Ensysce Biosciences, Inc.

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FIRESIDE CHAT

Boobalan Pachaiyappan

All right. Good afternoon, everyone. My name is Boobalan. I'm Managing Director and Senior Biotech Analyst at ROTH Capital. We have the Ensysce team. Why don't we have them introduce themselves?

Lynn Kirkpatrick

I'm Lynn Kirkpatrick, CEO of Ensysce.

David Humphrey

I'm Dave Humphrey, the CFO at Ensysce.

Boobalan Pachaiyappan

Great, Lynn, and Dave, welcome to the show.

Lynn Kirkpatrick

Thank you.

Boobalan Pachaiyappan

So why don't we start with a very high level introduction about Ensysce Biosciences and then maybe you can touch a little bit on your pipeline programs and then your clinical strategy and commercial outlook and then we can take things from there.

Lynn Kirkpatrick

That sounds great. Well, as you know, Ensysce really aims to disrupt the analgesic landscape for the treatment of severe pain because we're developing an entirely new class of opioids, what we call the next-generation of opioids. We're using a very different approach that's been used from the past. We're using chemistry, what we call clever chemistry, to actually inactivate the opioid and deliver the opioid. And that's different from the abuse-deterrent formulations that are actually marketed at the moment.

We modify the delivery and we refer to the delivery concepts as TAAP and MPAR. And we have clinical data to actually validate that these technologies work as we've designed. And we can talk about that a little later. Our goal is actually to make these very effective analgesics safer and make people in pain more comfortable taking an opioid rather than suffering.

So we can talk about TAAP. TAAP stands for Trypsin-Activated Abuse Protection. It's our clever chemistry. As I said, we modify the opioid and with this modification, an individual has to swallow our product, in order to have it exposed to an enzyme in our small intestine that is purposeful for digesting our protein products. This is called trypsin and that starts the activation process. We actually have designed a two-step activation.

So the first step is exposure to trypsin. You don't have trypsin in your nose or your mouth or in your bloodstream. And with the chemistry, we also control the rate of release. We've designed our lead product, PF614, which is an oxycodone TAAP product to be slowly released. And with our chemistry, it's very difficult to change the slow release into a fast release product. And that is what people who actually abuse opioids really crave, that initial rush of a fast relief in opioid. That's where our TAAP product is different from other formulations which can somehow and sometimes be manipulated. And we've actually showed clinically that this works.

Now, MPAR, we've layered on top of the chemistry, another layer of protection for overdose protection. And this is a combination of our TAAP opioids with a trypsin inhibitor. Now, it sounds a little counterintuitive, but we designed it so if you take your prescription, the pain relief is delivered as designed. If however, you've forgotten you've taken the prescription, you take a double dose, you're also taking double the dose of your inhibitor, which blocks that first step that we talked about, the trypsin activation. It prevents activation release of more opioid until it passes out of the body unchanged, preventing the overdose. And one should take this seriously because we have proven clinically it works.

The FDA has looked at our data. They've given us Fast Track status for PF614 and Breakthrough Therapy designation for PF614-MPAR. And that's the only opioid to actually get that designation. So we're very happy.

Boobalan Pachaiyappan

Okay, all right, so let's take one thing at a time. So let's start with PF614. And essentially, you have a technology like a clever chemistry you mentioned that could deliver opioids in the way that you wanted. And humanity has known opioids for almost 8,000 years. And you're probably rewriting the narrative of opioid delivery, to put it very simply.

So let's talk about 614. You are a 505(b)(2) company, which means you don't have to do all the clinical studies that are required to take it to the approval stage. So tell us what kind of data you can rely on based on the OxyContin's previously known data. And how are you leveraging that to go all the way to the regulatory Phase 3 and regulatory approval?

Lynn Kirkpatrick

Correct. We are using the 505(b)(2) path, and we've undertaken five clinical studies to-date. We've shown first of all, the chemistry works as designed. When you swallow PF614, in the intestine, converts to oxycodone and releases it. And we've been able to design the chemistry so it releases in a bioequivalent manner to OxyContin. That allows us to refer to the OxyContin labeling. We've also evaluated PF614 for liking. In other words, recreational drug users have evaluated PF614 versus an immediate-release product.

And they have indicated they don't particularly like it and they wouldn't take it again because other things are more pleasurable. So that allows us to appreciate our chemistry as abuse-deterrent.

Boobalan Pachaiyappan

That's exactly what we want to see.

