Ensysce Biosciences, Inc.

Corporate Update Call

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CORPORATE PARTICIPANTS

Lynn Kirkpatrick, PhD, Chief Executive Officer

Dave Humphrey, Chief Financial Officer

CONFERENCE CALL PARTICIPANTS

Thomas Flaten, Lake Street Capital Markets

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; 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 judgment 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'd like to turn the call over to Ensysce's Chief Executive Officer, Dr. Lynn Kirkpatrick. Lynn?

Dr. Lynn Kirkpatrick

Thank you, Operator. Good morning everyone and thank you for joining us. I am pleased to welcome you to our corporate update conference call. Before I begin, I want to direct your attention to the slide deck posted and accessible via our investor relations website at ir.ensysce.com. This slide deck is our latest investor presentation, inclusive of the recently released clinical data from the PF614-102 and PF614-MPAR-101 studies which I am very excited to review with you in detail this morning.

For those of you new to Ensysce, we are a clinical stage biotech company using sophisticated chemistry to improve drug safety and performance. Our technologies, TAAP and MPAR, I will go into more detail

shortly on both, 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 powerful and safe.

Our focus is to utilize our transformative technologies to address the ongoing opioid crisis. We have applied our chemical approach to a number of opioid and ADHD therapies, and our lead program is an oxycodone product to replace OxyContin in the marketplace. Our lead agent PF614 has received Fast Track status from the FDA and we believe we have a shortened path to registration through the 505(b)(2) regulatory process. We have over 100 patents issued in 25 countries, supported by over $100 million in investment since our inception. We have been progressing our lead products through clinical development and exploring other means to apply our technology. Additionally, I am supported by a strong team to aid me in achieving our goals. One example of the depth of our management bench is the recent addition of Dr. Nily Osman, as our chief medical officer. Dr. Osman is a highly versatile board-certified neurologist, migraine and pain specialist with over ten years of experience in both R&D and medical affairs within the pharmaceutical, CRO and medical device industries.

Before I continue with our update, I want to describe our two technology platforms in detail. This will be helpful background before I review the clinical trial results. For those following along in the slide deck, I would like to turn your attention to slides 5 and 6. The first technology, TAAP, stands for Trypsin-Activated Abuse Protection. Trypsin is a digestive enzyme that is only active in the small intestine. TAAP is a chemical modification that inactivates the drugs in Ensysce's opioid products, including our lead agent PF614. This chemical modification protects from non-oral abuse, provides resistance to manipulation of our products, and is meant to reduce other forms of recreational drug abuse.

The second technology platform, MPAR, stands for Multi-Pill Abuse Resistance. MPAR is a smart overdose protection platform, designed to be combined with our TAAP prodrugs to prevent patients or abusers from overdosing. This protection from oral overdose exists only when more than the prescribed dose is taken.

Importantly, applying our technologies to opioids does not limit the ability of our products to provide a high degree of pain relief for those in severe pain.

Opioids have been used for thousands of years. Ensysce believes it will introduce a new class of opioids that are differentiated from the abuse deterrent formulations (or ADFs) that have been marketed for over 20 years. These ADFs did not solve the crisis of opioid abuse as the numbers dying from opioid related deaths have been increasing despite this approach that was designed to limit abuse. The market is huge for painkillers, both in the US and globally, evident on slide 8.

Looking at slide 9, you will see Ensysce has an extensive patent portfolio that may allow us to explore opportunities for our TAAP and MPAR products outside of the US.

Now, for the primary purpose of our call today. While we will touch on our financials from our last week earnings release during this call, I will take this opportunity to review how our technology works and to show the recently reported data from our PF614-102 and PF614-MPAR-101 clinical studies. I recently presented this data at the 22nd annual SMi Pain Therapeutics Conference in London UK on May 5, 2022.

Slides 11 through 18 summarizes how TAAP and MPAR work and give some examples of our animal data that supported the development of these abuse and overdose protection technologies.

On Slide 12 we see that our TAAP prodrugs, or Trypsin Activated Abuse Protection prodrugs, need to be swallowed and exposed to trypsin in our small intestine to activate and release an opioid. This feature, directly correlated to the mission of Ensysce, reduces the ability to abuse by chewing, manipulating and snorting or injecting our opioids.

