Transcript of the videoconference, November 2, 2021 – 7.30 pm CET

Participants

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David Heuzé

Hello everyone, welcome to this conference today dedicated exclusively to the results of the phase 3 of our mdc-IRM product, which were presented this weekend by our partner Teva at the Psych Congress in the United States. So today, our meeting will be dedicated exclusively to this subject.
We will have the opportunity to talk about the rest of the portfolio within a month when the half-year results will be presented. Today, to talk about the phase 3 results presented this weekend, I am with Christophe Douat. Hi Christophe.

Christophe Douat

Hello David.

David Heuzé

And we have the pleasure to have with us Doctor Marc Antoine Crocq, hello Doctor.

Doctor Marc-Antoine Crocq

Hello David.

David Heuzé

So, doctor, you are a psychiatrist, you are based in Alsace (France). You're the author or co.-author of 75 publications, including one, published a few years ago, about long-acting treatments for the treatment of schizophrenia.
Morevover, you were the coordinator of the French translation of the DSM-5, the bible of psychiatry. Today you have a consultation in Alsace. You see a lot of adolescents and young adults, a lot of people who suffer from schizophrenia, in the early-stage of the disease and in the follow-up of patients
That's right?

Doctor Marc-Antoine Crocq

Exactly exactly.

David Heuzé

Well. So, before addressing you, doctor, I first turn to Christophe.
Christophe. Today we have people with us who do not necessarily know MedinCell and its technology. In a few words, can you tell us about the company and the BEPO technology?

Christophe Douat

Yes of course. David, then. MedinCell is developing a new generation of Long-Acting Injectables. What is that? It is the sustained release of drugs, through a single injection, subcutaneously. I often take the image of a virtual mini

pump which is injectable under the skin, which will release its medication for a chosen period of time until the next injection.
Sometimes it's a week, sometimes six months. So, when I describe it, it sounds simple, but it's very complex and that's what our 100 engineers, pharmacists, doctors, scientists do. they develop the formulations so that the drug is released in a stable manner at the therapeutic level and obviously avoiding any overdose which would create side effects.

David Heuzé

This weekend our partner Teva presented the results of the first phase 3 study with one of our products. It is a product which is dedicated to schizophrenia. Why schizophrenia, Christophe?

Christophe Douat
Schizophrenia is really an area where there is a need for adherence. The patients must take their treatments for this indication, but as in many others, half of the patients take it badly or stop their treatment. And when it's schizophrenia, there are a lot of consequences and I'll let Dr. Crocq talk about it.
And therefore, this is the field in which there have been the greatest successes in long acting injectables, precisely to help support patient compliance.

David Heuzé

About compliance, perhaps it is not clear to everyone. It is the fact of following the doctor's prescription well, of taking your medication to say things clearly.

Christophe Douat

Our collaboration with Teva to develop these products is seven years of work. Teva had chosen us from 150 technologies around the world to develop a new generation of long-acting injectable that had all the attributes demanded by caregivers and patients.
That's what we did. This first product has successfully completed phase 3. There is a lot of excitement at MedinCell, and this is the first in a series of three.

David Heuzé

Thank you, Christophe. I turn to you, doctor. Can you tell us a little bit more about schizophrenia which, I believe, affects almost 1% of the world population?

