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VRP.L - Q1 2018 Verona Pharma PLC Earnings Call

EVENT DATE/TIME: MAY 08, 2018 / 1:00PM GMT



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PRESENTATION

Stephanie Carrington - *ICR, Inc. - Managing Director*

Good morning or afternoon depending on where you are and welcome to today's call to review Verona Pharma's results for the first quarter ended March 31, 2018.

On this call, I'm joined by Jan-Anders Karlsson, Chief Executive Officer; and Piers Morgan, Chief Financial Officer. I trust you have seen the press release that was issued this morning before markets opened. It includes the results for the three months ended March 31, 2018, as well as the operational update. If you have not, the press release is available on the Investor Relations portion of Verona Pharma's website.

On today's call, Jan-Anders will provide a clinical development and business update for the first quarter 2018. Piers will then review the company's interim financial results for the three months ended March 31, 2018. We will then open the call to your questions and expect this call to last approximately 60 minutes.

As a reminder, the conference call is being recorded and will be available on Verona Pharma's Investor Relations website shortly following the conclusion of today's call.

During the call today, the team will be making forward-looking statements and we remind you of the company's safe harbor language. All statements that do not relate to matters of historical facts should be considered forward-looking statements, including but not limited to statements regarding RPL554 as a potent bronchodilator and anti-inflammatory agent; our ability to provide a promising therapeutic effect through the delivery of RPL554; the timing of topline data for our ongoing clinical trials; changes in our clinical development plans based on additional data; and the potential for certain formulations of RPL554 to address larger markets; and our plans to explore these formulations in cystic fibrosis and other respiratory indications.

These forward-looking statements are based on management's current expectation. These statements are neither promise nor guarantees but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from our expectations expressed or implied by forward-looking statements. Any such forward-looking statement represents management's estimates as of the date of this conference call. While the company may elect to update such forward-looking statements at some point in the future, it disclaims any obligation to do so, even if subsequent events causes view to change.

With that, I will now turn the line over to Jan-Anders. Go ahead.



Jan-Anders Karlsson - Verona Pharma plc - CEO

Thank you, Stephanie. It's a pleasure to have the opportunity to provide you with the clinical development and business update today. We're very pleased with the continued progress and development of RPL554, unique, first in class inhaled, dual inhibitor of the enzymes phosphodiesterase 3 and 4, designed to have bronchodilator as well as anti-inflammatory properties. It is currently being developed for the treatment of COPD patients and for the treatment of patients with cystic fibrosis.

We report a very positive data from the most important clinical trial today with RPL554 in late March. This Phase 2b dose range in clinical trial of nebulized RPL554 for maintenance treatment of COPD was completely fostered and planned and data reported ahead of schedule.

As a reminder, this four-week double blind placebo controlled parallel group Phase 2b multicenter European study evaluated efficacy, safety and dose-response of nebulized RPL554 administered twice daily as a maintenance treatment in 400 patients with moderate to severe COPD.

There were four dosing arms of RPL554, 0.75 milligram, 1.5 milligram, 3 milligram, and 6 milligram in this study, in addition to placebo, and patients were required to withhold use of regular long-acting bronchodilator therapy for the duration of the study.

The study method's primary endpoint with RPL554 producing a clinically and statistically significant improvement in peak force expiratory volume in one second or FEV1 at four weeks in patients with moderate to severe COPD compared to placebo. Furthermore, the peak FEV1 was significantly improved at all time points over the four weeks of dosing, with the last dose being as effective as it was on the first day.

The key secondary endpoint measured COPD symptoms and quality of life during the trial. The clinically meaningful and statistically significant progressive improvement in COPD symptoms over the four-week treatment period support the potential clinical benefits of RPL554 for the treatment of COPD. Importantly, RPL554 was very well tolerated in these patients with adverse events being similar to those in the group of patients that received placebo.

RPL554 continues to be well tolerated in our clinical trials conducted to-date and it has not been observed to result in the gastrointestinal or other side effects normally associated with PDE4 inhibition.

This was the largest and longest trial with RPL554 completed to-date. We are in the midst of conducting an in-depth analysis of the data set from this trial and we plan on disclosing a broader dataset at the European Respiratory Society International Congress to be held in the middle of September in Paris.

