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ONTX - Q1 2017 Onconova Therapeutics Inc Earnings Call

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PRESENTATION

Lisa Sher - *MBS Value Partners - IR*

Good morning and welcome to Onconova's first quarter 2017 earnings call and webcast.

(Operator Instructions)

Please note that the remarks today will include forward-looking statements and that actual results could differ materially from those projected or implied in our forward-looking statements. For a description of important factors that could cause actual results to differ, we refer you to the forward-looking statements in today's press release and the note on forward-looking statements in the Company's SEC filings.

It is now my pleasure to turn the call over to Onconova's CEO and President, Dr. Ramesh Kumar.

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

Welcome. Joining me from Onconova's management team is the CFO, Mark Guerin.

We had a productive start to the year, advancing the Phase 3 INSPIRE trial of our lead clinical candidate and securing additional funding to support our late stage trial as we position Onconova for multiple key milestones.

During the quarter, our targeted Phase 3 study of IV rigosertib for patients with second line higher risk MDS, continued to advance. The INSPIRE trial is now open in 18 countries. And consistent with our earlier guidance, we are on track for interim analysis and full enrollment targets over the coming year.

We're also on track to submit the protocol for a pivotal Phase 3 trial for first-line patients with MDS for oral rigosertib in combination with azacitidine with the FDA. We plan to pursue special protocol assessment, SPA. We recently initiated the scientific advice process with the EMA for this study, having completed the end of Phase 2 meeting with the FDA last year.

While designing the new trial, we have expanded our Phase 2 trial to obtain additional efficacy and tolerability data for the combination routine across a large number of sites. We believe that this additional data will be helpful for the new Phase 3 trial.

We reported positive data on two promising pre-clinical candidates in this quarter. In particular, I would like to highlight data on our third generation CDK4/6 antagonist demonstrating potential advantages over second generation CDK inhibitors, now in the market for breast cancer indications.

We secured additional funding last month and we are well positioned to execute our clinical development plan, as we seek to advance innovative treatments for patients with MDS and other cancers.

2017 represents an important year in our clinical development, with interim analysis of our INSPIRE pivotal trial expected in the second half of the year. Considering that INSPIRE patient population is highly selective, we are pleased with the progress of the trial to date.

We've activated 163 sites across 18 countries, including 33 in Japan, 44 in North America and the rest of the world. We expect the final three to four countries to join this study in the coming months.

Reflecting the complex operational process and interval between activated sites and first patient enrollment, as of April 30, only 60 of the active sites have enrolled patients, with the first patient enrolled in Belgium, Ireland and Israel, as well as Italy during the months of March and April.

We intend to provide updates on enrollment statistics only after we open all the sites, which we expect to be in the second quarter of 2017.

Recently, we also completed our second pre-planned Data Monitoring Committee review. After review of safety data from enrolled patients in the INSPIRE trial, the DMC recommended that the study proceed as planned.

I would like to reiterate a point I made in the last call. The INSPIRE trial is highly selective and requires us to search extensively to identify appropriate candidates that meet stringent entry criteria. These criteria are based in part on the learnings from our previous Phase 3 ONTIME trial.

Since currently there are no approved therapies for second-line higher-risk MDS patients, several early stage clinical trials as well as the alternative of no treatment are competing with our pivotal trial. This is one reason for the broad-based trial approach we are pursuing.

The ONTIME trial identified several previously recognized prognostic factors, and subgroups that appeared to exhibit improvement in the primary endpoint of overall survival. By leveraging these prognostic factors in the design of the INSPIRE trial for patients who are refractory to prior hypomethylating agent therapy, we are aiming to increase the probability of the trial's success.

In addition, the provision for interim analysis provides another window into the progress of this new trial. Our statistical analysis plan, now under review by the FDA and EMA, will provide the basis for data analysis at the interim and top-line intervals. We expect this review to be completed in the second quarter.

In this analysis, the INSPIRE study design permits two looks into the study populations, ITT, as well as a predefined IPSS-R very-high-risk subgroup, providing two shots on goal with the data. Based on our progress to date, we continue to project full enrollment by the first quarter of 2018 or sooner if enrollment further accelerates after all sites become active in the second quarter of 2017.