Lynn Kirkpatrick

Yeah, exactly. We don't want people to try to manipulate, they can use something else. Our intent is to develop PF614. And we've designed our Phase 3 clinical study based on another clinical trial we did, a time

of onset study knowing you have to swallow and there is a little time before the product is released and absorbed to understand when is the maximal effect of PF614. So our Phase 3 study is going to be a post-surgical pain study. We will pre-dose with PF614 so that by the time the individual is out of surgery, we will see an effect. And our primary endpoint will be measuring area under the curve 48 hours, in other words, taking pain measurements for 48 hours after the surgery to understand how the patient is doing. And this is a little different from other analgesics where they deliver it post-surgery. They allow the patient to experience pain first and then they measure their pain reduction with their analgesic and they're kind of chasing the pain rather than controlling the pain from the start.

We believe PF614 will provide better pain experience for those individuals having surgery. They'll have opioids for a few days and we transition them to a non-opioid product. That's our intent for the acute pain space. We also know our products will be very well used in the chronic pain space and our intent is then to develop our MPAR product for that particular use.

Boobalan Pachaiyappan

Fantastic. So let's talk about your Phase 3 clinical trials. So one of the challenges of doing pain related clinical trials is that all patients are getting good standard of care, including those who are on placebo, which means there's a chance that the placebo readout could be much better and it could lower or shrink your delta. So how are you thinking about it, what steps you're taking to make sure that you can separate signal from the noise.

Lynn Kirkpatrick

Yes, and that's a very critical thing when you're designing your Phase 3 study and selecting your clinical sites, having those sites, understanding that placebo effect. We still believe there'll be a differentiation from PF614 to placebo. And we'll be able to monitor that with the rescue medication. So our primary endpoint is area under the curve for 48 hours versus placebo. We also have secondary endpoints, obviously the morphine milligrams equivalents that individuals are taking and we are comparing it to an IR opioid control arm, although that's not our primary endpoint. So part of the way you manage your Phase 3 trial is picking sites that understand the placebo effect.

Even when somebody is going in taking pain scores, an individual may respond to that person in a positive or negative fashion. So we have to have all of the scoring done very similarly between our sites. We're also using minimal sites for the trial. And we believe this particular abdominoplasty trial will enroll very quickly so that the fewer sites we use, we feel you can control the placebo effect much better.

Boobalan Pachaiyappan

Okay, I know you are interacting with the agency to the extent that you can. So has the agency provided any guidance in terms of the efficacy they wanted to see to rapidly or quickly advance the molecule to the approval stage?

Lynn Kirkpatrick

Well, they've indicated the safety database that we're doing, obviously with 505(b)(2) pathway, we are referring to some of the documentation that OxyContin has reported and uses in their label. But we still need a safety database and in other words, a number of subjects exposed to our product, PF614. I'm happy to say to-date we've shown very good safety profiles. And in a study we're doing right now with our MPAR technology, I'm actually very astounded at how few adverse events we're actually seeing with the product.

So the biggest indication, obviously we need to show efficacy, oxycodone, whether it's coming from PF614 or OxyContin, has shown efficacy in the past. We're expecting that. But really what we'd like to show with our 12-hour half-life, which is almost twice as long as the products that are on the market, will give us that better pain control as well as a good safety readout.

Boobalan Pachaiyappan

So your Phase 3 study is a randomized control study.

Lynn Kirkpatrick

Correct.

Boobalan Pachaiyappan

And obviously, you're going to evaluate the drug response, which is placebo. But are you under pressure to show a better efficacy versus OxyContin or that something totally out of the book?

Lynn Kirkpatrick

Yeah, we're not trying to show superiority. We're using the label to say we're just as efficacious. What we do want to show is some of these other secondary endpoints. One, I think abuse potential or abuse resistance is superior, the 12-hour half-life is superior. And the ability to layer on overdose protection is something that nobody else has.

Boobalan Pachaiyappan

Okay, so let's talk about your clinical trial data timeline. So when do you expect the enrollment to complete and when do you expect to do the data release and potential steps that you wanted to achieve in terms of how quickly you can go to the NDA stage?

Lynn Kirkpatrick

Our plan is to initiate our Phase 3 trial in second quarter of this year. We've already evaluated clinical sites, we've interviewed CROs to run this study, made selection, and we are preparing to actually launch as quickly as we can. As I mentioned, we're anticipating very quick enrollment and part of that is due to abdominoplasty being very favorable these days. We will take an interim look, but we are anticipating enrolling within this year. So potentially data readout in the fourth quarter of this year and we're working towards getting our NDA filed in 2026.