We also plan to conduct a further Phase 2a clinical trial to evaluate RPL554 when dosed in addition to LAMA/LABA therapy or triple therapy compared to placebo. We anticipate starting this study in the third quarter of this year with topline data expected in the first of 2019. And currently, we're developing RPL554 on both pressurized metered dose inhaler or PMDI, and dry powder inhaler or DPI formulations for the maintenance treatment of patients with moderate to severe COPD.

Estimated in the United States, approximately 4.5 million patients with moderate to severe COPD use inhalers for maintenance therapy. Successful development of an MDI or DPI formulation of RPL554 for moderate disease would greatly expand the addressable market for the drug and represents a multibillion dollar potential opportunity. Development of these new formulations is progressing according to plan and we now expect to complete the clinical studies for RPL554 with this formulation in the second half of 2018. Followed by the first clinical trials in healthy subjects or patients with COPD that are targeted to commence in the first quarter of 2019.

Turning to cystic fibrosis, we reported positive topline data in early March from the Phase 2a clinical trial evaluating the pharmacokinetic, PK, and pharmacodynamics, PD, profile effect on lung function and the tolerability of RPL554 in cystic fibrosis patients. The trial demonstrated that the investigational therapy has a favorable PK and PD profile, with single doses achieving statistically significant with less than 0.05 increases in average forced expiratory volume in one second in patients with cystic fibrosis. This data consistent with our other findings on the PK and PD profile in COPD patients and provide a solid foundation for further development of RPL554 for the treatment in CF.



The progressive development of nebulized RPL554 towards start of Phase 3 studies. We focus on the maintenance treatment in moderate to severe COPD. The preliminary analysis of the market research we have conducted indicates that there's indeed a very high, unmet medical need for a novel drug that can be used as an add-on treatment for the standard of care for these patients. This plan to progress the development of RPL554 takes into account our market research that [could add to] our clinical data that will involve more than 730 subjects in 12 different studies to-date, with anticipated outcome of the clinical add-on study that we will be starting in the first quarter this year, and the overall commercial opportunity.

We will continue to keep the market informed as these plans progress. I will now turn the call over to our CFO, Piers Morgan, who will provide a financial overview. Piers, please.

Piers Morgan - Verona Pharma plc - CFO

Thank you, Jan-Anders. Good day everyone and thank you for joining the call today. I will provide a brief recap of our financial position, our results for the three months ended March 31, 2018, as well as our financial outlook. I want to refer you to the press release that we issued this morning and the 6-K that we filed. The release includes income, balance sheet and cash flow statements for the three months ended March 31, 2018.

Given the way our headquarter is in the UK, our financial results are in British pounds. We have included a translation to U.S. dollars using the period end exchange rates on March 31, 2018, for your convenience.

Turning to the income statement, our operating loss for the three months ended March 31, 2018 was GBP5.9 million or \$8.2 million compared to GBP4.1 million for the prior year period. The loss after tax for the period was GBP15.2 million or \$21.4 million for the three months ended March 31, 2018 compared to GBP1.9 million for the prior year period.

Operating expenses increased due to an expansion of research and development activity. This represents a loss of 14.5 pence per diluted share or a loss of \$1.63 per ADS for the three months ended March 31, 2018. This compares to a loss of 3.7 pence per diluted share for the prior year.

The fiscal comprehensive loss was calculated as follows. Research and development costs for the three months ended March 31, 2018 were GBP4.4 million or \$6.2 million, an increase of GBP1.3 million compared to GBP3.1 million for the prior year period. Increase was predominantly attributable to GBP0.5 million increase in clinical trial expenses relating to the continued activities of the Phase 2b clinical trial of RPL554 in 2018.

In addition, we increased spending on contract manufacturing, another formulation work by GBP0.5 million, but this was partially offset by a decrease in preclinical development by GBP0.3 million. Our share-based payment charge increased by GBP0.4 million as we issued long term incentives to our staff to drive development of RPL554.

General and administrative costs for the three months ended March 31, 2018 were GBP1.5 million or \$2 million, an increase of GBP0.5 million compared GBP1 million for the prior year period. This increase includes an increase of GBP0.3 million in our share based payment charge.

