

# Transcript of the webcast, December 13, 2021 – 6.00pm CET

#### Participants

Hervé Affagard, CEO and co-founder, MaaT Pharma

**Professor Mohty,** Professor - Sorbonne University and head of the Clinical Hematology and Cellular Department - Saint-Antoine Hospital

John Weinberg, MD, Chief Medical Officer, MaaT Pharma

#### Hervé Affagard

### <u>Slide 1 – 2 - 3</u>

Hello Ladies and Gentlemen, I'm Hervé Affagard, CEO and co-founder of MaaT Pharma.

I'm very pleased to be with you today for this webcast.

Today I'll be joined by Dr. John Weinberg, our Chief Medical Officer, and Professor Mohamad Mohty, a specialist in hematological diseases, in particular blood cancers and Head of the Clinical Hematology and Cellular Department - Saint-Antoine Hospital in Paris.

This webcast will be in French, with English subtitles. I would like to remind you that today's discussion contains forward-looking statements that are subject to various risks and uncertainties.

The presentation will last a total of 30 minutes and will be broken down into 3 parts. During the first part, I will explain our MET platform and how it allows us to generate drug candidates in oncology. The second part will be presented by Professor Mohamad Mohty and will focus on the results recently shared at the ASH conference. Finally, for the third part, I will provide a corporate update on recent and upcoming developments for the Company.

Finally, we will dedicate 10 minutes for a Q&A session taking place both in English and in French. We will answer in the language used to ask the question.

The webcast and the presentations will be available for download in English and in French on our website.

## Slide 4 & 5 – Microbiome Ecosystem Therapies in Oncology

Without further ado, I will present our MET platform.

As previously mentioned, our MET platform allows us to generate drug-candidates to modulate the immune system. As you are probably aware, 80% of the immune system cells reside in our gut. Therefore, there is a sort of partnership between the gut microbiota, meaning a permanent recognition between the immune system, which is part of the host, and our microbial world that is the gut microbiota.

Pretty often, patients treated for cancer will show severe alteration of their gut microbiota illustrated by a loss of richness and diversity which means that the immune system will end up missing its microbial counterpart.

Let's take the example using a game of tennis. Imagine you are playing on a rebound wall and the rebound wall suddenly disappears. This is what kind of happens here and that is when a series of phenomena may happen on the immune system side of things, such as hyper-inflammation which is deleterious to the patient, can result in disruption of the immune system. In this context, some anti-cancer treatments, including immunotherapy, could be ineffective.

This is exactly what we are focusing on at MaaT Pharma: restoring the gut microbiome's diversity and richness as both are key functions.

## <u> Slide 6 – Diversity Matters !</u>

What is diversity? let me explain, each individual has about 250 bacterial species in their gut microbiota. Each bacterial species is made up of a number of individuals. This diversity is very important and is usually an indicator of what could happen to the patient during its cancer.

For example, we can see on the 2 charts on your left, that for patients receiving a stem cell transplantation, the greater the diversity, the better the survival.

If we compare the red curve and the black curve, the latter represents the patients with high diversity, and we see that the survival of the patients with high diversity is multiplied by almost 2. The graph, right next to it, explains essentially the same thing.

In solid cancers, we also see that the higher the diversity or richness, the better the response to immunotherapies, resulting in a shrinking of the tumor.

This notion of richness is extremely important, and our drug-candidates will aim to correct the loss of gut microbiome's richness and as a result, reduce the impact on the gut microbiome's functions, which play a protective role for the individual.

## <u>Slide 7 – Cutting-edge platform generating a diversified product range</u>

To do so, we have developed several product lines using the two pillars of our MET platform: the gutPrint<sup>®</sup> platform, an artificial intelligence platform, and our platform cGMP (*Good Manufacturing Practices*) manufacturing capacities.

Our first line of drug-candidates are native products, while the other one is cofermented products. Native products come from donors, meaning that we collect fecal microbiota to be used in our biotherapeutic drug -candidate.

