
**Corporate Update Call**

**April 11, 2023**

## CORPORATE PARTICIPANTS

**Lynn Kirkpatrick, Ph.D.,** *Chief Executive Officer*

**Dr. William Schmidt,** *Chief Medical Officer*

**Dave Humphrey,** *Chief Financial Officer*

## CONFERENCE CALL PARTICIPANTS

**Thomas Flaten,** *Lake Street Capital*

**Hunter Diamond,** *Diamond Equity*

## 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, Ph.D.**

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.

Before I get into the full background on the Company, I want to restate our mission and highlight three major achievements that have moved Ensysce forward in the last year.

We're still losing over 200 Americans everyday to opioid overdose; yet we also have countless Americans with severe pain who cannot get access to their prescriptions. I believe this is unacceptable and the Ensysce team believes we have a solution to reduce this crisis.

The three key points that we achieved this year are pivotal to our long-term success. Firstly, strong efficacy. Our bioequivalent study demonstrated that PF614 will deliver powerful pain relief equivalent to OxyContin. Secondly, less abuse. Our two human abuse potential studies were successful and demonstrated that PF614 is not attractive to individuals who may seek to abuse opioids. Thirdly, less overdose. Our PF614 MPAR study demonstrated that this unique platform works and can deliver the first ever product that may prevent overdose if too many pills are taken.

In the next few minutes I'll expand on this data, but the important take-away is we have the first product with strong efficacy, lower abuse and overdose protection. This is a real breakthrough that we believe could save many lives.

For those of you new to our story, we are a clinical-stage 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 the goal of creating new classes of prescription medicines that are intended to be both powerful and safe.

Our first endeavor is to bring to market the next generation of analgesics for the treatment of severe pain. I will review our two technology platforms and then explain our clinical trial progress over the last year.

2022 was a year in which we made important progress across all of our clinical development programs, accomplishing key milestones that further advance our two lead programs. We are highly focused on positioning our technology platforms, TAAP and MPAR, opioid abuse deterrent, and overdose protection programs as next-generation opioid products.

TAAP stands for Trypsin Activated Abuse Protection. In simple terms, it is a chemical modification that makes a drug inactive until its swallowed and reaches the small intestine, where it's exposed to the natural enzyme trypsin. Trypsin, which is only found in the small intestine and responds both for digesting the proteins and meats we eat, starts the activation process to release the free opioids. In other words, our TAAP products are activated or turned on through normal digestive processes in our own bodies. The subsequent rate of release is further designed into the chemistry which determines either an immediate or extended release profile. We refer to TAAP as sophisticated chemistry since it limits opioid release to oral administration, and it determines 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.

Our second technology platform, MPAR, stands for Multi-Pill Abuse Resistance. MPAR is a smart overdose protection technology, an industry first. It is designed to be combined with our TAAP prodrugs to prevent patients or abusers from overdosing. MPAR 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've 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 a potent opioid, like oxycodone, should be indicated for. There are many types of pain where opioids are not appropriate, and hence not the focus of our current programs. We know that controlling severe pain appropriately may prevent someone from developing chronic pain and requiring opioids long term.

As I said, these medications are used to treat severe pain when other therapies are contraindicated or likely to be ineffective, as per the recent updated CDC guidelines for the clinical practice of prescribing opioids. We do know that in certain circumstances, such as severe traumatic injuries or invasive surgeries where having pain is inevitable, and controlling pain is the role of our lead product, PF614.

We also know that overly broad opioid use has led to the current opioid crisis; yet our TAAP and MPAR technologies have been developed to address and reduce both abuse and overdose of these prescription pain products.

This is something other marketed abuse deterrent formulations of opioids have failed to achieve. We believe these two technologies can give both patients and prescribers more confidence in their medicine's safety.

Although we are focusing on developing our lead product, PF614, please remember that both TAAP and MPAR can be applied to many more prescription drugs; therefore, for providing us with ongoing opportunities. As our pipeline shows, we have an applied TAAP chemical modifications to a number of opioids as well as drugs to treat ADHD and we have a discovery program focused on novel TAAP agents for treating opioid use disorder.