Finance income for the three months ended March 31, 2018 was GBP0.2 million or \$0.2 million compared to GBP1.8 million for the same period last year. The decrease in finance income was primarily due to an increase in the fair value of the warrant liability during the first quarter of 2018, which was recognized as a finance expense, compared to a decrease in the fair value of the warrant liability in the same period last year, which was recognized within finance income.

Finance expense for the three months ended March 31, 2018 was GBP10.3 million or \$14.5 million compared to GBP0.2 million for the same period last year. The increase was due to an increase in fair value of the warrant liability of GBP9 million arising from changes in the inputs and other underlying assumptions for measuring the liability of warrants, if used in the July 2016 placements, including the price and volatility of our ordinary shares. The increase in the fair value of the warrant liability during the period contrasts with the decrease in the same period last year, which was recognized within finance income.

Taxation for the three months ended March 31, 2018 amounted to a credit of GBP0.8 million or \$1.2 million, an increase in the credit amounts of GBP0.2 million from the prior-year period. The credits were obtained at a rate of 14.5% of 230% of our qualifying research and development expenditure, and the increase in the credit amount was primarily attributable to our increased expenditure on research and development.

We ended the first quarter of 2018 with GBP72.6 million or \$101.9 million in cash, cash equivalents and short term investments, which comprised cash deposits of maturity of more than three months. This includes the net proceeds from our NASDAQ IPO completed in April 2017. Our net cash used in operations for the three months ended March 31, 2018 was approximately GBP6.2 million which reflected an increase in operating costs driven by higher research and development costs.

We expect that our existing cash, cash equivalents and short term investments will enable us to fund our operating expenses and capital expenditure requirements through the end of our Phase 2a and 2b developments of nebulized RPL554 for the treatment of COPD, and our pivotal concept studies of DPI and MDI formulations of RPL554 for the treatment of COPD, as well as our Phase 2 development of nebulized RPL554 for the treatment of cystic fibrosis.

And with that, we'd like to turn the call back to the operator for questions.

QUESTIONS AND ANSWERS

Operator

Thank you. (Operator Instructions) We shall now take our first question from Alex Schwartz of Stifel. Please go ahead, sir.

Alex Schwartz - Stifel - Analyst

Just looking at your most recent slide deck, you indicate you now plan on pursuing RPL554 and GOLD guidelines C and D population first with potential label expansion in the B population second. Maybe can you talk to what KOL physician feedback is on RPL554, it's value proposition in this setting, and why you're deciding to pursue these later stage patients first?

Jan-Anders Karlsson - Verona Pharma plc - CEO

So, hi, Alex, thank you. It's Jan-Anders. Thanks for the question. Did I understand right, you were saying that we position it for the more severe patients first and then expand to milder population?

Alex Schwartz - Stifel - Analyst

Yes, I'm curious what -- your KOL feedback, your physician feedback, what helped you -- what informed you to this decision?

Jan-Anders Karlsson - Verona Pharma plc - CEO

Yes, great, thank you. So, it is -- it is correct, we've had lots of discussions with physicians and KOLs, and actually payers also. And as we knew before, now has become more confirmed, is that there really is a large, large patient group of COPD patients that are already on maximum treatment and they still continue to progress and have symptoms and, of course, exacerbations, and there's no further therapy for them. That is the group of highest medical need among the COPD patients.



And we think that we have showed with RPL554, this new mechanism of action, it's a very nice add-on treatment. It gives profound extra boost to lung function, reduces symptoms both in short term treatment and in long term treatment, as we have shown, and we think this will really be helpful to patients with the most severe disease.

We think also it is clearly the positioning where there's little competition as we understand it today from the approved product, and we think that is for us a very appropriate way to start the -- towards the Phase 3 in the clinical -- end-stage of clinical development with RPL554.

Having said this, of course, if we have a contribution to these patients that really changes as we hope the situation, quality of life. Of course, we also then afterwards, we'll see that there is an opportunity to move it into earlier stage of treatment. Why would you want to wait if you have an opportunity to have this add-on treatment already at an earlier stage, I think that's a natural expansion into that stage.

