimy - *Stifel - Analyst*

Okay. All right, let me just move on to the segmenting of the patients. So, I just want to make sure I understand the significance of that secondary endpoint. What was the purpose of including that secondary endpoint? Does the FDA segment the market like that when they look at drugs in development? And if you are able to change the endpoints for Rocket 2, how does that change the powering of the trial?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

So, both of those -- both of those are good questions. I'm going to have Brian sort of deal with that. So, the FDA doesn't require that we do this but don't forget we did a similar thing with the original Rhopressa study, Phase 2 trial where we looked at above and below 26 millimeters of mercury. So, what we wanted to do was to see whether that difference continue, meet the difference meaning that as we lowered the patient's entry pressure, that our efficacy continue to improve or worst case didn't change because we knew the timolol would. So, that was the original intent there.

But let me turn it over to Brian, he can answer the balance of your question.

Brian Levy - *Aerie Pharmaceuticals - Chief Medical Officer*

Yes, so hi Annabel, so what Vince just said is correct. I mean we're looking at a drug that is unique. It's got two unique activities in terms of its trabecular outflow and EVP and we're learning about the activities of these mechanisms and I think this trial is another trial that we've learned from but we also knew that we wanted to see what happens at lower baseline.

And so we did put that 24 -- less than 24 millimeter analysis into the statistical analysis plan ahead of time because we knew we wanted to see that. So in terms of Rocket 2, we're analyzing right now we haven't locked the database of course and we haven't finalized the statistical analysis plan.

So we are taking a good look at the patients, all fully enrolled and we're looking at what percentage of patients that has been enrolled fit into the below 24 and we will work out the power and the sampling size from that and estimate whether we have sufficient patients and power to analyze it at that level.

Annabel Samimy - *Stifel - Analyst*

If you don't, can you enroll more patients?

Brian Levy - *Aerie Pharmaceuticals - Chief Medical Officer*

Yes, we can.

Annabel Samimy - *Stifel - Analyst*

Okay. And then just on that last point of -- so how does the FDA sort of the segment the market, do they -- do they look at drugs for different parts of the market like that in terms of development programs?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

No, they actually don't. The endpoints are the same and what they require for approval is the same and so basically you always get the exact same label which is for the ocular hypertension over the treatment of glaucoma. What they do is in the clinical study section where you write up the results of your clinical trial. It will simply show the range of the IOPs or the average IOP if you will that were studied in the trials.

And so as you'll -- for illustrative purposes and you take a look at the Lumigan labels, the higher concentration of Lumigan, rhe original trials were done with an average IOP of about 26 millimeters. Then when they drop the concentration to the lower one, they actually dropped the average IOPs by 3 millimeters. And so they further constricted the range that they allowed the patients to commit on and so -- but if you look at the labels, they're all identical except for the clinical section.

Annabel Samimy - *Stifel - Analyst*

Okay. Can I ask one last question on the discontinuation rate, it seems like overall it's about 10%, 11% but when you segment between the different arms, Rhopressa looked to be about 17% and timolol which is on 7%. So can you speak to the difference and the discontinuation, what's that have to do -- is that related to the hyperemia that you're seeing?

Brian Levy - *Aerie Pharmaceuticals - Chief Medical Officer*

Right, so interestingly it wasn't. The discontinuation rate between the two groups was relatively similar and it was really distributed to a number of things. The -- we look at two things of course. We looked at the ocular effects and we looked at systemic effects and any AEs that occur that could potentially cause a patient to end the study.

And as you can see there's adverse events, protocol violations, withdraw of consent, lack of efficacy and investigative decision, and these are pretty well-distributed. In fact, again, these are top line data but as I look through adverse events, the terminations due to that, there was actually only one patient that terminated from each of the arms for hyperemia. So even though that was the adverse event that we saw the most, didn't cause patients to exit the study.

Annabel Samimy - *Stifel - Analyst*

Okay, great thank you.

Operator

Thank you. Our next question comes from the line of Corey Davis with Canaccord Genuity. Your line is now open, your question please?

Corey Davis - *Canaccord Genuity - Analyst*

Yes, thanks very much. I think I know the answer to this but could you ever get approval of Roclatan without having a separate monotherapy approval for Rhopressa?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Yes, if you take a look at the combination guidelines from the FDA, it does envision that what you have to be able to do is show that your drug actually -- the drug you're comparing i.e. in this case Rhopressa that it actually decreases pressure. And I think we have generated quite a bit of data to show that it really does and so the guidelines allow for it.

Corey Davis - *Canaccord Genuity - Analyst*

So, are you saying that it's a possibility that you got enough data to show that for example hypothetically you beat placebo and therefore you decrease pressure, so in your Roclatan studies, as long as you beat the individual components, that might be enough for approval without having your monotherapy alone approved?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

If you look at the current FDA guidelines, that's exactly what it says.

Corey Davis - *Canaccord Genuity - Analyst*

Okay, it will be interesting, there's a separate path to getting one of these to market.

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Yes.