Both MaaT013 and MaaT033 are designed to rapidly restore high richness and high diversity. This applies particularly to MaaT013, a very high-density product, presented as a 150mL liquid enema for rectal administration.

What we are looking for with MaaT013 is to solve these problems of loss of function of the microbiota as quickly as possible. As an example, the targeted population with MaaT013 are patients with only 22% of survival rate at 2 months, for whom we must intervene very quickly.

For MaaT033, this is an oral form, a capsule, just like any other drug, and we have more time to use it. Based on our current data, we currently believe that 7 days of treatment with MaaT033 is roughly equivalent to one administration of MaaT013. This allows us to treat different populations; indeed, MaaT033 is intended for use in all patients receiving a stem cell transplant.

Our fermented product has a different mechanism of action. We continue to leverage the restoration of gut microbiome diversity, but in this case, we design a dedicated microbiota in order to make patients responsive to immunotherapies. Once again, we define the composition using our AI-powered gutPrint<sup>®</sup> platform. However, this time, we will not use donors, but we collect the microbiota using our own "Microbiome Ecosystem Banks", which have been developed over many years at MaaT Pharma, and then the products are manufactured using fermenters.

I'm done summing up our drug-candidates line. One last thing on MaaT013, that will be at the center of the next part of our presentation, this is our current lead product candidate. We have completed our Phase II and are now entering Phase III. As you will see in a few seconds, we have very promising results, and I will now hand over to Professor Mohty to present these results. Thank you.

#### <u>Slide 8 - MaaT013 for the treatment of graft vs. Host disease</u>

Thank you so much Hervé, and it's a great pleasure to be with you today.

I'm Mohamad Mohty, professor of clinical hematology and head of the clinical hematology and cellular therapies department at Hospital of Saint Antoine, and University of Sorbonne in Paris and today I'm going to share with you our clinical experience with MaaT013.

#### Slide 9 - An urgent medical need in acute Graft-vs-host-Disease (aGvHD)

Before that, I would like to set the stage and show how graft-vs-host disease, aGvHD, is an urgent medical need today, for which we don't have any effective therapeutics options to cure the patients.

What is aGvHD? We have patients who suffer from bone marrow cancer, blood diseases, malignant diseases like acute leukemia, lymphoma, and myeloma. These patients, during their treatment journey, will need, in some cases, an allogenic stem cell transplant (also called an allogeneic bone marrow transplant). One of the major complications of this curative therapy, that is meant to cure them, is graft-vs-host disease; it will target different organs, including the gut. That's where the notion of microbiota and dysbiosis are involved.

Today, we have plenty of scientific data, research, and hindsight to show that in these patients, who have received an allogenic hematopoietic stem cell transplant, there is a loss of diversity of microbiota, that is called dysbiosis, that predisposes them to infections and many complications including the aforementioned acute GvHD.

Today the only validated treatment is corticosteroids. But unfortunately, 50% of these patients will be steroid refractory and the most severely affected, prognostic-conditioning organ is the gut. In aGvHD patients with steroid resistance, the mortality can be high as 90% if there is no curative treatment performed.

### <u>Slide 10 - MaaT013 aims to restore interaction between the microbiome and the</u> <u>immune system to treat aGvHD</u>

MaaT013, as a drug, represents an extremely attractive therapeutic option. In fact, there is a scientific data rationale suggesting that, thanks to its very high [microbiome] diversity and richness, and especially the Butycore, this drug, in the allogenic stem cell transplant patients for which I will show you the data from our experience, allows to increase [the patient's gut microbiome] diversity, to inhibit, pathogenic bacteria, and to increase metabolic production and favor maintenance or restoration of the intestinal barrier integrity. All of this is essential for preventing the infections and ultimately, this leads to a restoration of immune homeostasis, including among other things, the induction of regulatory T cells. The diversity will favor the butyrate production and immunoregulation. This restored homeostasis will allow the improvement of the aGvHD symptoms.