Doctor Marc-Antoine Crocq

Indeed, schizophrenia affects 1% of the population. Tt is a neurodevelopmental disease which often begins at the end of adolescence, typically around fifteen or sixteen in men, a little bit later in women. And it is a disease that progresses, a chronic disease that tends to evolve, with an alternation of acute phases called relapses, followed by remission phases. The problem is that the relapses are toxic, in a way for the brain. And these phases of acute relapses condition the long-term prognosis of the disease.
So when the patient relapses, so toxic in his brain, it's deleterious. Often the patient relapses because he stops the treatment. And when you restart treatment after the relapse, there is a deterioration. So, we restart the treatment at a lower level, at a lower level of performance than before the relapse. The previous status quo. And why do patients often not take treatment for schizophrenia? It is somewhat linked to the nature of the disease itself which means that there is a lack of insight, a lack of awareness and that the patient has difficulty constantly understanding that he must take its treatment. It's difficult for him to measure the negative effect of a relapse.
Therefore, the treatment of schizophrenia involves antipsychotics. If we take a step back, it is the discovery of antipsychotics that emptied psychiatric hospitals. The first antipsychotics were Largactil, Chlorpromazine which was discovered in 1952.
And that's what emptied mental hospitals. And already, with the first antipsychotics, we discovered quite quickly that we could do long-acting injections and these long-acting injections have allowed that we see the patients no longer in the hospital but in town in dispensaries. And the rise of dispensaries and
The rise of what was going on in dispensaries, a psychological and social care, it is finally, the consequence of the antipsychotics, then the invention of the antipsychotics with prolonged effect. At one point there were new antipsychotics that appeared, atypical or second-generation antipsychotics that were effective with fewer side effects.
And at a time when there were no more side effects, we forgot a little. We lost the habit of prescribing the old antipsychotics which had long-acting formulation. And for a while, we rediscovered long-acting antipsychotics. These new long-acting antipsychotics were based on risperidone, olanzapine, Aripiprazole. And it's really these long-lasting injections
These long-acting enable compliance with the treatment, regular compliance with the treatment, with the minimum effective dose that allows the patient not to relapse and control minimal doses, it also allows the patient not to be overdosed, not to have side effects.

In most cases the current recommendations favor treatment with long acting injectables. These are official

recommendations, the recommendations of all countries are consistent at this level, but unfortunately these long-acting injectables are relatively little used, resulting in frequent relapses in schizophrenia and relapse, and rehospitalizations that means costs for society. And for patients it means above all a phase of deterioration of his condition, degradation of cognitive functions, brain functions which will pave the way for a negative evolution, i.e., dominated by deficit symptoms and cognitive difficulties.

David Heuzé
If I summarize, it is 1% of the world population. It is treatments which have already made the revolution, which have made it possible today, as you said, to empty psychiatric hospitals. But it is also recommendations that are not necessarily followed, in particular the recommendation to use long acting injectables.
And if I also come back to what you have just said, relapses are major events in the life of a schizophrenic patient and can have very, very negative consequences. So, precisely,
So, precisely, that was the primary endpoint of Teva's study.

David Heuzé

So, I turn to you again, doctor. What does this study tell us about that, about relapses?

Doctor Marc-Antoine Crocq

The Teva study looked at a new formulation of long-acting risperidone and the main result of this study is that indeed, people who are treated with the active product will relapse much less or much later than people treated with placebo.
And the main goal of the study was to see when people relapse and therefore to classify them by time, when they relapse. And so, it gives a sort of survival curve, like what we see in cancer studies as well.
If people do not relapse, the curve remains more or less a straight line over time. If people relapse, we see that the curve is turning down and that the patients who have not relapsed, it is survival, in a way without relapse, are less and less numerous.
It is a statistical method which is always used in this type of study, which is very powerful and gives very reliable results. And there, we can say, with a very high degree of probability, of certainty, that the use of this mdc-IRM product makes relapses much rarer and much later.
So, and once again, this is crucial for the patient who suffers from schizophrenia to not relapse. As we said, relapse is accompanied by deterioration of brain function and restarting treatment after a relapse means restarting treatment at a lower level, a lower level of functioning than where the patient was before.

David Heuzé

That was the primary endpoint. the primary endpoint of the study which effectively shows, as you said, a time to relapse before relapse multiplied by five, I believe, if I read correctly compared to the placebo group.
Maybe we can make a stop to talk about the design of the study. we have a study that is done with the treated group, in fact two treated groups, because there are two products, 1-month and 2-month, versus placebo.
Can you confirm that this is a usual study design for this type of product?

Doctor Marc-Antoine Crocq
Yes, it is a classic design which is even superior to what is done in other studies. We note that the patient inclusion time was very long, it could be over two years, and that the number of patients is very large.
We have many patients who were followed for a long time, which made it possible to have a long observation period and to measure during this long observation period the time to relapse.
And it's true, there are fewer relapses. It can be explained in different ways. We can present this result in several ways. That is to say that relapses are less frequent. If you use a given period of time, there are significantly fewer relapses in the group, much less relapses in the
Group treated with the active compound. The relapses are much later in time. Time to relapse is multiplied very significantly if you are under treatment compared to the placebo. And if you are on a placebo, there is a steady progression.
That is to say that the number of patients who have not relapsed regularly decreases over the entire observation time and that the decrease in this curve is much smaller in patients who are treated. Most of the patients who are treated will not relapse.
This was the main endpoint of the study. The main result of the study. This study measured many other endpoints.
An important result is that there are no more side effects with the injectable form of the product than with the oral form, and even less side effects.
Less dose-dependent side effects, maintaining a minimum effective dose.