Corey Davis - *Canaccord Genuity - Analyst*

...in the event that you couldn't get this one in. And then just to be clear --

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

No, we're not convinced that we can't get this one in as we think that the drug does work. It's just in this particular case, you know, had we just simply changed the upper entry criteria to drop it by a millimeter, we would be having this totally different call here.

Corey Davis - *Canaccord Genuity - Analyst*

Well that was -- that brings me to my second question, so even if you drop it to 26, you hit the 9 out of 9 at 1.5 but it wasn't clear to me that you hit the majority at 1.0. You said they were numerically there but did they really hit the criteria for non-inferiority?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Yes, so the non-inferiority was hit at all 9 at below 26 and then we had --

Corey Davis - *Canaccord Genuity - Analyst*

Would the primary endpoint had them hit if both upper entry criteria was 26 millimeters of mercury.

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Yes.

Corey Davis - *Canaccord Genuity - Analyst*

Okay. It didn't seem the way you worded it that that was the case but I got the answer.

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

You did.

Corey Davis - *Canaccord Genuity - Analyst*

In thinking about a different way to design a trial, is there a different comparator that you could use besides timolol?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

If we had missed huge or nothing worked, let's say we were only dropping pressure 2 or 3 millimeters, then we could always consider using an alpha-blocker or something that decreases pressure not quite like timolol does in this particular case when it's IOP-driven. And again with just a 1 millimeter difference at the top end of the range, by dropping it we could have hit it. It doesn't seem like we need to go to the extreme of changing comparators at this point.

Corey Davis - *Canaccord Genuity - Analyst*

Okay. And then last question, I get the explanation for the drifters but one of the big broader questions going into the study is does the drug lose efficacy over time. And I think the answer is yes and you're saying but only in certain patients for which we have plausible explanation. But if you step back and ask the bigger question, does the drug lose efficacy over time, is the answer yes or no?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

The overall drug itself doesn't appear to lose efficacy over time. We do have patients where the only reason we called them drifters because they happen to respond on the first pay and then not thereafter. And so, we're not sure whether it's just as soon as the drug hits, it sort flushes something through and so it works great and then after that for whatever reasons, it just seems to lose its effect but it looks like and it's pretty -- it's so consistent when as you're coming down that pressure line that the lower the pressure, the less drifters we have and it's again by the time we get to 24, it's no different than for timolol.

So, we take it the drug continues to work on the majority of the cases and by the way, the way this will work out in a doctor's office is they bring these patients back, these glaucoma patients back every six months. And so even though they're -- they're going to be aware that there's going to be some patients who don't respond well to this drug, we'll obviously have to remind them of that when they stop prescribing this drug once we get it approved.

And what will happen is, they will bring them back and if he happens to be what we now described as one of these drifters, then you go add on another med or take him off Rhopressa and use something totally different. But, we still think it's pretty viable for -- at least in this study based on the studies where 80% of the patients did fine.

Corey Davis - *Canaccord Genuity - Analyst*

Other than the b.i.d. arm, is there any other thing that we could look forward to that's different about Rocket 2 that might be encouraging?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

For safety components, we'll have three readings for safety once we get past the 90-day efficacy component which is what we'll report out in Q3 but at each of those safety visits we will also take a look at the 8:00 a.m. pressures. So, we'll continue assessing the viability of the drug as part of that safety program.

Corey Davis - *Canaccord Genuity - Analyst*

In terms of like the design, the enrollment, everything else was at the -- for the 90-day efficacy is virtually the same as Rocket 1 right?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Yes.

Corey Davis - *Canaccord Genuity - Analyst*

Okay, all right, that's all I had, thanks.

Operator

Thank you. Our next question comes from the line of Caroline Corner with Cantor Fitzgerald. Your line is now open, your question please?

Caroline Corner - *Cantor Fitzgerald - Analyst*

Hi guys, sorry about the disappointing top line. I have a question about the Rocket 2 trial and Rhopressa in general, you said that the pressures from 20 to 26 millimeters are about 80% of the market. So assuming FDA let's you move forward with another trial and you can address that 80% of the market in the 20 to 26 range, aren't most of those people with glaucomas in that range already on PGAs?

And then if your reason for the trabecular meshwork getting shot in the higher pressures, isn't over time that also going to affect the PGA patients that are in the 20 to 26 range and what I'm trying to get a handle of is, if you do get approval in that 20 to 26 millimeters of mercury range, how much of that 80% is actually your addressable markets?

Thomas Mitro - *Aerie Pharmaceuticals - President, Chief Operating Officer*

Sure, this is Tom Mitro, let me try to address that. So if we did get approval and if the FDA took the highly unlikely tact of limiting our label that is putting a range of pressures in our indication or something along that line. I don't think it will have an inventory effect on our commercialization because just as you said, the vast majority of people are under 26 to begin with.

They may already be on a PGA and they just need a second drop which is ideal for again for Rhopressa because if the prostaglandin has taken them down from, pick any number you want, from the 25 down to 20. And now they need a second drop, that's right again in our sweet spot, that is -- as the study begins to point to again, the lower IOPs is where our products certainly excels. So, we don't think it limits -- would limit the marketplace at all. We just think it happens to be right where our sweet spot is and we think that's the majority of the market.