We will provide updates. We anticipate final data in 2018, allowing for global filings and commercial launch in 2019. We believe this Orphan opportunity represents a compelling global commercial proposition.

Turning to our oral formulation of rigosertib in combination with azacitidine, a synopsis of this pivotal trial has been prepared. Recently we submitted a briefing book to the EMA for scientific advice. As I mentioned earlier, we expect to submit the protocol for SPA to the FDA during the third quarter.

We've also expanded our Phase 2 trial of oral rigosertib in combination with azacitidine. The key objectives of the study are to obtain additional data on efficacy and tolerability of the combination regimen by continuing dose exploration and quality of life assessment in the new cohorts.

We expect to open more than 10 sites in this extension of the Phase 2 trial, including all three sites that participated in the original study. And we expect to enroll up to 40 new patients. The first two patients have been enrolled in this expansion study.

Earlier this month, we presented clinical data at the 14th International Symposium on MDS in Valencia, Spain, alongside our collaborators from Mount Sinai School of Medicine and The Cleveland Clinic.

Our oral presentation of data from the Phase 2 combination trial highlighted the duration of benefit in patients with complete remission and presented a case study of a HMA failure patient who continued to benefit from the combination therapy for more than two years.

Then, in a poster presentation, a new prognostic tool being developed at the Cleveland Clinic was applied to retrospective analysis of ONTIME trial data to highlight the heterogeneity of the enrolled patients. The new INSPIRE trial eligibility is designed to include a more homogeneous patient population.

As a reminder, front-line MDS represents a much larger medical need and opportunity due to the increased number of patients and longer potential duration of treatment.

I would also reiterate that during our meeting with the FDA, we determined that the expected endpoint for the upcoming Phase 3 trial will be based on response rather than overall survival, thereby potentially reducing the trial's cost. As all study patients will be receiving an approved or experimental treatment, we also expect the enrollment to be relatively fast.

During the first quarter, we also reported new data about two preclinical compounds, underscoring the depth of our pipeline. Positive preclinical data was announced for a first in class dual inhibitor of CDK4/6 + ARK5, as well as the Type 1 novel inhibitor of FLT3 and Src pathways as a novel strategy for AML. And these presentations were made at the AACR conference in D.C. in April.

ON 123300 is a third generation potent CDK4/6 inhibitor that also inhibits ARK5 with low nanomolar potency. And this compound was found to be as effective as Palbociclib, the new breast cancer drug called Pfizer's Ibrance in an Rb positive xenograft model. Moreover, the molecule may have the potential advantage of reduced neutropenia when compared to Palbociclib.

There is a need for next generation CDK4/6 inhibitors given the limitations of second-generation compounds that depend on a second molecule for therapeutic use. We are particularly excited about ON 123300 because of its potential to act as a single agent, as a dual inhibitor of CDK 4/6 + ARK 5, which could be suitable for indications that may not be amenable to Palbociclib-like second generation compounds.

We also presented data on a novel FLT3 plus Src inhibitor. ON 150030 is a Type 1 inhibitor which is differentiated from Type 2 inhibitors such as Quizartinib that do not work against mutated kinases. We're actively seeking partners for our early stage development programs as well as regional partners for rigosertib.

I would like to share with you that we're initiating a collaborative program focusing on diseases with well-defined molecular basis in defects in the Ras Effector Pathways, which are the targeted by rigosertib.

Based on new data published last year, we are developing preclinical and clinical collaborative programs with the National Institute of Health, National Cancer Institute, as well as academic investigators and patient advocacy groups. The NIH/NCI scientists are developing a broad ranging rigosertib clinical protocol for pediatric rasopathies.

A CRADA will be executed with the NIH/NCI to permit the clinical trial with rigosertib in these indications.

Another therapeutic focus will be JMML or Juvenile Myelomonocytic Leukemia, a well described rasopathy affecting children, which is incurable without an allogenic transplant. Further details of these programs will be presented in a KOL -- Key Opinion Leaders --session expected to be held in New York during the third quarter of 2017.

I will now hand the call over to our CFO, Mark Guerin.