Now with Fast Track status, there's potential for – priority review, potentially rolling review, but it's up to the agency for that. I'm not entirely sure of the timeline, but we are anticipating, as I said, working towards an NDA in 2026.

Boobalan Pachaiyappan

Okay, fantastic. So let’s talk about the market opportunity, right? So you indicated that PF614 would be first – your primary focus would be on acute pain, and then later on you could expand to, let’s say, chronic pain and things like that. So tell us, because this market has already been educated by those abuse deterrent formulation technologies, including OxyContin. So you could leverage not only their clinical data, but also the market education that they have already done. So tell us like how it’s going to help you as you think about commercialization strategy.

Lynn Kirkpatrick

Sure. You mentioned the acute and the chronic market. It’s interesting that no other extended release oxycodone product has been approved in the acute market. So this will be a niche market for us and actually add on to the potential that we have in the chronic space. Our intent is to launch there because we feel we can get into that market more quickly and as I said, give the patient a better pain experience. And hopefully we can show that clinically.

With launching, the steps to get there include obviously education. We’ve started in the past presenting at PAINWeek talking about this product coming. And it’s very interesting that we have a very positive following

of physicians saying that they're waiting for this product to reach the market. Certainly moving from PF614 from acute into chronic will take a little time, but we'll focus on then having our MPAR product undertake that particular step.

And then we'll have both products having the opportunity to be prescribed for either acute or the chronic space. And as you know, that market in the chronic space is over $2 billion. OxyContin holds the majority of it. Xtampza, the most recently approved abuse deterrent formulation, which is still a formulated product has had good market share, but we feel launching our products as a new class, differentiating it based on chemistry, not a formulation, and educating the market about that and potentially reimbursement as well to say this provides a better safety profile to other products. So those are all the things we're thinking about in our launch and marketing.

Boobalan Pachaiyappan

Absolutely. And just to reiterate, 614 cannot be abuse through, let's say like through intranasal routes or intravenous routes. And you cannot even chew it or break it into pieces and take it. It's not going to work that way.

Lynn Kirkpatrick

Exactly. That's why we designed it to be activated by trypsin. Trypsin is an enzyme only found in your small intestine, it's not in your nose, it's not in your mouth, not in your bloodstream. And we've demonstrated that even if it's – PF614 itself - is absorbed into the circulation, it's excreted very quickly, it doesn't convert. And that is what we believe reducing the ability to abuse by those routes. But also the kitchen chemistry, which is another measure the FDA puts on an abuse deterrent formulation, meaning can you manipulate the product in your kitchen with using alcohol or acids or enzymes? And we've shown with our drug itself, no, it's very difficult. You don't get very much oxycodone. So that is another means that reduces the ability to abuse our product. And again, we have to market that and demonstrate that it will be less abused.

Boobalan Pachaiyappan

Yeah. And one of the differentiation factors that I'm looking at when I look at PF614 versus other abuse deterrent formulation is the half-life, which not many people talk about it, but it's actually a very important metric because this molecule, PF614, it's a bonafide twice daily. And others, they claim they're twice daily, but there's a very high chance that they're taking more than two drugs every day.

Lynn Kirkpatrick

Well, and that's what – even physicians have admitted. They prescribe OxyContin, the branded product, up to three, sometimes four times a day because it's not lasting. And that's what led to some early abuse. It was prescribed twice a day. People would have breakthrough pain and they start self-medicating as you're going through that pain and pain relief cycle. And potentially it could have led to some of the earlier addictions that people were getting from oxycodone delivered by a formulation.

We feel having a 12 hour half-life, keeping that very steady pain relief. When you have severe pain and we are talking severe pain here, we're not just talking is something that you can take an NSAID for. This is somebody who has a pain that really requires an opioid that we're promoting our product for.

Boobalan Pachaiyappan

Okay. So let's spend 30 seconds on your manufacturing and commercialization strategy and then we'll move on to MPAR. So tell us how easy or difficult it is to make 614 in a commercial scale.

Lynn Kirkpatrick

Well, we know how to make it. Obviously it is oxycodone with manufactured tail. We're able to make that tail separately. And then we have the manufacturing of PF614. We've identified a commercial group to actually

manufacture that for us. We can make it highly pure. It's exquisitely stable once it's manufactured. So that gives us the opportunity to manufacture and even have shelf lives for years from the product. And we've identified a very capable drug product manufacturer to make capsules for us.