Now let me update you on our lead program, PF614, an oxycodone TAAP product which is designed to replace OxyContin in the marketplace.

PF614 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.

During 2022, we initiated three clinical studies to advance PF614 through development. I could not be prouder of the work our team has achieved. With the successful completion of these three trials, we are now positioned with a growing safety database that allows us to move to an end-of-Phase 2 meeting with the FDA to discuss our Phase 3 plans and to map out the last steps to commercialization. All three studies conducted over the last year delivered positive data in line with our ambitious target profile. In July, we announced positive data from the study, PF614-102, that directly compared PF614 to OxyContin for bioequivalence.

For those unfamiliar, bioequivalence is the clinical comparison of two dosage forms, or active ingredients, showing that they provide similar blood concentrations; therefore, resulting in the same therapeutic effect. With the positive measure of bioequivalence, a product may use the shortened 505(b)(2) regulatory pathway to commercialization, potentially saving time and cost.

In our oral bioequivalent study, PF614 was found to deliver oxycodone at the same rate and level as did OxyContin. However, the important advantage observed for PF614 is its longer half-life. Meaning, the pain relief should last longer than OxyContin. The data supports our hypothesis that PF614 should be a true twice-a-day pain medication, which is a major patient benefit.

Additionally, we believe PF614 has superior abuse deterrent properties and ultimately with MPAR can be launched as the first-ever opioid analgesic with overdose protection.

We believe the data will support our goal of PF614 replacing OxyContin in the marketplace. We also expect the positive data from this study will support the 505(b)(2) regulatory path for clinical development of PF614, reducing time to launch.

We also initiated two human abuse potential studies to evaluate how well recreational drug users like PF614, versus OxyContin when crushed and inhaled or just taken orally. These HAP studies are required to support abuse deterrent labeling upon final approval of PF614. HAP studies are conducted to

determine if a new opioid has less abuse potential, both orally through crushing or chewing, and nasally by inhaling or snorting, compared to traditional opioid products.

During 2022, we reported that our nasal study, PF614-103, was very successful. Inhaled PF614 had significantly reduced "Drug Liking" when compared to inhaled, crushed, immediate release oxycodone.

Overall, the data means that drug users did not like PF614 and would not take drug again due to an inability to abuse by snorting, unlike the oxycodone comparator.

In October, we received guidance from the FDA that an acute pain indication may be appropriate for PF614. While not binding, the guidance is encouraging and states that our proposed clinical development approach of conducting two well controlled trials in two different pain models with appropriate controls appeared to be reasonable to support a new drug application for PF614 for an acute pain indication. This guidance is important, as it provides us with a shortened development path for an acute pain indication that may be filed for approval much earlier than approval for chronic pain indications.

The FDA advice letter also provided additional guidance with respect to nonclinical studies in addition to the clinical trials we have planned. As a result of the FDA guidance, we are moving forward with clinical trials to support PF614 for acute pain, such as postsurgical pain, while we also continue our chronic pain development program. We believe the longer half-life of PF614 compared to OxyContin may better control severe pain on a day-to-day basis, ultimately preventing acute pain from becoming chronic.

Additionally, in late 2022, we initiated and completed enrollment of a second TAAP study, PF614-104, comparing oral administration of PF614 to oxycodone and placebo. Recently, we announced positive results from the study, meeting both our primary and secondary endpoints. We successfully showed PF614 at significantly lower "Drug Liking" and ""Take Drug Again" scores than the comparator OxyContin tablets. Further, the data from this clinical trial showed that PF614 even at doses double that of oxycodone did not increase its abuse potential. We believe these data were the result of PF614 taking a longer time to reach maximal blood levels, a feature that cannot be changed by manipulating through crushing or chewing.

Lastly, I want to stress our programs are protected by a global patent portfolio of over a hundred patents issued in 25 countries, ensuring an opportunity to address the need for safer pain medication globally. We have built a strong team to assist in achieving the milestones we have set for each program and we now have a goal of advancing our lead products through the last stages of clinical development in an attempt to bring our lead programs to market as quickly as possible.

