Transcript of Isofol Conference call 4th August 2022 – Topline results

CEO presentation

Ulf Jungnelius

Thank you so much and good morning everyone and we will present to some of the information around the results of the phase three study mestatic colorectal cancer with Arfolitixorin.

If we go to the next slide, #2.

So of course this company presentation it's being prepared for not as a prospectus so keep in mind, we would walk through Slide #3 and do a recap on the design of the phase 3 study and what we wanted to achieve.

So keep in mind that our intention was to demonstrate at least a 10% improvement compared to the control arm on objective response rate with Arfox and Avastin versus Folfox, modified Folfox, with Avastin, the standard of care in the US.

A key secondary endpoint was the measurement of progression free survival.

Unfortunately, and very disappointingly, the top line results show that neither the primary endpoint of objective response rate nor the key secondary endpoint of progression free survival achieved statistical significance.

So what do we know then? Well, the study patient population after discussions with FDA, they were increase in Japanese patients to 490 patients.

So our data on objective response rate represents the 490 patients and we did not see a statistical significant improvement in objective response rate over the control arm with at least 10%.

The secondary objective we are still having maturing data, so the top line is the only the top of the iceberg and there would be more patients coming in.

Yeah, but at this time point we are not seeing any progression Free survival, significant in full benefit so we did not meet the primary objective on the top line itself.

Of course there is patients who were still undergoing treatment.There are patients in follow up that had not had a progression.

So I'll come back to that.

And if we go to the next slide, what are our next steps? Well, of course this is an ongoing study and and we will finalize this study.

This means that by the end of the year, we would probably have all the data regarding subgroups, geneexpression data and safety data.

So the only data we had at topline was the objective response rate and some of the progression free survival data.

Our final study report is expected by the end of the year, and of course once we have an understanding of the subgroups and keep in mind, for example, that there are patients who underwent surgery.

We don't know the distribution of those. The gene expression data will be analyzed. We don't know then how gene expression impact on outcome was. And after we have all this data, of course we will go to the relevant regulatory agencies.

FDA, EMA, and PMDA, and the Australian agency and have a discussion about what can we do with this drug and how do we get it on to the market.

My absolute conviction is that yes, we will try to get this drug on the market, one way or another.

And of course we will need to really dissect and understand the data from the full data set to understand how we will be able to do this.

So the next step related to the clinical program will be decided then after we have the final study report and that has to be completed and and once we also have had interactions with the regulatory bodies to understand our pathway forward and I'll leave the goal now and Roger, do you have any additional comments?

Roger Tell

Yeah, thank you and so yeah so we all both surprised and disappointed of course, uh, we have, had a short discussions with our Advisory Board that we met during the ASCO meeting here earlier this summer and and we will continue to discuss with the advisors when we have the full data in our hands to discuss the subgroup analysis. But also, as you mentioned, the gene expression, the bio marker data and also the safety data to decide upon the path forward and that needs also of course to be discussed with with the regulatory authorities in each region.

How to look at the data and the file, the value on the asset, so we will come back on this information here later.

Ulf Jungnelius

OK, I think this is the part of the presentations we are now open for questions.

Q&A

Moderator

Our first question comes from Patrik Ling, DNB Market.

Patrik Ling, DNB Market.

- *Thank you guys and good morning Ulf and Roger, could I just ask a few questions. You talk about patients that are still in treatment that still hasn't progressed. Can can you give us a feeling for how large proportion of total 490 patient that is still in treatment?*

Ulf Jungnelius

Uh, let me say it this way, we don't have the exact numbers because we haven't access to the full data set yet and and it is one of the reasons that we are, we don't even have the safety data and so we do know that there are patients in treatment, especially in Japan who were the last patients to be enrolled.

And we also have patients who have not had a progression. So the number I don't know and we will see that when we get access to the final data batch.

Patrik Ling, DNB Market.

- *If you could speculate a little bit, do you think that there are any chances that patient still in treatment could change the overall top line result or will those potential patients merely sort of have an impact on different subgroups of patients?*

Ulf Jungnelius

Yeah, I'll answer and then I'll let Roger speculate.

Uhm, keep in mind, when it comes to the objective response rate that data set is mature, we have 490 patients with data on objective response rate. We did not meet the significant level. Uh, so for that part, the primary objective is not to change.

And when it comes to the progression free survival I let Roger take that question.

Roger Tell

Yeah, thank you and thank you Patrik for your questions.

PFS events on the patient still under treatment or follow up.

We will of course, uh, follow these patients. I don't expect, uh, a major difference from the results that we have presented today. Uh, we also have some patients that we are still looking into from, and to discuss with the team that are reviewing the CT scans to judge if it's a progression or not by definition but these patients, together with the patients being in treatment, they are too few to do a major change of the result.