#### <u>Slide 11 - Two complementary approaches generating data on MaaT013</u>

This has been verified clinically so on the patients through 2 main types of clinical testing:

First, we have conducted a phase II clinical study, called HERACLES. We also now have a large cohort of patients treated as part of a compassionate access program.

The prospective Phase II HERACLES study has included 24 patients in 4 countries, with only severe acute gastro-intestinal steroid refractory aGvHD. Patients received 3 doses of MaaT013 as a monotherapy over 2 weeks. MaaT013 is used as second line in patients who have failed a first line of therapy. Follow-up is at 28 days.

Under the compassionate access program, naturally, we assessed a wider group of patients with 52 patients treated, also with severe acute aGvHD but this time, ranging from grade II to IV. They can be steroid-refractory or steroid-dependent, meaning patients that could not stop corticosteroid treatment. So, it's just as bad, I would say, as cortico-resistance. These patients also received 3 doses of MaaT013 as monotherapy, but in this case, this group of patients had previously received up to 6 lines of therapy, which goes to show how severe these patients are. Follow-up was performed at 28 days and of course we also looked at survival.

## Slide 12 &13 - HERACLES Phase 2 Clinical Trial

On this slide, are shown the very promising results of HERACLES study. Once again, there are patients with very severe disease of grade III to IV. This study included 24 patients; as you can see here 96% with grade III and 4% with grade IV, and all of them were resistant to corticosteroids. What do we see? The gut response at day 28 reached 38%, which is a very elegant number, and the best gastrointestinal response at 28 days exceeded 50%, actually it's 54%. I underline the 21% of complete response and up to 38% in best GI response, as these patients, as you will see, will really have better outcomes. This benefit is obtained while having a good safety and tolerability profile, as there were no severe adverse effects that may compromise the future of patients.

We really have the proof of concept that microbiota diversity of responding patients increases with the MaaT013 treatment, allowing to improve their survival.

You can see on the diagrams, on the left-hand side, at the top in red, this is the MaaT013 product. Then we compare the responders' patients represented by the black boxes and the non-responders patients illustrated by the white boxes. If you look at each analysis time, what we call visit 1, visit 2, visit 3 and visit 4, we notice that the responders are the ones who benefitted from MaaT013: their gut microbiota gets progressively richer and as you can see from visit 4, they get closer to richness of the drug they have received. This is an elegant demonstration of the proof of concept, and this translates in a real benefit for the patients. At 6 months, the overall survival of responders is 44% while the non-responders are at 20%. What is even more interesting is that this overall survival is maintained at 12 months, 44% versus just 13% for the non-responders. Unfortunately, 13% is what is expected in these refractory patients in the absence of other therapeutic options.

#### Slide 14 &15 - Early Access Program (EAP)

On this slide are shown the early access program data confirming the HERACLES study results, in a more diverse population, but also in a sometimes in more heavily treated patients.

Here we are looking at multiple lines of treatment, as I said before, a larger cohort of 52 patients, out of which 83% were steroid resistant and. 94% with grade III aGvHD, so here too a very severe population and, by definition, all patients had a gastrointestinal involvement. I would like to point out that 77% of patients had previously received ruxolitinib which is now seen as I would say the most available salvage therapy among different options. And here again, we can see that the response rates are even better than what we had seen in the HERACLES study. We are at 58% of positive GI response at day 28 and we reach 67% when considering the best GI response. A third of patients achieve remission, a complete response and all this with a very good safety and tolerability profile in a population which, as you can guess, is a very fragile population.

When you look at the survival rate of all patients in this compassionate cohort, we observe 38% at 1 year and 49% at 6 months. This is very similar to the Phase II of HERACLES study, and this is even more impressive when you compare the responders versus the non-responders. So, we really see consistent and reproducible data between the Phase II of HERACLES study and the compassionate (EAP) program.

#### Slide 16 - Next Step: ARES Phase 3 Clinical Trial

Of course, we will not stop here because in view of all these data and promising results that bring a lot of hope to the patients, we have already planned a Phase III clinical trial called ARES, which is, I would say, the last step in the validation of the medical benefit of MaaT013 [in this indication].