Now I'm pleased to turn over the call to Dr. Bill Schmidt, our Chief Medical Officer. Bill is very experienced in analgesic drug development and will discuss in more detail the recently reported positive data from our second TAAP clinical study, PF614-104. Bill?

**Dr. William 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 have worked in analgesic drug development throughout my career and I'm very excited about the new data Ensysce just reported.

We have developed a new generation of opioid analgesics, which promises strong efficacy with less abuse and less overdose potential, something that industry and society really needs. Our goals in the last year were, as Lynn described, mission critical in demonstrating that PF614 was not only effective but also unattractive to people who may seek to abuse opioids.

I would like to begin by outlining that PF614-104 oral human abuse potential study. Human abuse potential, or HAP, studies are required by the FDA to demonstrate that a drug with a potential for abuse has fewer desirable features than traditional opioid products used by recreational drug users. In other words, we want our drug products to be effective for moderate to severe pain but not liked to the same extent as other oxycodone-containing products by recreational users.

The PF614-104 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 analog, or VAS, scale that measures both desirable and undesirable drug effects. For our oral HAP study, we compared three doses of PF614 capsules to a 40 milligram tablet of immediate release oxycodone and to placebo by prequalified recreational drug users who know how to recognize opioid drugs.

We recently announced the main results from the study, which showed that PF614 has a significantly lower peak "Drug Liking" and significantly less appeal to "Take Drug Again" than the comparator oxycodone tablets. Our study was done in 28 nondependent recreational drug users who typically use oxycodone or other opioid drugs to get high 10 or more times in the past year. These data are very important in establishing that we have an effective agent with the appropriate protection to discourage any abuse in the dose range which we intend to launch.

Study subjects were previously qualified to assure that they could recognize a referenced 40 milligram oxycodone tablet as something that they considered desirable or liked. The test subjects then received each of the five following treatments in a complete crossover fashion. There was one treatment in each of five treatment periods with a five day or longer washout period in between each. The test drugs were administered in a randomized, double-blind manner; meaning neither the subject nor the person administering the treatment knew which one they were getting following a fasting period of at least eight hours.

In each test period, the subjects received either a PF614 50, 100 or 200 milligram capsule or oxycodone HCl immediate release 40 milligram, which was overencapsulated to look identical to PF614 100 milligrams, which it was equivalent to or a placebo capsule. These were taken orally and then over a 24-hour period. Each subject was asked a number of questions to rate how much they liked each test product.

The primary measure was maximum effect, or Emax, for "Drug Liking". This measure, which is known to correlate with a drug's potential for abuse, is the primary endpoint recommended by the FDA and their guidance on Assessment of Abuse Potential of Drugs.

For the second measure, subjects were also asked to rate whether they liked the drug enough to want to take it again. Specifically the primary endpoint for the study, "Drug Liking" at this moment, was measured at time periods up to 24 hours after dosing using the 100-point VAS scale. PF614 produced statistically lower effects than oxycodone, the lowest dose $p<0.0001$, and statistically significant overall "Drug Liking" at both the low and the mid doses $p<0.0001$ and $p=0.0025$, respectively. PF614 took a significantly lower median time to reach Emax for "Drug Liking" than oxycodone at all three dose levels, which is highly important for reducing drug abuse.

Similar findings were noted with a second endpoint we evaluated, where we asked each subject if they liked the drug enough to want to "Take Drug Again". The secondary endpoint was met at both the low and mid dose of PF614 with highly significant values of $p<0.001$ and $p=0.0038$, respectively, and was numerically lower than comparator even at double the dose, demonstrating that recreational users would be less motivated to abuse PF614 compared to immediate release oxycodone.

The study was an important step in establishing that unlike the current opioid analgesics on the market, which can be manipulated and abused to release higher concentrations of opioids more quickly through

chewing or crushing to defeat the time release formulation. PF614 has a much lower risk of showing a favorable "Liking" score by recreational drug users.

Remember, the time release features of PF614 cannot be altered by these means. The study supports our hypothesis that the very low "Liking" scores for PF614 should reduce the risk of misuse, abuse and diversion through oral administration.

I want to also 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 if injected for purposes of recreational drug use. As Lynn said before, the only way to activate our TAAP prodrugs is to take them orally and allow normal digestive processes to initiate the activation cycle.