There might be some some slight defencing in the final outcome, but I don't expect it to be a major one.

Ulf Jungnelius

Another comment, that, keep in mind what we know is and that we don't have access to.

We know that a fairly high number of patients went to surgery, a fairly high number of patients were censored and we don't know in which arm they were censored and of course when we do the subset analysis, looking at them, there would be things that are sticking out and this is where we will have a discussion with the regulatory agencies how to manage for example, the impact of Covid on this, etc.

But as Roger was saying, overall on the two key endpoints we don't anticipate any major changes.

What we don't know is if we have subgroups, and I take the gene expression as one example.

If there is a subgroup that really had no advantage of Leucovorin compared to Arfolitixorin, of course that is something that we can build on, so the biomarkers and sub groups analysis become really important for us to understand and then also the impact of, as I said surgery, COVID yeah.

Patrik Ling, DNB Market.

- ***I mean, there's been some discussions about how to evaluate the patients with the new set of evaluations from the old. Could you tell us if this top line data has been evaluated by what you had in the protocol or do you think that there could be any differences if it's evaluated with the new set of guidelines for this?***

Ulf Jungnelius

At this point, I don't think we can get into the details.

And I think what we need to understand is that when we have access to the full data set and right now it will be speculation only to look at, you know subsets of subsets.

We will understand the impact, though they're using the new sensing rules, but as Roger said we don't anticipate any major changes, the results are fairly robust.

Roger, any comment?

Roger Tell

No, I echo you Ulf.

And then we will look into these different strategies to censoring patients and look into the final data set to look carefully into this and also we have mentioned all the subgroup analysis, including the bio markers to see if there is any advantage in some of the subpopulations and then to go back to the agencies and discuss it further.

Patrik Ling, DNB Market.

- *Last question for me, and then I'll jump back into the queue when you look at the primary and secondary endpoint, do you have any understanding of whether you were sort of on the positive or the negative side, or if it was completely neutral compared to the control arm?*
- *Did you have any improvement at all in in PFS and ORR?*

Ulf Jungnelius

Yeah, I can give you a high level answer. Arfolitixorin it's an active drug, no doubt about it, and that's clear. End of sentence.

Magnus "Bernard" (inhearable)

- *I was wondering in which medical congress or medical congresses would be in line for presenting the top line results so we can know more about the top line result.*

Ulf Jungnelius

The answer to that is that we have passed the timelines for ESMO.

Uh, we will have more data by the end of the year, so the next conference that we would looking at would be ASCO GI. If we miss that one and we don't have much time, it will be the annual ESMO meeting.

And and, uh, it's a good question and one of the reasons we've been (host host) discreet with the numbers is, of course that if we display the numbers we will not have a chance to be at any Congress or Publication, right so not showing the data gives us the opportunity to come into the Congress with the data and for Isofol this is extremely important.

Moderator

Questions from the message board.

Thanks, we have received a couple of questions and I think you've answered the questions relating to specific numbers and more details on the differences between the treatment arms, but there's a couple of other questions as well and one is:

- *Is it standard procedure to occupatiants to switch to the standard of care arm even though the experimental arm is better although not statistically significant?*

So when you have a phase 3 study and you don't see that you hit the primary objective then the study by default, in the eyes of the scientific community and regulators, is a negative study.

We don't have access to the safety data we know that both arms are very active and so no doubt about it that patients benefit. It is up to the investigator, the physiscian, to look at if the patient has a benefit from the treatment in the experimental arm, I would hesitate to take that patient off the treatment as long as the patient derives a benefit, and so again I need to emphasize that both arms are very efficacious, it's the difference between their arms that we did not reach statistical significance, but Arfolitixorin is a very active drug.

No doubt about it.

Moderator

- *What kind of subgroup analysis were predefined by the protocol.*

Roger Tell

Yeah, so I mean there are several sub group analysis defined by the protocol and also knowing some of the most important ones that we know that will make a big difference this is used for stratification of the patient.

Uh, I don't want to go into all the subgroup analysis that we do, but we have focused on the anatomical side and other features of the disease that we know could make an impact on the outcome so and this is of course of the discussion we had with the other experts and also the regulatory authorities, how to design the trial in the best way so we will have a lot of data out of this phase three study with almost 500 patients.

Uh, so there there will be a huge work here during the coming months to review all the data, including also the biomarkers than to add another layer on the results.

Moderator

- *If you will be able to sort of track any positive signs from these analysis, do you think that you need to confirm those in additional trials or will this be sufficient?*

Ulf Jungnelius

That's a good question. Of course, from a regulatory standpoint this is a negative study, uh, if we find that there is the subset of patients that have a significant advantage, of course, that's a discussion with the agency how to manage those.