David Heuzé

We don't have the peaks and valleys of oral medication. Another endpoint was the general improvement of the patient. What does the study show?
What does the study say about these criteria?

Doctor Marc-Antoine Crocq

So, there are several reference scales that have been used to measure what is called the quality of life. One of the consequences, one of the advantages of treatment, as they say, is that with antipsychotic treatment, the patient can leave the hospital and live in the community.
So he can live in the community and can there, in the community, be helped, and benefit from psychological and social care and the patients who are treated by the product, compared to those who are on placebo, will have better quality of life, on scales that explore many different aspects of the life of the patient. His ability to use the means of communication, his ability to go to appointments, his ability to be independent for accommodation, for food, for shopping. So, it explores the freedom that the patient can have in everyday life and also the pleasure he can have in living in better psychological conditions, with less symptoms. These different scales shown that the patient can flourish more, live better independently and pleasantly in daily life. And so that's a whole aspect of the patient's life, the rediscovery of life that is made possible by the treatment.
If there was no treatment, the patient relapses and unfortunately, he would spend more time in the hospital. But above all, if the patients relapse it means that the evolution over the years will be more negative, whereas if we maintain a treatment, it is the best chance to see a remission and a good level of functionality.

David Heuzé

So, if I sum up, less relapse, an improvement in quality of life compared to placebo, good tolerance to the product, no more side effects, or even less than what is found on treatments that already exist in the form of oral or even under long acting.
And then, Teva accompanied this study with surveys of the patients who received the product and the caregivers who administered it. And I think we are coming back to the very characteristics of the product.
Can we talk about a plebiscite?

Doctor Marc-Antoine Crocq
Yes, that's it, it's important. It was said that long-acting injections are recommended by all international recommendations, national and international societies, but yet they are relatively little used. Often this is because these injections can be unpleasant to use, difficult to use or disturbing for patients and caregivers.
The patient can be reluctant by receiving an injection if it hurts. If the injections are very frequent, for example every two weeks. If the procedure for initiating treatment is complicated, i.e., the injection is not enough, because it does not take effect immediately because of a particular kinetics and therefore for several weeks, it is necessary to continue to take the oral treatment in addition to the injection or when the injection does not take effect quickly enough, several injections are needed soon at the start of treatment. It can also be complicated for therapists if the product is difficult to store.
If the product must be reconstituted, if there are several syringes, if it is necessary to make manipulations to reconstitute the product so that it is ready to be injected. It is more complicated than if you have a product that is injectable and that can be easily stored. And so, that's why it's important to make the injections as easy as possible to use.
And we know that if the patient does not like the injection or if the therapist does not like the injection, these injections will not be started. There is a big advantage in making products that are easy to use and accepted by therapists and patients.

David Heuzé

This is what you see in your practice, with the patients you follow. Without going into detail.

Doctor Marc-Antoine Crocq

I see that there are a lot of psychological barriers, and a lot of misconceptions. The consequence is that long-acting injections are not used enough in the treatment of schizophrenia. So, there is a paradox. All the studies show that the long-term course of schizophrenia is better if one quickly uses long acting injectables and that relapses are reduced. But despite this scientific knowledge, many patients continue to take oral forms of the drug and in practice do not take it regularly, almost always and finally relapse. Many therapists are unaware of this.
Many therapists imagine their patient is taking the treatment when they are not actually taking it. When we ask therapists what percentage of their patients do not take the treatment. The therapist will have good self-esteem. He's going to say that all of my patients are taking the treatment. On the other hand, if we ask the therapist what percentage of patients of its colleague do not take the treatment, the therapist will be much more realistic. He'll say most of my colleagues' patients don't take their treatment, so the therapist himself always has a kind of euphoria about his own competences. He thinks he has convinced his patients to take the treatment, but it often just doesn't work out that way. And we must see that when there is a relapse. We could compare with diabetes, which is easier to understand.
There are a lot of young teenagers who have type 1 diabetes. When they are teenagers, they say I want to live freely, I want to live without treatment. And many teens will not take insulin therapy at this time.
When the diabetes is unbalanced, when there is no insulin, it will deteriorate, it will have a toxic effect, harmful on many organs. It will indeed have a harmful effect on the retina, so it promotes blindness, it will have a harmful effect on the kidneys.
So that can lead to dialysis. It's a bit of the same thing happening in a more complex way on the brain when you treat a schizophrenic disorder. it is not so easy to imagine than a toxic action on the kidneys or on the retina.
But it is somewhere neurotoxic for the brain, and it is a factor of degradation and poor prognosis. That is the