Caroline Corner - *Cantor Fitzgerald - Analyst*

Okay. And then in the press release you said, with Rhopressa, you could expect to file an NDA by the end of 2016, can you just walk us through what has to happen for that to occur? I'm assuming it includes the 90-day Rocket 4 trial and then pretty near term successful communications with FDA?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

That's exactly what it entails. So the fact that we'll have Rocket 1 and 2 completed, we'll have incremental data from Rocket 3, assuming that it would go at risk, we may be able to start a trial, Rocket 4 here over the next few months. It will be the same protocol design as what we currently have for Rocket 1 and so we can get that into the market and basically at risk prior to seeing Rocket 2 results.

And so assuming all that moves forward and we continue to have positive discussions with the FDA, then that means that Rocket 4 should be done some time in the middle of next year. But in the meantime, we could write the balance of the NDA and so -- so that the only thing that's left is the incremental or the final Rocket 4 data results as well as integrating the database. And so, that's why we feel comfortable that given the timelines that we can still get an NDA filed before the end of next calendar year.

Caroline Corner - *Cantor Fitzgerald - Analyst*

Okay and then are your going to present the intend to treat data as well?

Brian Levy - *Aerie Pharmaceuticals - Chief Medical Officer*

Yes, so as soon as we get all of our tables for all of the analyses, we will have the intent to treat but the top line or currently the intent to treat looks similar to the per protocol.

Caroline Corner - *Cantor Fitzgerald - Analyst*

Okay. Thank you, that's all I have.

Operator: Thank you. Our next question comes from the line Difei Yang with Brean Capital. Your line is now open, your question please?

Difei Yang - *Brean Capital - Analyst*

Yes, thanks for taking my question. I'm sorry about the Phase 3 results. So just a couple, I assume that you would not have any additional opportunities to modify the protocol of Rocket 2 is that right?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Well modifying the protocol is correct, right, because we've already finished the enrollment. So what we're talking about modifying is what is the final endpoint and so -- and that's what we were describing earlier.

Difei Yang - *Brean Capital - Analyst*

Okay.

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

But not the protocol itself.

Difei Yang - *Brean Capital - Analyst*

Okay, okay. And then just a hypothetical scenario. Let's say Rocket 2 you have it positive and now Rocket 1 you have it negative, so is it a sure thing that FDA will want to see a Rocket 4 or in the case where you have the one positive, one negative, there might be some leeway?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

No, I'm not sure that I would go to the bank with something like that and that's why we would always want to -- that's why we're considering starting a Rocket 4 trial at risk but certainly that won't be the first time that the FDA has approved a drug where one study worked very, very well and the other one didn't work quite as well but there was enough indication in the quote study that didn't work so well, that the other drug did work Okay.

It's just either luck of the draw or some other factor that played in there. And obviously, this is a little bit dated but that's how RESTASIS got approve based on a subset analysis. It was not pre-specified and by the way they didn't have either study work but both of them were sort of afterthoughts assessments and they got approved. So, it is possible, you can't discount that but at the end of the day, our job is to make sure that we move this thing forward, so that's why we're considering just moving forward with Rocket 4.

Difei Yang - *Brean Capital - Analyst*

Okay, okay, thanks. And then my other question is that, so it seems like we're seeing lots of efficacy at least on the subset of the patients, would you conclude that's basically a class effect?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

You know we haven't - the honest answer is I don't know. We had to -- we had to take a look at some of the data for example on the [Cal] product. It seems to hold its efficacy pretty well but we don't have access to the actual data, so I don't know whether that was based on some other assessment or not. So, we got to take a look at that.

Difei Yang - *Brean Capital - Analyst*

Okay and now that we know by day 90 we see lots of efficacy, how likely will the FDA based on this data request you to run a longer trial?

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

We're going to be looking at -- but again it's a loss of efficacy with the subset of the patients and so -- which seem to sort of go away to noise level by the time you bring the IOPs down to 24. And so, we'll have further efficacy data all the way through 12 months when we finish the safety. So, I don't think that the -- the FDA can always do something but we just don't think it's likely that they'll do anything prior to seeing that data.

Difei Yang - *Brean Capital - Analyst*

Okay, all right, thank you.

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Yes.

Operator

Thank you. I'm showing no further questions on the phone queue at this time. I would like to turn the call over to Dr. Vince Anido, Chairman and CEO for final remarks.

Vicente Anido - *Aerie Pharmaceuticals - Chairman, CEO*

Hi guys, well we try to be as open as possible like we promised we would be with the data and we're not pleased at all with the ultimate outcome here which was being inferior to timolol at the upper end of the range of 27 millimeters of mercury and on down but we obviously are very pleased with the rest of the data analysis that we completed. Some of them pre-specified and other pre-specified and others not.

We do think that we have a drug that it's worth pursuing and we certainly have the team in place and cash available in order to be able to move this drug forward and so we certainly look forward to the activities over the next few months and obviously the next major data point would be the unblinding of Rocket 2 in Q3.

So, thank you for listening and have a good evening.

Operator

Ladies and gentlemen, thank you very much for your participation. This does conclude the program. You may now disconnect.