I want to reiterate why these HAP studies are important milestones. They are key for gaining approval and to position PF614 as a new class of opioid when it enters the market. We believe that PF614 will offer a better solution to treat severe pain with less risk of abuse and overdose.

I will now turn the call back over to Lynn.

**Lynn Kirkpatrick, Ph.D.**

Thank you, Bill.

I'd like to again say how pleased we are with the positive topline results of the oral HAP studies.

I will now briefly comment on our overdose protection product, PF614 MPAR.

This product is truly groundbreaking and could save many lives. PF614 MPAR is designed to build on the efficacy of PF614 and deliver the first-ever agent with strong analgesic effect and protection against all forms of drug abuse: inhaling, chewing to make it release faster, injecting and, importantly, intentional or accidental oral overdose.

Last November, we completed the initial part of the first clinical trial to evaluate overdose protection of PF614 MPAR. This study is being undertaken in partnership with Quotient Sciences, using their integrated translational pharmaceutics platform for the clinical testing of PF614 MPAR. This platform has allowed us to complete our initial overdose protection studies in record time. The data from this trial, PF614 MPAR 101, demonstrated that we could achieve opioid overdose protection with PF614 MPAR at a 25 milligram dose level. The results also provided the first human data to show that the intact prodrug, PF614, when absorbed into the bloodstream following oral administration, does not convert to oxycodone since it will never be digestive enzymes. This information is important as it supports our contention that attempts to abuse PF614 by direct injection should be unsuccessful.

In January, we expanded the study into a second part to provide additional data to confirm overdose protection for PF614 MPAR. This study has completed enrollment and we are awaiting the bioanalytical results of the pharmacokinetic portion of the study.

Looking ahead at the milestones for the remainder of the year, we are setting even more ambitious goals designed to get us to the market as soon as possible. I'd summarize them as follows.

One, we expect final results from the PF614 MPAR 101 study midyear in 2023. Two, we expect midyear to initiate an experimental pain study to evaluate the onset time of analgesia for PF614 to support our Phase 3 plans for analgesic efficacy in postsurgical pain indications. Thirdly, we expect to complete an end-of-Phase 2 meeting with the FDA in the second half of the year. Finally, we expect to initiate one of the Phase 3 analgesic efficacy studies for PF614 by the end of 2023.

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

**Dave Humphrey**

Thanks Lynn.

As of December 31, 2022, remaining funding available from federal grants included $3.2 million for our Opioid Use Disorder Research Program, and another $1.4 million for the third part of the ongoing Phase 1 clinical trial evaluating the MPAR platform. This nondilutive government grant funding, along with our December 31 cash balance of $3.1 million, and proceeds from a $3 million registered direct offering in February, all support the ongoing development of our highly unique TAAP and MPAR technologies.

Operator, we will now take questions.

**Operator**

(Operator Instructions)

Our first question comes from the line of Thomas Flaten with Lake Street Capital. Please proceed with your question.

**Thomas Flaten**

Hey, good morning, everyone. Congrats on all the progress. Hey, Lynn, just sequencing-wise, I wanted to ask, so the time of onset study will be run and completed prior to the end-of-Phase 2 meeting, or will you—or is there a chance you can make the request for the end-of-Phase 2 meeting while that study's ongoing? I'm just trying to figure out timing and sequencing.

**Lynn Kirkpatrick, Ph.D.**

Yes. Thomas, thank you. Our plan is really to try and do things in parallel, so we will be initiating, we believe, midyear, this study, while we're putting in our meeting request. We're working on both of them at the same time. There is a potential we'll be finished the study prior to the end-of-Phase 2 meeting with the FDA, but both are ongoing at the moment.

**Thomas Flaten**

The time of launch is not required to successfully complete the end-of-Phase 2 and get the input you need?

**Lynn Kirkpatrick, Ph.D.**

Not specifically, but we believe it would put our Phase 3 plans in a better light with the agency as we discuss them. We will be really thinking about getting the trial initiated and completed very quickly so that it can be included in the end-of-Phase 2 package.