The idea is to position the drug as 3rd line treatment because it's where there is the highest medical need; indeed, as of today, there is no approved product except from corticosteroids and ruxolitinib which is beginning to appear. We are planning to treat 75 patients with also the severate and acute aGvHD. The study's schema is presented on this slide, but this one is similar to what we have done before. We are very optimistic and attentive to the next results that will arrive in the coming months.

I will stop here and, I will give back the speech at Hervé Affagard. Thank you so much for your attention.

#### Hervé Affagard

Thank you very much Professor Mohty. As mentioned in the introduction, today's presentation is also an opportunity to provide a corporate update.

## <u>Slide 18 – Value-creating milestones expected in the next 12 months, including</u> <u>MaaT013 entering Phase 3 clinical trial</u>

I will obviously start with the clinical part. As you will see, in the next 12 months, we will reach important milestones, and the main one is MaaT013 set to enter Phase 3 clinical trial soon in GhVD. We have already received regulatory approval in two major European countries, and we will, of course, communicate when the first patient is included.

At the same time, we are continuing our compassionate access program. I would like to remind you that this program, taking place in France, allows the company to earn revenues as we provide the products on demand to doctors requesting them.

We are also working with the U.S. regulatory authorities to expand the ARES trial in the United States of America. Pending US approval [of the trial], we are looking at expand to US sites in the second half of 2022.

Our other formulation, the MaaT033 oral capsule, targeting all patients receiving stem cell transplants, is currently undergoing Phase Ib evaluation. We have now completed the recruitment of 4 cohorts out of 5 in total and we expect the results in the first half of 2022. The timing is as planned, and this program is important as we will identify the dosage regimen for patients and therefore will should be able to move to a phase II/ III in the second half of 2022.

On the immunotherapy side, we are taking our first step in this field with MaaT013 that will be evaluated in combination to Immune Checkpoint Inhibitors during a Phase IIa. This clinical trial is ready to start in France and it has received authorization from the French regulatory Agency. AP-HP (Assistance Publique des Hôpitaux de Paris) is the sponsor of the clinical trial and MaaT Pharma's role is to provide the product and conduct all analysis of the gut microbiome.

This will be our first step towards solid tumors and immunotherapy.

Finally, we are also developing MaaT03X, our next-generation co-fermented product and we plan to enter the clinical phase in the first semester of 2023. On this part, to accelerate and secure our development, we were recently awarded a significant public grant of €4.26M. This grant will allow us to structure this program, both on pre-clinical and on clinical sides.

## <u>Slide 19 – Key differentiators of MaaT Pharma in the microbiome field</u>

I would like to remind you of our key differentiators compared to our competitors.

MaaT Pharma is a company specialized in the full ecosystem approach meaning that we restore and reset a complete gut microbiome. Other approaches, which are the more common amongst our competitors, focus on supplementing the microbiome with one or more bacterial species, also known as "cocktail". Our approach is to completely reset the gut microbiome This makes us quite unique, as we now master the science on the full ecosystem approach.

Furthermore, our focus is on oncology, and this has not changed since the company was created in December 2014. Therefore, we have a high level of knowledge as we are one of the most advanced companies in the fields of microbiome applied to oncology.

On the manufacturing side, we have had since 2016 the capacities to industrialize manufacturing processes. We have established the first biomanufacturing site producing full-ecosystem microbiome therapies in Europe and have developed significant know-how in this field.

Finally, we have established a proof of concept with the Phase II data presented earlier and have already demonstrated that the modulation of the gut microbiome can modulate the activity of the immune system. This validates our approach and what we want to accomplish with our current products MaaT013, MaaT033 and the upcoming ones such as MaaT03X.

## <u>Slide 20 – Q&A</u>

This is now the end of our presentation. I would like to thank Professor Mohty for participating to this webcast. Dr. John Weinberg, our Chief Medical Officer, Professor Mohty and I will be very happy to answer your questions.