I don't think you were alluding to metered dose inhalers or dry powder inhalers, which is of course a different population. So, the first is the nebulizer, which fits nicely with the patients' (inaudible) almost or prefer at least route to delivery and form of delivery, which a nebulizer could have -- for the end-stage patients obviously who are in hospital. Whereas the outpatients with either moderate disease of course will prefer a pocket inhaler. And that's where we think our drug RPL554 can really help a much wider patient population, by providing it in this much more accessible form. This is what we someday will have to do in partnership. But certainly, we'll do the first step, so clinical development into Phase 1, Phase 2, and Phase 2b potentially with -- both in MDI and also DPI over the next years.

Alex Schwartz - *Stifel - Analyst*

Okay, thank you.

Jan-Anders Karlsson - *Verona Pharma plc - CEO*

Does that answer your question?

Alex Schwartz - *Stifel - Analyst*

Yes, that's very helpful. And then just a second question on something that you just touched upon. In terms of a potential RPL554 partnership, maybe can you talk to what stage in clinical developments, as well as what formulations are most interesting to pursue a partnership? What are you looking for in a partner and maybe what considerations are most important to you?

Jan-Anders Karlsson - *Verona Pharma plc - CEO*

Yes, so great question, thank you. I think it's important to clarify that there are segments of the population of COPD patients that we can address as say a smaller and growing company, and that is clearly the patients with the most severe need and would maybe even prefer to use a nebulizer.

I think in the nebulized form, it is also most advanced in our studies, it's the one that can be taken forward into Phase 3 and maybe even through commercialization in a segment of patients. It's not a small segment, it is a very specific segment, which has its own dynamics around it and a set up will be helpful actually for the company.

The partnership is where we -- with an MDI or DPI actually cannot compete for the Phase 3 studies and certainly not [commercialization] in U.S. or globally. That's where we would need a company with the service infrastructure, a commercial sales force of the appropriate training and relevance that can help us to actually get the compound through the last stages of development into the market.

We really need somebody with expertise in the area, also with the commercial infrastructure in place, and that would like to participate in helping us to drive this new (inaudible).



That relevant timing for that is when we have developed more data in clinical trials, we created more value, we have a better understanding about the dosing, the dosing frequency and the positioning of the metered dose inhaler or DPI. So that is not happening in 2018, and we may take a year or two before we are in the right position.

Operator

We shall now take our next question from Liana Moussatos of Wedbush Securities. Please go ahead.

Liana Moussatos - Wedbush Securities - Analyst

For Verona to go after the severe COPD patients with the nebulized formulations, you mentioned starting with Phase 2 on top of LAMA and LABA. What are all the steps that you need to do for Verona to start a Phase 3 in this population with the nebulized formulation?

Jan-Anders Karlsson - Verona Pharma plc - CEO

That's a great question, how long are you going to continue to try and get into Phase 3. So I think actually the -- in a way, we have enough data today to understand how it behaves and of course as an add-on to many of the available therapies out there. What we would like to clarify is the size of the response in addition to patients already on double or triple factors, LAMA/LABA or maybe LAMA/LABA/ICS. So we believe that there will be a response and we'll be surprised otherwise.

And what we would like to understand before we size the Phase 3 studies is what is the magnitude of the response and how should we think about that in terms of sizing the Phase 3 studies, the number of patients which we'll see in various Phase 3 studies that we envisage.

Apart from that, I do believe that we -- we will have to understand lower doses of the nebulized formulation, as you noted in the four-week study, the four doses that we tested between 0.75 milligram and 6 milligram, they all seemed to be at the -- actually in reality, when you look at the totality of the data, the lowest dose actually was not so robust as it would appear from the published figures that we've shown you.

So we do think that actually it's a nurturing dose response and we may need to have a small extra additional short, short study to confirm that if FDA would like to see that shorter data. Otherwise, I think it's more about creating the right package around CMC, around presentation form. Having enough data to discuss with regulatory authorities about dosing frequency endpoints. And most importantly, the patients that we want to select the treatment in the Phase 3 study, and as our plan and what we have mentioned, we expect that we would be in that position next year, that's later in the [year].

Operator

Our next question is from Yatin Suneja of SunTrust. Please go ahead.