Mark Guerin - *Onconova Therapeutics, Inc. - CFO*

At the end of the first quarter, our cash, cash equivalents as of March 31, 2017 totaled $15.4 million compared to $21.4 at December 31, 2016. This amount excludes the proceeds from the financing we completed in April, in which we raised approximately $5.2 million before underwriting discounts, commissions and offering costs in our public offering of common stock through Laidlaw & Company.

This also excludes the proceeds from the exercise of the underwriter's over-allotment option, which is expected to raise an additional $0.8 million before deducting discounts and commissions and costs. We believe that our cash and cash equivalents will be sufficient to fund our ongoing trials and operations to the end of 2017.

First quarter net revenue totaled $0.2 million in 2017 compared to $1.5 million in the year ago quarter. Research and development expenses were $4.9 million in the first quarter of 2017, versus $5.8 million a year ago.

General and administrative expenses were $2.1 million for the quarter, compared to $3.2 million for the year-ago period. Our first quarter net loss was $8.3 million, compared to a loss of $7.2 million in the year ago quarter.

I will now hand the call back to Ramesh for his closing remarks.

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

I believe we are making great progress on our late-stage trials, setting the Company up for multiple milestones over the coming 18 months.

We expect to present additional clinical data for IV rigosertib in HR-MDS at the 2017 ASCO Conference. An abstract of this presentation will be available later this week. This provides a first look at the 04-24 Phase 2B trial of IV rigosertib in second line HR-MDS patients at ASCO in early June.

We're also excited to present multiple abstracts, including updated data on the oral rigosertib plus azacitidine in combination trial at the European Hematology Association Annual Meeting in Madrid in late June. The abstract for these presentations will be released this Thursday.

With more than 17,000 patients in the US with high-risk MDS, MDS represents a compelling market opportunity. Despite the large number of patients with the unmet need, the current standard of care falls classically short.

Hypomethylating agents only work on a subset of patients and are not curative, plus they carry significant side effects, and the FDA has not approved a new drug since 2006 for this indication. There is a well-recognized need for new therapies, as well as synergistic combination therapies for the unmet needs for MDS patients. We are proud to be making advances in this treatment landscape and look forward to updating you on our progress throughout the year.

I would now like to open the call to questions.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions)

Jason McCarthy with Maxim Group.

Jason McCarthy - *Maxim Group - Analyst*

Ramesh, two questions, one on the IV and one on the oral. In the pivotal study now, 225 is the target. Can you give us a sense of how many patients have been enrolled to date? And in the frontline setting for the combo, in the Phase 2 study, you did have complete responses of 35%.

Can you give us a sense of what the expected HMA response or complete response would be in that population in the frontline setting? And for a pivotal study, would you be going after complete responses or overall responses or both? Thanks.

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

The answer to the first question is that we will give enrollment statistics and update it periodically, but only after all the sites are up. As you know, we are in a very competitive field of clinical trials and we don't want to discourage new sites by giving prematurely the enrollment targets.

As we have announced in the previous call, as well as reiterating today, we think interim analysis is going to be this year as previously planned and then full enrollment could be in the first quarter or sooner if the enrollment increases with all new sites on board.

It takes a while for an initiated site to start enrolling patients. That's just a vagary of how the eligibility criteria are, and therefore we will give the actual numbers as soon as possible, very likely in the next call or subsequently.

The second question is a very good one. Yes, we can use response, not overall survival as the approval criteria. FDA has asked us to tally up Complete Remission, CR plus Partial Remission, PR. So overall responses (CR plus PR) and the CR rates for the azacitidine on the label is 6% and people believe that with the new schedules and prolonged administration, you can get up to 20% CR plus PR, overall response, for the current standard of care.

So the 35% complete remission we reported at ASH is really a new benchmark and that allows us to design a trial appropriately. And as you know, the trial is now being designed. We are seeking scientific advice from the EMA because we intend to conduct a global trial, include Europe, USA and Japan in the same trial.

Jason McCarthy - *Maxim Group - Analyst*

And a quick follow up to that is how many patients -- I know you're putting the protocol together -- how many patients do you think you're targeting for a pivotal program in frontline?