**Thomas Flaten**

Got it. 2023 financials, just thinking about you, obviously, we're doing the HAP studies in the first quarter, and then it sounds like there will be a bit of a lull in the second quarter at least. How should we think about R&D spending in particular as you guys move or transition from study to study and end to the end-of-Phase 2 meeting?

**Lynn Kirkpatrick, Ph.D.**

Dave, did you want to take that one?

**Dave Humphrey**

Sure. Yes, as you mentioned, Thomas, I do expect that we'll see a decline in R&D spending in the next couple of quarters, beginning in Q2, at least. We've had, as Lynn outlined, multiple clinical studies going on in the last few quarters, and with some of those wrapping up, we do expect to see R&D spend come down to levels maybe of earlier last year, as opposed to the last couple of quarters.

**Thomas Flaten**

Final question, if I may. On the two HAP studies, anything that you saw in those studies that might raise questions for FDA or were they about as clean as you could have expected and required for successful FDA interactions?

**Lynn Kirkpatrick, Ph.D.**

Bill, would you like to take that one?

**Dr. William Schmidt**

Sure Lynn. Thomas, these really did come out in a way that they met my expectations. In fact, they exceeded my expectations. What we see is that PF614 clearly differentiates itself from either intact or crushed oxycodone HCl. But when we compare the data from this trial with that of competitor drugs, such as Xtampza, we see that we have liking scores that are 10 or 20 points lower than what we're seeing with Xtampza. With Xtampza data, they missed the opportunity to get abuse deterrence in the label. We think that we've got stronger data and we see the possibility that we will have abuse deterrence in our label.

**Thomas Flaten**

Excellent. Appreciate it. Thanks, everyone.

**Lynn Kirkpatrick, Ph.D.**

Thanks, Bill.

**Operator**

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

**Hunter Diamond**

Firstly, fairly comprehensive call, so I don't have too many questions. My one question was can you talk about the patent portfolio? For a small company you have a pretty robust patent portfolio. What's the IP strategy for the business as a whole?

**Lynn Kirkpatrick, Ph.D.**

Hunter, thanks for that. Yes, I'm glad you recognize we have a massive patent portfolio, and globally. Strategically, as a company, we're obviously focusing on the U.S. market at the moment. We have been doing outreach globally to try to monetize some of the ex-U.S. patents, and we'll still continue. I believe a lot of the companies that we've spoken to are very interested as, obviously, the opioid crisis not just a

problem here in the U.S.. But we do feel we'll be bringing our product forward here and then probably having a better opportunity to monetize in an ex-U.S. market as we bring PF614 to commercialization.

**Hunter Diamond**

Great. No, appreciate that. Makes perfect sense. My second question was on the nondilutive grants for financing. Obviously, I think it declined a little year-over-year. It's probably just an accounting item. But I would think there's a massive opportunity for nondilutive financing given the opioid crisis in the country and government initiatives behind that. Maybe just more color on what you're seeing on grants and the opportunity for nondilutive financing for the business.

**Lynn Kirkpatrick, Ph.D.**

Thanks. Again, I'll take this one. We've been very successful. In fact, very pleased that we received two large awards from the National Institute on Drug Abuse. Obviously, we believe that's a very important factor as well to supplement our other financing and we are continuing to try and access funds, specifically for the opioid, or the MPAR program, but we also are looking at opportunities to utilize our platforms, TAAP and MPAR, for other indications and we're continuing to explore those both this year and in the future.

**Hunter Diamond**

Great. No, perfect. Makes a lot of sense. Again, congratulations on the results and thanks for taking my questions.

**Lynn Kirkpatrick, Ph.D.**

Thanks, Hunter.

**Operator**

I would now like to turn the call back over to Dr. Kirkpatrick for her closing remarks.

**Lynn Kirkpatrick, Ph.D.**

Thank you, Operator.

I would like to thank each of you for joining our corporate update conference call today and look forward to continuing to provide ongoing progress and growth reports. With our continued progress, there is increasingly more to discuss on our update calls and we look forward to this cadence continuing throughout the year. I hope you share our optimism that we have some life-changing programs approaching the market. I look forward to speaking with you and updating you on our additional progress very soon.

Thank you.

**Operator**

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