Corporate Update Call

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CORPORATE PARTICIPANTS

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CONFERENCE CALL PARTICIPANTS

Thomas Flaten, *Lake Street Capital*

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PRESENTATION

Operator

Good morning, and welcome to the Ensysce Biosciences Inc. Corporate Update Call.

As a reminder, this conference is being recorded.

Your hosts today are Dr. Lynn Kirkpatrick, Chief Executive Officer; Dr. Bill Schmidt, Chief Medical Officer; and Dave Humphrey, Chief Financial Officer.

Before we begin the formal presentation, I would like to remind everyone that statements made on the call and webcast may include predictions, estimates, or other information that might be considered forward looking. While these forward-looking statements represent our current judgement on what the future holds, they are subject to risks and uncertainties that could cause actual results to differ materially. You are cautioned not to place undue reliance on these forward-looking statements, which reflect our opinions only as of the date of this presentation. Please keep in mind that we are not obligating ourselves to revise or publicly release the results of any revision to these forward-looking statements in light of new information or future events. Throughout today's discussion, we will attempt to present some important factors relating to our business that may affect our predictions. You should also review our most recent Forms 10-Q and 10-K for a more complete discussion of these factors and other risks, particularly under the heading Risk Factors.

At this time, I would like to turn the call over to Chief Executive Officer, Dr. Lynn Kirkpatrick.

Lynn.

Lynn Kirkpatrick

Thank you, Operator, and good morning, everyone. Thank you for joining us. I am pleased to welcome you to today's Corporate Update Conference Call.

Although some of you are familiar with Ensysce, I've historically kicked off these calls spending a few minutes reviewing our technology platforms and overall company focus for those of you new to our story.

First, we are a clinical stage biotech company using sophisticated chemistry to improve drug safety and performance. Our technology platforms TAAP and MPAR are designed to improve delivery and reduce abuse and overdose of prescription drugs, with a goal of creating new classes of prescription medicines that are intended to be both powerful and safe.

Our first effort is to bring to market the next-generation analgesics for strong pain relief. I will review our two technology platforms to offer background before we review recent clinical trial results.

TAAP stands for Trypsin-Activated Abuse Protection. TAAP is simply a chemical modification that makes a drug inactive until it is swallowed and reaches the small intestine where its exposed to an enzyme, trypsin. Trypsin is only found in the small intestine where it is responsible for digesting the proteins and meats we eat. This exposure to trypsin allows our own body to 'turn on' our TAAP drugs by starting the release process. TAAP allows us to deliver medicines orally, and we refer to it as 'sophisticated chemistry' since we can use the chemical modification to fine-tune how quickly or slowly a drug is released. TAAP can be applied to most types of medicines to either make them safer or actually perform better. We have applied TAAP to opioid products in an attempt to reduce recreational drug abuse.

Our second technology platform, MPAR, stands for Multi-Pill Abuse Resistance. MPAR is a smart overdose protection technology designed to be combined with our TAAP program prodrugs to prevent patients or abusers from overdosing. TAAP 'turns off' the release of the active ingredient in an overdose situation. This protection from oral overdose is designed to activate only when more than the prescribed dose is taken.

As mentioned, we have applied these transformative technologies initially to opioid products to produce the next-generation analgesics to treat severe pain. Now, I stress severe pain, which is what an opioid is indicated for. There are many types of pains where opioids are not appropriate, and not the focus of our current programs. As an example, there are those individuals who may require an opioid to control pain on a limited basis after major surgery, such as hip or knee replacement, whereby controlling pain in these situations appropriately may prevent one from developing chronic pain and needing opioids long term.

The CDC has just released guidelines for the clinical practice of prescribing opioids, recognizing the need for these medications for severe pain when other therapies are contraindicated or likely to be ineffective. We do know that in certain cirumstances, such as severe traumatic injuries or invasive surgeries, having pain is inevitable, but we feel suffering from severe pain should be optional. And that is a role for PF614. We also know past opioid use has led to a crisis, yet our TAAP and MPAR technologies have been developed to address and reduce both abuse and overdose of these prescription pain products, something that other marketed abuse deterrent formulations of opioids have failed to achieve.