Usually that ends up being that the agency says OK, run a smaller study in this population because we anticipate the difference between the standard arm and the control arm will be much bigger.

The other thing is that to understand from a regulatory standpoint, the real impact as I mentioned earlier, COVID, surgery, etc.

So things that were not anticipated when we started the study. Could those skew the data, the other question, I think from a scientific standpoint, is how much more can you make 5-FU more efficacious, even if you have fantastic drugset, increase the level of MTHF, the active metabolite, how much better can you make 5-FU, that's another thing we need to look into.

Keep in mind Arfolitixorin by itself is not an anti tumor drug, it the potentiator of 5-FU that is Leucovorin. Uhm, we just happen to be the active metabolite and we see from the data, at least they work as potientiator but how much better can we make 5-FU by increasing the active metabolite in the cancer cell.

And so we need to look at the data and then of course, It's a huge disappointment there.

I think the key thing here is this is a disease, metastatic colorectal cancer that haven't seen basically in all comers ??? for over 40 years or 20 years. And the need to have new improved treatment is very high and for us and for the staff at the hospital, for all the patient is in huge disappointment and of course as an investor in the company, I'm also sad, but this is the risk you have in biotech.

It's high, high risk. If you are lucky high, high reward.

What we do know is that we have an active drug and the company will do whatever we can to see if there are any things that we can use and my own belief is that yeah, one way or another we will try to get this drug onto the market.

With that I'm I'm very hopeful.

Moderator

- *Relating to the financial status. So could you give us some some guidance on the cash status and the burn rate?*

Ulf Jungnelius

So the burn rate, Today, let's say this way and of course with these results there are things that we will stop doing like starting new studies that we have budgeted for etc.

So we have a very strong financial position. We have money that takes us well, including next year and as we are now downsizing a number of things, cash is not the problem that we have.

It's understanding the data and we have ample time to do that and also if without the way forward just to start understanding how we would execute on that way forward.

Moderator

- Final question, is there any sense that this study has been designed in a wrong way, by any chance?

Ulf Jungnelius

No, this is a a very conventional phase three study.

We have only switched out one component in the standard of care and inserted our own drug, and so the study went through what's called an SAP, Special protocol assessment procedure, in the US with the FDA and the only thing that FDA could not tell us was how long do we need to follow the patient for overall survival.

So in that way, no the study is correctly designed and has been executed through the pandemic in a very nice way. Uh, so again the staff that at the hospitals, the staff at Isofol has done a fantastic job and so sadly the drug didn't actually perform as we had hoped and we will now try to understand what we can do with the study results, and then again I have to say that Arfolitixorin is an active drug there's no doubt about it.

So you could ask yourself, OK, should we have done a study in another population?

Keep in mind we were asked by the FDA and EMA authorities to run the study on this population and when the regulators tells you to do that, you do that.

Moderator

- **Thank you and we just received another and additional questions relating to the prospects of a separate approval in in Japan given the high rate of colorectal cancer in that country?**

Ulf Jungnelius

It is the same answer, we need to understand the data and, uh, for Japan these were the last patients who were entered into the study. So getting the mature data from the Japanese patients will be the last data that we actually receive.

And so we'll see, that´s one subgroup we need to look at that did the Japanese patients, the Asian patients behave the same way as the Caucasian patients, right?

So, again, a lot of work lay ahead of us and we need to understand the data completely.

Moderator

- *Yes, another questions relating to the European market. Could you elaborate of getting an approval in Europe, how will that be handled then?*

Ulf Jungnelius

Yeah, so again there have been instances when the drug was not approved in the US based on the outcome of the study but approved in EU.

The same answer goes here. We need to understand the whole data set. I just need to emphasise, we only got the objective response rate data and the PFS data.

We don't even have the safety they yeah so.

We are sitting on a very small data set from the study and then the key one will be, of course safety, is there a difference between the on the safety side?

And there are things we need to understand before we go forward.

So in that case I will end the audiocast by saying again, our study did not meet the primary and secondary objective in this study.

It's a huge disappointment for patients, for all the people at the hospitals working with the drug and of course, for Isofol and all the investors.

The study will continue as it should to the end and we will analyze the data as it comes in. And again, we think that by the end of the year we should be able to understand the whole data set and then write up a final study report before we can engage regulators in discussions on how to take this drug forward.

As I said myself, I'm very hopeful that we will be able to take the drug on the market specifically in the US but that remains to be seen.

That is my conviction. But I may have been wrong sometimes before. But again, I am convinced that when we understand the data, there will be a path forward.

Thank you so much.

Thank you Roger for helping out.