important point, it is almost the most important thing that we have to say today. That the only way to administer treatment that best prevents relapses is long-acting forms.

David Heuzé

Moreover, looking at the study, we were still surprised, and it was not necessarily obvious, that 60% of the patients who were questioned, who took part in the study and who were questioned because that it is not all the patients who have been. They say they prefer an injection and therefore, a priori, to be ready to go under this type of treatment, which goes a little in the direction of what you have just said. So today, you tell us that there is still a lot to do for long-acting injectable to be more widely adopted,
Christophe, maybe you can tell us about the product we are developing with Teva and what are its characteristics that make it a drug that has the potential to be well received, because it is easy to use.

Christophe Douat

So, what is BEPO? Our technology is its code name, let's say.

David Heuzé

Its usual name.

Christophe Douat
What has BEPO made it possible to do? And it made it possible to develop these essential attributes precisely, to facilitate, as Doctor Crocq said a moment ago, the adoption of the injection. First, it is a product by subcutaneous injection which is not an intramuscular injection. As it was said just a few moments ago, it is a product that makes it possible to reach the therapeutic level almost immediately, therefore that does not need an oral supplement or by another injection. It is a product which offers flexibility in the frequency every 1-month or every 2-months.
But we can also note in the study that 75% of patients prefer the injection for 1 month. BEPO enables to offer these features. This is the disruptive nature of our technology, and this is why Teva has worked for seven years now to develop mdc-MRI.
And maybe I'll conclude David by saying and it's written on one of the Teva's posters and it's a little bit hidden in the text. But what is really quite surprising is that among all patients who received the BEPO, mdc-IRM injection, 90% say they no longer want to go back on their previous treatment, whether oral or injectable. And that is an extremely important figure which shows the qualities of the product.

David Heuzé

And its potential. So, if all goes well, I will remind you that the marketing authorization application is currently being studied in the United States by the FDA, our partner and ourselves,
We hope to have a favorable return and a commercialization by 2022. That will make a new product in a market which is however already very dynamic. Christophe?

Christophe Douat

Yes, exactly. As it has been said during this discussion, long acting injectables are already used in the maintenance treatment of schizophrenia. Today, the market worth more than 7 billion in the world, including 4 billion in products based on risperidone or very close to risperidone and it is this segment of 4 billion that Teva targets.
Just to give you an idea. 4 billion revenue per year. If it was a single product, it would be in the top 20 products of world pharma. So, the stakes are colossal, and we understand that Kåre Schultz, the CEO of Teva, is now talking about it at each of his analyst meetings.

David Heuzé

He talks about it. He even talks about it as saying that he has the potential to be the "preferred product."

Christophe Douat

He said it a few months ago. Patients tell us that in the study. I've been saying this for a long time.

David Heuzé

We'll see what happens next year. I think we should not go too fast. For the moment, as I said, the file is under review with the FDA.
So, a very dynamic market. You gave us market sizes, but also a market that is growing very quickly.

Christophe Douat

And it's important to look at the dynamic of the market along with its size. And it is a market that is growing at 15% CAGR. This is the technical term. That means 15% per year. And 15% per year, if this trend continues, it means that it is a market that is doubling every five years.

David Heuzé

And with also, I'm not sure that the formula is very good, but going back to what you said earlier, many patients today still under oral treatment and who could perhaps switch in the years to come, or start their treatment Maybe, I insist, with long acting injectables.

Christophe Douat

Yes, I would like to have Doctor Crocq's opinion on this because one of the theses was that with a simpler subcutaneous injection, we could treat less severe patients, therefore more upstream in the disease, may be younger.
And I wanted to know a bit what the impact of a product like this could actually have on these two topics.