It is important to note that although we are focused on developing our lead product, PF614, both our TAAP and MPAR technologies can be applied to many more prescription drugs, therefore providing us with ongoing opportunities. As our pipeline shows, we have applied TAAP chemical modification to a number of opioids as well as drugs to treat ADHD, and we have a discovery program focused on novel TAAP agents for treatment of opioid use disorder.

Our main focus today is to update you on our lead program, PF614, an oxycodone TAAP product, which is designed to replace OxyContin in the marketplace. TAAP has received fast-track status for use in chronic pain from the FDA, demonstrating that the Agency feels PF614 may fulfill an unmet therapeutic need. We continue to make significant strides in bringing our lead product to market, and we recently reported that PF614 was shown to be bioequivalent to commercially available OxyContin, an outcome

that may provide a shortened path to registration and commercialization through the 505(b)(2) regulatory process.

For those unfamiliar, bioequivalence is the clinical comparison of two dosage forms or active ingredient showing that they provide similar blood concentration levels, therefore resulting in the same therapeutic effect. In other words, the data from this study means that PF614 will be as effective in treating severe pain as OxyContin. The advantage of PF614, however, is that PF614 has a longer half-life; meaning pain relief should last longer than OxyContin, and possibly be a true twice-a-day pain medication. Additionally, we believe PF614 has a very superior abuse deterrent properties and also can be supplied with overdose protection, as with our PF614-MPAR product.

Our extensive early discovery programs provided us with over a hundred patents issued in 25 countries. We have built a strong team to assist in achieving the milestones we have set for each program and we have been advancing our lead products through clinical development in an attempt to bring our lead programs to market as quickly as possible.

Just this week, on Monday, we announced we received guidance from the FDA that an acute pain indication may be appropriate for PF614. While not binding, the FDA guidance is encouraging and states that our proposed clinical development approach of conducting at least two adequate and well-controlled clinical trials of two different pain models comparing PF614 to placebo and to another immediate release, or IR opioids, such as IR oxycodone, appears to be reasonable to support a new drug application for PF614 for an acute pain indication. Now, this guidance is important, since in the development path for an acute pain indication should be less costly and have a shorter path to commercialization than that for chronic pain.

The FDA advice letter also provided additional guidance with respect to the nonclinical studies in the clinical trials we have planned. As a result of the FDA guidance, we now intend to initially pursue clinical development of PF614 for an acute pain indication while we continue with our chronic pain development program. We believe that the longer half-life of PF614 compared to OxyContin may ultimately prevent acute pain from becoming chronic pain by better controlling severe pain on a day-to-day basis.

Now for the primary purpose of our call today. While Dave will later touch on our recent financial results at a high level, I'm pleased to turn the call over to Dr. Bill Schmidt, our Chief Medical Officer, to review the recently reported positive data from our PF614-103 Human Abuse Potential clinical study.

Bill.

Bill Schmidt

Thank you, Lynn. It’s wonderful to be here this morning to discuss the continued progress we are making with our clinical program for the development of PF614. I would like to begin by outlining the PF614-103 nasal human abuse potential study for which we recently reported positive results just two weeks ago. Human Abuse Potential or HAP studies are a requirement by the FDA to demonstrate that a drug with a potential for abuse has FEWER desirable features than other products used by recreational drug users. In other words, we want our drug products to be effective medications for pain but not ‘liked’ to the same extent as other oxycodone-containing products by recreational drug users. These HAP studies are vital for obtaining abuse-deterrent labeling upon final approval by the FDA.

The PF614-103 study examined PF614 for these ‘features of liking’. The primary measure was Maximum Drug Liking by the subjects and the secondary measure was whether the subjects felt they wanted to ‘Take Drug Again’. These features of PF614 were rated on a 100-point scale using a visual analogue or VAS scale that measures both desirable and undesirable drug effects and compared PF614 to both crushed oxycodone and a placebo by recreational drug users.