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

This is really a matter of negotiation with the agencies, because the total number of patients, as you know, in a randomized study is determined by the hypothesis, what percentage improvement are we shooting for. And that's what we're discussing in our outreach to the EMA first and then in our SPA dialogue with the FDA.

So we're hopeful that in the next quarter, we'll be able to talk more about it. And the SPA process is time consuming, but as soon as we have that nailed down, we'll be able to discuss the design. The design is simple, one-to-one randomization azacitidine plus placebo compared to azacitidine plus oral rigosertib.

Operator

Yale Jen with Laidlaw & Company.

Yale Jen - *Laidlaw & Company - Analyst*

First question I have is to follow up on the previous one, which is, let's just assume that you will be able to do the interim analysis towards second half, maybe toward the end of the year and you'll be able to complete the patient recruitment in the first quarter of next year or shortly after that.

What was your projection that the topline data will ultimately come in 2018 or late 2018 or in 2019? What is your best read right now?

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

The best way to respond really is that what we know with some level of comfort, is the number of months between reaching the topline events and then the data. And the reason for that is that we have a good idea of how many months, unfortunately months, the patients are expected to live on the control arm. And the trial hypothesis tells you what we're expecting in the treatment arm.

So using the known facts, we're able to model this and our expectation is that within four months or even less, you should be able to get to topline analysis after full enrollment. So this is also based on our experience with the ONTIME trial. To just remind you, we had 300 patients, 200 in the rigosertib arm, 100 in the control.

In this case, in INSPIRE we have 225 patients, 150 in the rigosertib arm, 75 in the control. So we do expect the end of the trial and the topline analysis to be within a short period of time, within six months at the outset.

It could be as little as three months. So if the enrollment is completed in quarter one, which is our expectation right now, we expect that the topline analysis could be as early as the third quarter in 2018. And obviously we will provide guidance and interim analysis.

The timing of the interim analysis will give us very good outlook on when to expect the topline analysis of the data.

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

-- and just to remind you, we have orphan indication for this drug and this is an unmet medical need, so very likely various designations, including fast track, will become available to the Company.

Yale Jen - *Laidlaw & Company - Analyst*

Just to follow up a little bit on the statistical plan we understood that you will get the feedback in second quarter of this year and respond to that.

As your best analysis at this point that just in case that you do need to choose, very high risk instead of intent-to-treat route, do you anticipate a significant or substantial population, or extended the timing to complete the study or you think that overall that this timeline you suggested earlier still holds, regardless either way of the options that the study may take you?

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

I can say that our expectations in the trial based on eligibility, based on the Lancet Oncology paper we published last year and based on what's known about IPSS-R scoring, our expectation is more than half of the patients will be IPSS-R, very high risk.

And the trial hypothesis is more aggressive based on the data for the IPSS-R very high risk. Just off the top of my head, whereas the trial hypothesis from ONTIME subgroup analysis is in the 0.5 range for the ITT, and the hazard ratio was 0.27 for the IPSS-R very high risk.

So basically what I'm really saying, long answer, sorry, is that we expect that the IPSS-R VHR analysis will include a large subset of patients and those patients will have a better hypothesis because of the lower hazard ratio. So we would expect that we won't need too many more patients than initially planned for analysis based on only this subgroup.

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

-- I hope that was the answer to the question you asked.

Yale Jen - *Laidlaw & Company - Analyst*

So I just want to reiterate that you anticipate you could have almost half of the patients enrolled initially will be IPSS-R so that in the high risk category. So, you will not be substantially changing the protocol or amend the protocol to have many more patients to be able to achieve the expected targets for your enrollment. Would that be fair?

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

First of all it's fair and right that we do expect 50% or more of the patients to fall into the subgroup of IPSS-R VHR. The second one is hard to answer because that has so many variables. And that's the exact reason why we are going through this SAP statistical analysis plan, the process so that it's all nailed down.

So that we actually have more certainty of what we're going to do at that point. And therefore I can't really answer that at this point.

Yale Jen - *Laidlaw & Company - Analyst*

And the last question here is that I know that we looked at CDK4/6, the 123300. It's very promising. I understand also you have laser focus on the rigosertib development right now. At this moment or in the next 12 months, will there be any resources be used for the basic development for this drug or you are solely want to get the drug product out when you can?