Yatin Suneja - SunTrust - Analyst

Maybe just Jan-Anders, could you maybe provide a little bit more detail on the LAMA/LABA trial, the size, the duration of that trial? And also on another point, we have not seen much data on how RPL554 works on exacerbation, or how it helps with exacerbation. So could you comment on one, if that's something you might be looking at in the LABA/LAMA trial, and what might be a reasonable duration to capture effects on exacerbations?

Jan-Anders Karlsson - Verona Pharma plc - CEO

Yes, thank you, Yatin. Hi, thank you. That is a good -- good questions. We have not on purpose announced all the details in the LABA/LAMA trial. Suffice to say that it will be quite similar to the study we did as an add-on study to Spiriva or Tiotropium, which was a short study in a moderate number of patients and it was a cross-over study. We'll have a similar design. We will measure similar parameters. We want to understand the effect on large airways, sputum onset and the other measurements we had in that study. But of course, we want to increase the number of subjects that are being crossed over in the three different treatments, two doses and [we'll try again with] placebo.

So we will increase the number of subjects in the study. But otherwise, it will be very similar to the one we did. And the reason for doing it that way is twofold, one, is that we think a short waiting period on lung function will translate into a very similar effect after prolonged period, based on the studies we have done so far. So, we think that's represent.

We also believe that the effect on smaller airways or residual volume, as we have seen in two previous studies, that's the add-on effect, also should translate into an improvement in symptoms, and that's of course what we are now demonstrating in the four-week study. So I think [already a] smaller studies can give us good guidance on what you would expect in a much larger and much longer studies. So that's the reasoning behind doing a shorter and sharper study as an add-on now to LAMA/LABA and triple therapy.

For the other question you had I believe was around exacerbations and are we measuring them or not in the study. So actually, the study is far too short. So see if it's less than half a year to a year, it is usually not acceptable and actually FDA would want to see a year-long study. And I think you would need, based on historical data from other compounds and studies, you will need probably six months data at least to be able to catch a change in the number of exacerbations of quite a large number of COPD patients. Because on average in these studies, they are actually not that frequent. So over a year is maybe an exacerbation per patient. So we are not doing that.

And actually the strategy is to -- if we are going to hit the market as soon as possible, we'd like to do it on the basis of an approval around a bronchodilator effect, improvement in lung function and reduction in symptoms, and we also want to have evidence of secondary effects to inflammation, which would be for example improvement in symptoms as we said and not a (inaudible) the totality could be an interest in and clinically meaningful addition to a standard of care.

So that's how we would like to structure the first step. Of course, we need to discuss this with the FDA and other regulators, and we need to get some agreement, of course. But this is our expectation today.

Exacerbation studies, of course, they are important. It will probably not change the price much, but it will certainly change the uptake and widen the accessibility of the compound. So, certainly that's a very important step, either during the Phase 3 for the first indication label, or perhaps once we are on the market. So, we haven't forgotten about it, but it's a very long and very costly [undertaking] and we really want to delay that until we are well underway with the first set of studies (inaudible) first approval.

Does that answer your question, Yatin?

Yatin Suneja - SunTrust - Analyst

Yes, very comprehensive, and I appreciate that. Maybe just touching another property of therapy in COPD, what is the significance of trough FEV1 level? How important of a measure that might be for any novel therapy, do you think that's important to get in order for an approval, just trying to understand. Because I think in the previous trial, I understand it was a shorter trials, so there was not much separation there on the trough FEV1 level, but just trying to understand the significance of that?

Jan-Anders Karlsson - Verona Pharma plc - CEO

Yes, thanks, good question. So indeed, we have actually in all our trials of three days or longer duration and some are actually also [do] single-dose studies, and when we have measured it, we have seen a good effect of at least one of the doses or a couple of the doses on trough in every study.

This time, we did not see an effect consistently. There was statistical significance but it was not distributed in a dosed response way that we had expected, and that's why we needed to understand it better before -- and so we can communicate our message exactly around what the data was, which doses were active, et cetera. So, that's why we [phrased] the doses were, and there will be more data coming.

I think what's -- so your question is good. For almost all, if not all over the last several years now, LABAs and LAMAs bronchodilators that have been approved, they have all been studied almost without exception on no -- patients with no background therapy. So, of course, FDA and other regulators would expect that you have total coverage of 12 hours or 24 hours, and then most important thing is to prevent the patients from losing lung function during that time, if as a first-time treatment or using a new compound.