Eligible subjects were previously qualified to assure that they could recognize a reference opioid product as something they considered desirable, or 'Liked". The test subjects then received each of the 3 following treatments in a cross-over fashion (1 treatment in each of 3 treatment periods). The test drugs were administered in a randomized, double-blind, manner following a fasting period of at least 8 hours: either powdered PF614 from a 100 mg capsule; an equivalent opioid dose of crushed oxycodone HCl IR 40 mg; or a placebo powder. These were placed in dark jars for the subjects to inhale nasally, and then they were asked to rate how much they "liked" the test products. The primary outcome measure, maximum effect or Emax for 'Drug Liking' is recommended as the primary endpoint by the FDA in their Guidance on "Assessment of Abuse Potential of Drugs." This measure is known to correlate with a drug's potential for abuse.

This study was an important step in establishing that, unlike the current opioid analgesics on the market, which can be manipulated and abused through nasal inhalation, PF614 has a much lower risk of showing a favorable "liking" score by recreational drug users. PF614, as Lynn explained, must be exposed to trypsin in order to actively release oxycodone, and the only way that this can happen with nasally administered drugs is for the users to swallow a portion of the nasally administered product down the back of their throat. The study confirmed our hypothesis that the very low liking score for PF614 should reduce the risk of misuse, abuse, and diversion through nasal administration by those who use recreational drugs. I note that the FDA previously excused us from having to do intravenous abuse liability studies since PF614 will never see trypsin in the blood and hence will never be converted to oxycodone.

The topline results from this study, which compared intranasal administration of PF614 powder to crushed oxycodone immediate-release tablets, were recently announced and showed that PF614 had a significantly lower peak "Drug Liking" and significantly less appeal to 'take drug again' in non-dependent, recreational opioid users (n=26).

Specifically, the primary endpoint for the study "drug liking at this moment," was measured up to 24 hours after dosing using the VAS scale. As mentioned, in the study, PF614 powder produced significantly lower peak "Drug Liking" when compared with intranasal crushed IR oxycodone (with a p value of 0.0133) using the full 26 subject population. Furthermore, analyzing a smaller group of subjects following their exposure to the FIRST drug they were administered – call the first period analyses – a similarly strong difference was noted between PF614 (in 8 subjects) and crushed IR oxycodone (in 10 subjects) (with a p value of 0.0175), even with this smaller cohort of subjects.

Similar findings were noted with the second endpoint we evaluated, where we asked subjects if they liked the drug enough to want to "Take Drug Again". The study showed a statistically significant difference with a lower wish to take PF614 again versus crushed IR oxycodone, with a p value < 0.0001, also using the smaller group of subjects in the first period analysis. Such a highly significant value in the small group of subjects speaks to the difference between PF614 and oxycodone for those who wish to use these products recreationally.

These results are consistent with our prior findings that showed PF614 needed to be swallowed to release oxycodone and we believe demonstrate PF614 will provide unique advantages when compared with currently marketed products.

During the last quarter we also initiated a second HAP study, PF614-104, to evaluate the oral abuse potential of PF614, and subject dosing is continuing. This study is designed to test and confirm that PF614 will have less potential for 'Drug Liking' versus immediate release oxycodone at equivalent drug dosages when taken orally.

The PF614-104 study will examine the desirability of three doses of PF614 versus a current marketed equivalent and placebo in recreational drug users. Eligible subjects in this study will receive five treatments (one per treatment period) in a randomized, double-blind, crossover manner, meaning the

order of exposure of each treatment will be mixed for each subject. The primary outcome will again be to assess 'Drug Liking' for each treatment regimen and the key secondary endpoint will evaluate whether the subjects would 'Take Drug Again.'

We are looking forward to reporting the data from this trial, expected in the first half of 2023.

I want to reiterate why these HAP studies are important milestones — they are key for gaining abuse deterrent labeling for PF614. The studies help us further understand the tendency for drug abusers to like the effects achieved after taking PF614 either orally or nasally, compared to that of similar products, for example, crushed OxyContin.

I will now turn the call back over to Lynn.

Lynn Kirkpatrick

Thank you, Bill.

I'd like to again say how pleased we are with the positive top-line results of the nasal HAP study. I will now briefly comment on the initial clinical data from our overdose protection product, PF614-MPAR, that we reported in May.

We believe that this data from the PF614-MPAR study, where we combined PF614 and the trypsin inhibitor nafamostat, provided the first evidence of a product that could protect from an overdose. The results also provided the first human data to show PF614, when absorbed into the blood stream, does not convert to oxycodone, supporting our contention that attempts to abuse PF614 by direct injection should be unsuccessful.