PF614 can actually be dissolved in water and still have its abuse deterrent properties, which we're making powder in a capsule. We can open it up, dissolve it, improve the ability for somebody who has trouble swallowing or even have pediatric formulations because of this chemical modification versus a formulation.

Boobalan Pachaiyappan

So what's your current thinking in terms of commercializing 614 in the acute setting – acute pain setting?

Lynn Kirkpatrick

As far as thinking about the commercial launch?

Boobalan Pachaiyappan

Yeah.

Lynn Kirkpatrick

Well, we do have a plan. We're getting that in place. We have the manufacturing lined up and over this year we'll have product to move into the market probably hopefully end of 2026.

Boobalan Pachaiyappan

So do you like to do it alone or you wanted to have a partnership?

Lynn Kirkpatrick

Yes, at the moment we're anticipating doing it alone.

Boobalan Pachaiyappan

Okay. That's smart. All right, so for the next three minutes or so, let's spend little time on MPAR, even though you know it deserves a fireside on its own. As a medicinal chemist and you are a medicinal chemist, we both are very psyched about the technology and the commercial potential and all of that. But maybe at a very high level, so MPAR, can you sort of summarize some of the clinical work you have done and the high level takeaways? And how you are thinking about in terms of regulatory development?

Lynn Kirkpatrick

Great. PF614-MPAR, again is the combination product of PF614 and a trypsin inhibitor. We've evaluated that in a clinical setting because what we want to do is deliver oxycodone if you take it two pills twice a day. But if you take three pills or four pills, what we want to do is have overdose protection. So we've designed the combination with a formulated nafamostat trypsin inhibitor to do just that. And that's what we got breakthrough therapy for.

That was our first clinical trial. We evaluated a 25 milligram dose unit. Obviously we want higher dose units. We had to answer the question, does it still work with 100 milligrams of PF614? And that's our second clinical trial. Our clinical data to date says yes. We're working to have a discussion with the agency in June of this year to understand our full clinical path.

We're intending to launch PF614-MPAR for chronic use, refer and use the 505(b)(2) path with OxyContin. For that we still have preclinical studies to complete and I'm happy to say the federal government has given us a large $14 million grant September of last year to undertake both this second clinical trial as well as the number of the non-clinical studies we need to do. Our intent is to finish that and then build the database.

And PF614-MPAR would launch then shortly after PF614.

Boobalan Pachaiyappan

All right. Great. So one last question before I move to Dave. So do you think market understands the difference between TAAP, which is abuse protection technology, and MPAR, which is abuse resistance technology?

Lynn Kirkpatrick

Well, MPAR is overdose protection. I believe the individuals we speak to do because we do have a very positive response when we talk about our MPAR technology. The Holy Grail for opioids has always been oral overdose protection. We're the first product or first company to have a product with oral overdose protection. We believe our TAAP technology is superior to formulated technology.

But MPAR is a game changer and there are different markets. Obviously if you're in a hospital setting, you don't need MPAR. You're having your product delivered to you. When you go home, you have MPAR to take home. So we do feel there's a segment in the market for both of our products. And MPAR definitely is something differentiated from everything else.

Boobalan Pachaiyappan

I agree with that. All right, so let's switch gears and talk about finance for the last one minute or so. Can you remind us your cash position and then the runway and then the anticipated milestones that you can get through with your current cash?

David Humphrey

Sure. Our cash position right now we've got runway through about mid-year. We've been taking a lot of steps to reduce our cash burn. We've currently been burning less than $2 million a quarter. And what's really helped us to keep that low is, as Lynn mentioned, the NIH grant for MPAR. We had a $14 million grant over three years. We've got about $10 million of that left and that's going to support the MPAR clinical program.

We also had NIH grant funding for an opioid use disorder program with a methadone alternative that's in an earlier stage of development and there may be opportunities for additional grant funding in that area. So the real needs are going to be for the Phase 3 trial for PF614 and we'd be looking to raise capital to support that in the next few months, something on the order of $25 million to $30 million over the next 12 to 18 months. And that'll be our approach and we're looking opportunities to bring in capital and support our focus on Phase 3.

Boobalan Pachaiyappan

Absolutely. So that's it from us. Thanks so much for your time. We really enjoyed discussing insights with you guys.

Lynn Kirkpatrick

Thank you, Boobalan.

David Humphrey

Thank you.