So, that's how they have been developed. We have a different approach. We would like to study the patients that will need a newer medication. Many patients may or may not need the fifth, or the sixth or the seventh LAMA. But what they need is a new and different treatment, and we think RPL554 as an add-on treatment offers quite something important for the patients when there are no alternatives anymore. It's, of course, later stage or end-stage COPD.

And we therefore also believe that we can have a discussion with the FDA on which is the most appropriate measurement of lung function, FEV1, so you can measure peak, which has been used in approvals, also you can measure AUC, which has been used in approvals, or you can measure trough, which also have been used in approvals. But nothing has been approved in this setting, so I think it's a good rationale to having an open conversation with regulators on what is the better endpoint.

In addition, we of course believe that we will have a good effect on symptoms. And symptoms is a -- because of "exacerbation," so it's very clear that the more symptoms and the worse patients get, they are more likely to have (inaudible) exacerbation. So, we think there's a direct link and we think that would also be an important endpoint to capture in this severely sick patients, so really cannot afford to have more frequent exacerbations on what they have already (inaudible).

So, that's why we believe it's of course an important endpoint for first-line treatment, but not necessarily for add-on treatments in patients that have no alternative options.

Does that, Yatin, answer your question?

Yatin Suneja - *SunTrust - Analyst*

Yes, yes, absolutely, yes. And then, just finally, just one more question, I'll get back in the queue. How are you thinking about the CF development pathway going forward, what you might be doing to maybe accelerate it? Could you just maybe talk about, what the next trial might look like? Thanks.

Jan-Anders Karlsson - *Verona Pharma plc - CEO*

Yes, thank you. So, we like CF, we think it's an important opportunity for the compound; for patients, of course, it's even more. What we saw in the first study, which was just a single dose, was actually an excellent -- excellent in the sense that the compound was absorbed intact and actually also had an effect on [their lives]. So, we had hoped for it, but it was not clear that this would happen.

Now, with the data, I think we are really encouraged to move on to the next step, and then what's the next step. So, first of all, there are two things. One is around a longer exacerbation study or hospitalization study, which would be one, two, three months perhaps in such a group of patients. There are some examples of those types of studies. Or perhaps to do a step-wise approach where we look at some of the anti-inflammatory parameters of RPL554 in the CF patients. Because we do believe that we actually can treat all CF patients, it's mutation agnostic, so different from treatments in development now, around potential (inaudible). And that our anti-inflammatory effects would be appropriate for patients both with the new treatments, but also those that have no treatment options. And that would be an important contributor to wellness of these patients, to be seen of course in [clinical findings].



So, we would like to see that opportunity and we have to discuss now with a focus on first COPD, moving our compound towards or into Phase 3 as soon as possible, and in parallel, but somewhat behind CF -- behind [COPD] also continue with the CF development. I understand the -- both their anti-inflammatory effects in patients with CF, which we think will be the important [part]. The bronchodilator effect is important, but it's probably the anti-inflammatory effect that will be most important in the long run.

So in short, it will be a staggered approach with the CF lagging slightly behind the COPD and moving on to (inaudible).

Operator

We shall take our next question from Patrick Trucchio of Berenberg Capital Markets.

Patrick Trucchio - *Berenberg Capital Markets - Analyst*

I have two. Just first, what's the status of the dose ranging study or the data in COPD that you previously mentioned would have to be conducted or shown to the regulators that there is a non-therapeutic dose of RPL554? Is that data going to be generated in a LABA/LAMA combo study, or will you conduct a separate study to generate that data? And then, secondly, can you tell us what the status is of the search for a new Chief Medical Officer?

Jan-Anders Karlsson - *Verona Pharma plc - CEO*

Yes. Hi Patrick, thank you very much. So, on the first topic, we envisage actually that we should discuss it with the FDA, and ask if they really do believe that they will want to see a lower dose. Because in other studies, we have demonstrated that lower doses are less effective. For example, in an asthma study, a 0.4 milligram dose was clearly less effective than 1.5 milligram or 1.6 milligram. So, we have data to that extent.