We are continuing the PF614-MPAR study to fine-tune our drug product profile. Additional data from this part of the study is expected before the end of this year, and will allow us to test the concept of overdose protection by delivering increasing doses of PF614-MPAR in the final Part 3 of the study in the first half of 2023.

During the quarter, we announced that this study is being undertaken in partnership with Quotient Sciences, using their integrated Translational Pharmaceutics platform for the clinical testing of PF614-MPAR. Our findings from this study are important, because the MPAR combination technology is the first approach we expect may prevent all four forms of abuse: injecting, chewing, inhaling and, importantly, oral overdose.

Looking ahead at the milestones for the remainder of the year, I summarized them as follows:

We expect to report data from the oral Human Abuse Potential study PF614-104 during the first half of 2023.

We expect the full data from PF614-MPAR-101 Part 2 to be reported before the end of this year, 2022, and data from the final Part 3 of the study in the first part of next year.

I will now welcome our CFO, Dave Humphrey, for a short financial summary.

Dave.

Dave Humphrey

Thanks, Lynn.

As of September 30, remaining funding available from federal grants included $3.3 million to support our OUD research program, and another $2.6 million to support the third part of the ongoing Phase 1 clinical trial evaluating the MPAR platform. With this non-dilutive government grant funding, and our September 30 cash balance of $4.5 million, we are on track to advance the development of our highly unique TAAP and MPAR technologies through the end of the year.

I'll now turn the call back to Lynn for closing remarks and questions.

Lynn.

Lynn Kirkpatrick

Thanks, Dave.

Before I turn the call over to the Operator for Q&A, I want to take a moment and acknowledge all our company constituents as we forge ahead on our mission to provide patients in severe pain a unique therapeutic option. Developing any new drug involves a complicated and sometimes tortuous path and we are pleased that the FDA has provided us its recent feedback that will allow us to finalize our path toward commercialization in the coming months. We believe our recent clinical data that we highlighted today point to the potential for PF614 to be a safer pain medication and a highly novel option for those who experience severe pain.

Operator, we will now take questions.

Operator

Thank you. Our first question is from the line of Thomas Flaten with Lake Street Capital. Please proceed with your questions.

Thomas Flaten

Good morning. Appreciate you guys taking the questions.

Lynn, I was wondering if you could provide some context for the interaction you had with FDA that generated the guidance from the acute indication. What was the question you were asking? Were you surprised by the outcome? I'm just hoping you can kind of set the stage for how we ended up with that press release you put out this week.

Lynn Kirkpatrick

Sure. Thanks, Thomas.

We have been interacting with the Agency now for almost a year, and considering various options for PF614 in an attempt to understand how we may be able to bring PF614 to the market in a, I guess, more direct path. As you know, with the COVID and supply chain issues, a lot of things have been delayed, and in order to potentially expedite some of the activity, we had asked the Agency whether an acute pain indication may be appropriate, which potentially would have a reduced timeline for us, both for the nonclinical activities, as well as the clinical path. We began our discussion about December of last year. We had additional questions for the Agency last March, and we were very pleased with our back and forth that they have agreed that a potential clinical development path for PF614 in acute pain, as well as chronic pain, would be appropriate.

This will allow us now to move, really build on the answers, identify specifically the clinical program we intend to utilize over the next few years, and hopefully bring the product to market more quickly than we could in the acute pain space.

Thomas Flaten

Great. And did they render an opinion about the chronic pain indication, or was this specifically to get them to agree to acute, just to confirm?

Lynn Kirkpatrick

Yes. We'd always intended and we still intend to develop PF614, because it is an extended release product in the chronic pain space, but this was specifically to address whether or not it might be appropriate for this type of agent, which has a delayed onset and an extended release profile, to be used for acute pain. And really, the CDC guidelines that has broken pain down really into three subcategories now, acute, subacute, and chronic, defines where our clinical trials may be most appropriate.

Thomas Flaten

Got it. In terms of upcoming interactions with FDA to move towards an acute development plan, what's on the horizon there? I'm assuming you're going to wait until you have the HAP studies done and be able to report those out. But can you kind of lay out for us what happens next?