Doctor Marc-Antoine Crocq
Of course, treating as soon as possible is really essential. It is often at the onset of the disease that there are the most possibilities to prevent an unfavorable development, i.e., the more relapses you have, the lower you fall.
But first relapses are often the most important to prevent. And it is by treating early that we get the best remission and the best disappearance of symptoms. It's very complicated because often people want to do several trials without treatment. Most of the time it takes several relapses unfortunately, for people to understand or realize that they have a disease that must be prevented. And that's why all the recommendations are unanimous on this. It is important to treat early and with prolonged injection forms and one can think that often the recommendations are published and put after a certain time to be accepted. But we can see that most of these recommendations will be discussed, will in fact leave their mark among all prescribers, and that logically, these recommendations will be taken more and more into account and that the share of treatment in long-acting injection is expected to grow.

David Heuzé

I turn to you Christophe. This is the goal in the interests of patients. But these treatments are expensive.

Christophe Douat

The treatments, which are patented, now cost $ 25,000 per year in the United States. I don't think it was mentioned, Teva today is number one in generics, but it is also a very important player in drugs, in new molecules, in patented drugs.
And it is by this department, in fact, that mdc-IRM is developed.

David Heuzé

So, I come back to my question anyway. So, these are drugs that are expensive, but that provide a real service, as Dr Crocq explains.

Christophe Douat

Yes, moreover, in one of Teva's posters, there is one extremely interesting, that shows the impact of injectable treatments on the costs of health systems. It is one of the last poster that shows the positive impact that can have an injectable on the costs of treatment of patients, on the number of hospitalizations and also the number of admissions to the emergency rooms.

David Heuzé

The logic is quite simple. less relapses or relapses later, and therefore effectively less heavy support by the health system. This is what we are trying to do with long acting. To finish, Christophe, I would like maybe that we come back a little on our partnership with Teva.
Okay, you said it at the start, it's a partnership that dates back 6, 7 years now. At the time, MedinCell technology was selected by Teva to develop this product among others, a lot has happened at Teva since, including a little difficult time in 2017.
And despite everything, this partnered project is one of the only R&D projects that have continued. What's the deal with Teva? What's behind it? What does MedinCell do?
What does Teva do?

Christophe Douat

So, the core competence of MedinCell is to develop the formulations. So MedinCell has partnered with Teva to develop a series of long-acting, next-generation, disruptive, long-acting antipsychotics. And the agreement with Teva aims to develop three products, the first of which is mdc-IRM.
We are also expecting in the coming months the transition to phase 3 of the second product. Our agreement awards MedinCell for each product $ 122 million in milestone payments, $ 122 million per product. About ten million of mdc-IRM have already been received by MedinCell.
There will be a supplement for the end of development. But most of that amount is related to commercial milestone payments. So, 122 million. Beyond these amounts, MedinCell will receive royalties based on Teva's income.
We do not have the right to disclose the amount, but it is single to high single digit royalties and therefore MedinCell will start collecting them from the first euro of sale, normally in 2022.

David Heuzé

Well, thank you very much. Doctor Crocq may I leave you the last word? We were happy to welcome you. Do you have something to add?

Doctor Marc-Antoine Crocq

I am very happy to see that we have a new product which should be available soon and above all which presents advantages of use, ease of use.

David Heuzé

Thank you so much. Christophe, a final word?

Christophe Douat

Thanks everyone. I remind you that MedinCell is mdc-IRM, but also two other products with Teva and another 6 behind which all have a potential to have a huge impact on the patient thanks to our technology. And we will talk to you a little more about it at the next meeting David.

David Heuzé

We will hold our next meeting at the beginning of December to present the half-year results. Indeed, this will be an opportunity to give an update on the development of our product portfolio in various therapeutic areas. I would remind you that all these products are developed with the same technology.
That's why we are experiencing an important moment at MedinCell right now. It's the first time we've seen phase 3 results on a product using our technology. It's a great moment for our company.
It is not often that a company reach that point. And then soon, we obviously hope, the commercialization. Thank you, Christophe. Thank you Doctor. Thank you for giving us some of your time and I wish you all a very, very good evening or a good day if you're on the other side of the Atlantic.