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

As the CEO of a biotech company, I have to go with the laser focus that you mentioned. Our number one priority is to get rigosertib to market. And the way we do that is to do everything possible to run a clean trial, get positive results and to file the NDA. So that's our number one priority.

So I'm under pressure both internally from scientists in the Company, as well as from many informed investors to also advance the CDK opportunity, which many people believe is a mega billion-dollar blockbuster drug opportunity. So -- and some people say oh, it doesn't take that much time or that much money or that much effort to take it to the Phase 1.

We realize that, but again it's a tough balance. So we're advancing it to the extent possible. But our number one objective with the CDK compound is to find a very good partnership, which allows us to speed development and also allows it to be fully developed, not just a single Phase 1, not just a single Phase 2, but multiple trials as indicated by the novel mechanism of the drug.

So this is a good problem to have, but at the same time this is a distraction if you're going to be focused completely on rigosertib. So we're happy to have this project and we're working very hard to find a partner that satisfies the needs of both focus and also expansion.

Operator

(Operator Instructions)

Kumaraguru Raja with Noble Capital.

Kumaraguru Raja - *Noble Capital - Analyst*

I had a couple of questions, the first one on the extension in the first line setting. What process would be tested there? And how would the data from that trial be used in the Phase 3 trial?

And for the CDK4/6, do you have the freedom to operate? And, how [would that present] with a mouse model compared to the competition? And, how differentiating is this reduced neutropenia going to be?

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

Thank you very much, these are very good questions. So the first question regarding the expansion of the Phase 2 data, there are multiple reasons to expand. One is we are frustrated that we can't immediately start the new pivotal trial because we have to go through the scientific advice process and then the SPA process. It takes time.

Meanwhile there are patients who are available to be enrolled, and the sites want to keep going. So this was a way to do a Phase 2B, to satisfy the needs of the patients, needs of the sites and for us to continue exploring this very promising combination.

Can we use this data for Phase 3? I doubt it because Phase 3 is a randomized study. This is a single arm study, but what we can use is to amend the trial based on this new data, if we need, to make the Phase 3 trial better for the patients, from quality of life standpoint and make it better to attract new sites by having more data.

There's never any negative in having more data. In one way it satisfies the need for having more data, which we can certainly present in future meetings. So that's the answer to the first question. Hope that was clear.

And to the second question, yes, very happy to report that our CDK4/6 + ARK5 compound for ON 123300, has issued patents. The patents are issued in the US, Europe, Japan, just about everywhere in the world. So from a IP point of view, it stands apart from Palbociclib, which is the Pfizer's Ibrance or from Ribociclib or Abemaciclib, which are the other compounds from big pharma.

So unique starting position, unique mechanism reaction involving CDK4/6 + ARK5. And to the extent that we know, because we haven't done clinical studies, the data, the efficacy data is very comparable to these three compounds from Pfizer, Lilly and Novartis.

There are some advantages, which we have presented on and published for example a cell culture study shows that our drug works both in Rb positive and Rb negative cell lines, which is a distinction. And new mice xenograft studies show that our drug works as a solo, single agent whereas those other drugs typically require a combination to be effective.

In addition, because of the ARK5 modality in the molecule, we're able to go beyond breast cancer, beyond solid tumors. We can go into blood cancer such as mantle cell lymphoma, and lymphoma itself. So it provides us, additional opportunities; perhaps a faster route to approval.

I want to clarify that all of these statements are based on published pre-clinical studies. We are not yet in the clinic and the way things are going right now, they could be in the clinic, if you wanted to push this program or have a partnership that pushes this program, within one year.

Operator

I'm showing no further questions in the queue at this time.

I'd like to turn the call back to Dr. Kumar for any closing remarks.

Ramesh Kumar - *Onconova Therapeutics, Inc. - President and CEO*

Thank you very much. Our goal is to make progress and to keep you continually informed and we'll provide various updates at conferences and then look forward to our next earnings call. Thank you.

Operator

Ladies and gentlemen, thank you for your participation in today's conference.

This concludes the program. You may now disconnect. Everyone have a great day.