We also have on the add-on studies, either a single dose or a three-day (inaudible), 6 milligram was superior to 1.5 milligram. So, it may be that the new baseline treatment of COPD patients, and that's why I think the compound is slightly more efficacious already in lower doses. Whereas if you already have an add-on effect, you can start to see a dose ranging in the doses that we studied here, the 1.5 milligrams and 1.6 milligrams, for example.

So, that I think is the case that we will make. If, and that's why we also mention it, if we still need to prepare and for ourselves do an additional study on dose ranging with a nebulizer in patients with COPD, I think we believe it can be a very short study and a very simple study, and yes, demonstrating the lack or lower effect of lower doses that are nebulized for a day or a couple of days.

This of course needs to be agreed with FDA, if they want to see something. But the lung function effects I think represent all other effects of the compound in a way, in a dose-dependent way. And therefore, that should be also enough to demonstrate the dose-dependency in [the short study]. At least that's the starting position and then we'll have to see with regulatory discussions.

And on the CMO question, so we are searching, we have an executive search underway. We are interviewing candidates and which we have very good candidates, and we are very confident that we'll find a great replacement of our previous CMO, which was very helpful and that it will take a little time for [various] standard reasons as you hire new people to new positions from (inaudible). And of course, we will have to (inaudible) as soon as we all are moving closer to selecting the right candidate. So, clearly this will take a little longer, but the process is well underway and I'm very confident that we'll (inaudible).

Operator

Our next question is from Ram Selvaraju of H.C. Wainwright. Please go ahead.



Unidentified Participant - *H.C. Wainwright - Analyst*

This is [Julian] on for Ram Selvaraju. The topline Phase 2b data on nebulized RPL554 for maintenance COPD were very encouraging. If the DPI, MDI formulation precedes efficacy testing for this indication as well, would you expect a similar study design?

Jan-Anders Karlsson - *Verona Pharma plc - CEO*

Thank you. Hi, Ram, thank you for the question. So, yes, we were very, very encouraged by the topline 2b data that were presented and we continue to be encouraged when we dig further down in the data and will hopefully be able to present that in September at the [RS in Paris].

So I think for the MDI and DPI, it's a little earlier. I can see it at the first studies that we haven't announced yet, that would have to start with single dose, around a standard dose response curve, a low to high dose to understand the therapeutic window, which we expect could be even better, so we think we have an extremely well tolerated (inaudible) in nebulized RPL554. And perhaps even on the inhaler like an MDI/DPI could even further expand the therapeutic window, which will be good.

The step after that would of course be to do longer and larger studies, and I can see that we can piggyback, if you can call it that, on all the data that we have accumulated with the nebulized for, it's the same compound. And you give a smaller dose, but you give more of it directly for the [evidence]. So, in essence, we would expect to see very similar effect and we should definitely very rapidly be able to move from maybe Phase 2a studies into week long and longer studies, and then coming to a Phase 2b study, which perhaps is not so different from the Phase 2b study that we run on now.

But without having discussed it in detail, I will say that, in an MDI and a DPI setting, it might well be that we could study those patients with no background treatment, as well as patients with some background. Because at that stage, we would have learned so much more about the compound that I think we'll be comfortable to position it much more closer to their commercial position and when we do the Phase 2b studies for the MDI and DPI.

Unidentified Participant - *H.C. Wainwright - Analyst*

I see, that's helpful. And just to jump back to the nebulized formulation, would you expect any changes in endpoints in pivotal testing of RPL554 for maintenance COPD?

Jan-Anders Karlsson - *Verona Pharma plc - CEO*

The endpoints, you meant for pivotal trials?

Unidentified Participant - *H.C. Wainwright - Analyst*

Correct.

Jan-Anders Karlsson - *Verona Pharma plc - CEO*

Changes in endpoints. Yes, I think we -- actually, there is no change in the endpoints, because we have studied all these endpoints in all our trials. Actually, we are publishing some of the data, we have already published it on poster, so we do have data on (inaudible) on area under the curve and trough. And every other way you can measure lung function in these patients. So, from that perspective, we will continue to measure in a way that we have done or before, and that everybody else is doing it. So, I think that's pretty straightforward.