Lynn Kirkpatrick

Well, we're currently meeting with our clinical advisory board to continue the discussions of exactly what our clinical programs will be so we can develop our protocols. We anticipate providing those to the Agency next year and discussing them. And as they indicated, two well-controlled studies, and for acute pain you do need to do both of bony, and a soft tissue study would be considered appropriate for an NDA in this indication.

We will be discussing those protocols with the Agency in the coming month.

Thomas Flaten

And then a final question if I might. Any adjudication on the 505(b)(2) question, or was that not part of the discussion most recently with the FDA?

Lynn Kirkpatrick

Good question. No, these questions were submitted much longer before we had the data, but that will be certainly in our upcoming discussions.

Thomas Flaten

Understood. I appreciate you guys taking the questions. Thanks so much.

Operator

Our next question is from the line of Hunter Diamond with Diamond Equity. Please proceed with your questions.

Hunter Diamond

Hello. Congratulations on the quarter so far.

I was wondering, in terms of the recent top-line results for intranasal administration of PF615, can you say why the field data supports advantages over currently marketed products?

Lynn Kirkpatrick

Bill, would you like to take that question?

Bill Schmidt

Sure. We compared this directly to crushed oxycodone HCl, which would be known commercially as Roxicodone. We used opioid-equivalent doses of both products, and when the subjects snorted the Roxicodone product, they got the expected rush that you'd expect from insufflation of an opioid product. They liked it. Some even hit 100 on the Visual Analog Scale in terms of how much they liked the drug and whether they would take the drug again. Those who insufflated placebo—and this was all on a double-blind basis and they didn't know what they were getting (it just looked like white powder), those who insufflated placebo had very neutral scores that indicated that they neither liked it nor disliked it. It didn't have aversive properties.

When they got to PF614, the liking scores were, let's say, very muted. They were substantially less than the scores that any of the individuals had recorded when they had snorted authentic oxycodone HCl. When we looked at this again for 'Take Drug Again', the scores were also low on the PF614 side compared to oxycodone HCl side. We believe that this is because they actually received exposure to less oxycodone derived from PF614 when they snorted PF614 because the only part that would convert to oxycodone is what they swallowed down the back of their throat. Previous studies have shown that that's only about 20% percent of what goes up their nose.

It would be the equivalent of taking, say, a 100 milligram tablet of oxycodone, which would be an enormous dose, but clearly instead a dose of 40 milligrams, which was the actual dose of oxycodone HCl. If you reduce that to 8 milligrams, so that's a 20% dose of oxycodone, it probably wouldn't engender very much liking or 'Take Drug Again.' It's probable that the recreational user would be looking for something else if they really wanted to get high.

That's what we showed in this study, that, given an alternative, recreational drug users would not take PF614 again. They would look for some other drug product.

Hunter Diamond

Great. Thank you. Can you provide some color on how investors view the acute pain indication for PF614? What exactly is the speed to market and what's—I mean, I kind of understand the overall market opportunity, but what's the speed here to market?

Lynn Kirkpatrick

Thanks, Hunter.

The advantage of us moving into the acute pain space means that we're not required to undertake some of the nonclinical studies which are required for chronic pain and would take up to two years to complete some of the carcinogenicity studies. That is eliminated from our development path. Additionally, in the chronic pain space, we would be required to have subjects exposed to PF614 for up to a year, so the clinical development path is also reduced. We have not identified our ultimate timeline to date. We hope to provide more clarity. But we believe this opportunity, although on a market basis is a smaller market, it

will be adding to the overall market when we are able to commercialize both for acute as well as chronic pain, and initially bring the product to market more quickly.

We're anticipating a significant reduction in time and cost, and we'll be providing more guidance on our expected commercialization date probably in the coming month.

Hunter Diamond

Thank you so much. Appreciate it.

Operator

Thank you. At this time, I would now like to turn the call back over to Dr. Kirkpatrick for closing remarks.

Lynn Kirkpatrick

Thank you, Operator.

I would like to thank each of you for joining our earnings conference call today. I look forward to continuing to update you on our ongoing progress in the coming year. I wish everyone a lovely holiday season and look forward to updating you on our next call. Thank you very much.

Operator

Thank you. This will conclude today's conference. You may disconnect your lines at this time. Thank you for your participation.