I think it's more from the point, as I mentioned earlier that, the patients with end stage or very late in disease progression could expect to see probably a slightly different effect of an add-on compound -- when you add it on to everything else that's already out there. And that's why I'm saying that perhaps we shouldn't be so dogmatic and view these patients as the moderate patients with no background treatment as everybody else has gotten the approval of bronchodilator drugs.

And the other aspect is of course we have -- we have the bronchodilator and we also have the anti-inflammatory effect, and we want to get the composite - not a composite as in the true meaning of the word, but we want to capture both aspects in our endpoints so that we can also use it in future commercial discussions. And that's why I'm saying that for us, it's important not only to make some trivial copy of what we've done before in a different setting, but really together with regulators to understand what's the most appropriate measurements of how these patients feel and how they have to improve.

And actually, we do think that symptoms leading to exacerbations, and of course, on top of that also being improvement in lung function are all important factors that needs to be put into a trial to come up with the right compound. Obviously, we live in a regulated world, we'll have to have these discussions with the FDA, but I think there's plenty of evidence to support that there is a new way for trying to [conduct] -- a new way of treating these patients which we think this is a unique opportunity.

Operator

Thank you. (Operator Instructions) We shall take our next question now from Naveed Siddiqi of Andera Partners. Please go ahead.

Naveed Siddiqi - Andera Partners - Analyst

Just a clarification question. When you say the next study is at LAMA/LABA add-on or LAMA/LABA/ICS, do you mean you are going to test both or one of those?

Jan-Anders Karlsson - Verona Pharma plc - CEO

Sorry, sorry, I missed this, we're breaking up. What was the last, so you talked about next double and triple study --

Naveed Siddiqi - Andera Partners - Analyst

Yes, the next study, you say that it's going to be across -- no, a similar design with either a LAMA/LABA add-on to RPL554 or a LAMA/LABA/ICS add-on to RPL554. So, just to understand what do you mean by or, does that mean that you still have to decide which one of these or -- yes, just clarification there.

Naveed Siddiqi - Andera Partners - Analyst

Yes, yes, okay, sorry, thank you. So, the sign is very similar and that's the [where] the crossover and the double-blind and the randomized design, the background treatment will be a LAMA/LABA, so everybody. And that background treatment will also in some patients is complemented with inhaled corticosteroids.

So in all our trials over the last several years now, we have stopped treatment with the bronchodilators before starting a study and we have also allowed patients to use, if they are on a stable dose of inhaled steroid, they can use that dose throughout the study period, as long as it doesn't change and as long as they don't need more, so it's been stable. So we already have exposure of course in previous studies, where they have been on no background except for inhaled steroids and many times this has been around 30%, 40%, 50% of the population.

So, we see a similar design here where we have a study planned, LABA/LAMA background, and those patients coming into the study already on [triple] or on maybe an inhaled steroid in whichever combination. They can continue to use the steroid, and we expect that there will be a significant portion of the patients that [have been further] study, but also then have had triple [therapy].

Naveed Siddiqi - *Andera Partners - Analyst*

Great, thanks for the clarification.

Jan-Anders Karlsson - *Verona Pharma plc - CEO*

Statistics -- yes, so statistics and there are various reasons why this is the design we ended up with. And we think that we will [roll] this in a number of patients that end up in this situation. So, we should have an interesting readout on patients we [dose that will have] the triple therapy this way.

Operator

Thank you. It appears there are no further questions at this time. Therefore, I'd like to turn the conference back to you, Jan-Anders, for any closing or additional remarks.

Jan-Anders Karlsson - *Verona Pharma plc - CEO*

Thank you. Thank you everyone for joining us today. The topline data announced in the first quarter continues to validate the uniqueness and potential of RPL554 as a novel and differentiated treatment of COPD patients. We look forward to updating you in the coming quarters on the commencement of additional trials and progress in moving RPL554 towards start of Phase 3 in the next year, as I previously outlined.

We have scheduled to present next week on Wednesday, May 15, at the Bio?quity Europe conference in Belgium, and we'll be conducting one-on-one meetings and look forward to catching up with some of you at that time.

We will also be attending the American Thoracic Society Congress being held from May 18 to the 23 in San Diego, that [took us to] presentations related to RPL554 that will be presented on Monday, May 21. And again, we look forward to meeting you there as well.

This concludes today's call. Thank you very much, operator.

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