Slide 13 and 14 demonstrate how we are very different from the abuse deterrent formulated products that can be manipulated to release the opioid faster than designed. I believe it's important to point out the ADFs have been unsuccessful, thus proving the growing need for our chemical approach.

Moving on, our MPAR technology is designed to prevent overdose. MPAR – Or multi-pill abuse resistance – is a combination product of our TAAP opioid with a trypsin inhibitor called nafamostat. When a prescribed dose is taken, the opioid is released as designed. If too much is taken, as when one forgets if they have taken their medication and doubles the dose by accident, or if it is intentionally taken in overdose to try to get high, the increasing amount of nafamostat present is able to block the first step of the activation process until the material passes out of the body unchanged. This is illustrated with animal data on Slide 17

Slide 18 shows the data from our previously completed Phase 1 study that demonstrated orally administered PF614 converted efficiently to oxycodone, it released oxycodone in a dose dependent manner and it was found to be safe.

Importantly as demonstrated on slide 19 we found that PF614 has a longer half-life as compared to OxyContin which was an unexpected result at the time. This longer half-life will provide what we believe will be a true twice a day product. OxyContin is prescribed twice a day, and reimbursed for twice a day dosing, but it does not last twice a day – so patient start taking the product more often beginning a path that may lead to further abuse.

While we have progressed nicely against our intended goals, I would like to turn your attention to slide 20 which illustrates the clinical trials currently in process or planned for 2022. I will provide updates on PF614-102 and PF614—MPAR-101. Additional clinical trials to evaluate PF614 are in the process of being initiated in the second and third quarters of 2022, including two human abuse liability, or HAL studies, that will be key for gaining abuse deterrent labeling. The studies will help us further understand the tendency for drug abusers to like the effects achieved after taking PF614 either orally or nasally, as compared to that of similar products, for example, crushed OxyContin.

PF614-102 was a 2-Part study to evaluate the pharmacokinetics and safety of twice daily oral doses of PF614 compared to similar doses of OxyContin in healthy subjects. The second part of the study evaluated single oral doses of PF614 compared to OxyContin for bioequivalence, again in healthy adult subjects. We reported on the data from the first part of the study where groups of 6 subjects received PF614 while 2 subjects received OxyContin ER twice daily for 5 days at 3 different dose levels. The doses selected had been determined from our Phase 1 work, to be bioequivalent – PF614 administered at 50, 100 and 200 mg corresponding to OxyContin 20, 40 and 80 mg.

The end points of the study were safety and the pharmacokinetics of released oxycodone or PF614.
Firstly, and importantly, there were limited treatment emergent adverse events, meaning potential side effects, for the administration of either PF614 or OxyContin. These events were similar in both treatment groups at each dose level. Mainly we observed opioid related events such as nausea, emesis, headache, dizziness and constipation.

On slide 23, you will see the pharmacokinetic data that confirmed our Phase 1 data and showed that the oxycodone release from PF614 or OxyContin produced very similar concentration versus time curves at each corresponding dose levels. Cmax (maximal blood concentrations) on day 1 and day 5 were also similar as shown on slide 24.

Similarly, the area under the concentration versus time curve, or AUC on day 1 were similar for PF614 and OxyContin on slide 25. Yet on day 5 we did see a separation, as expected, due to the longer half life of oxycodone delivered from PF614 versus OxyContin. Although OxyContin did show some accumulation over time, that seen with PF614 was more pronounced, demonstrated on slide 26.

This was a study with limited number of subjects, so we are now awaiting the data from the more extensive BE study which was part 2 of the 102 trial.

The second study that started enrolling subjects in December of 2021 on slide 27 was the Phase 1 PF614-MPAR-101, to evaluate our approach to reduce drug oral overdose. Again, PF614-MPAR is a combination product of PF614 and nafamostat, to provide protection from both abuse and overdose, that we believe is unique in the industry. The PK data reported here was generated from the first group of 8 healthy subject that were administered PF614 alone. Six of these subjects returned to receive PF614 in combination with 10 mg nafamostat – a simulated overdose situation.

The initial pharmacokinetic data for this study is shown on slide 28. On the left of the slide the blood levels of oxycodone released from PF614 when administered alone are shown in blue. When PF614 and nafamostat are combined to simulate an overdose situation, the oxycodone blood levels are shown in green. These data demonstrate a 47% reduction in the oxycodone maximal blood concentration due to nafamostat's inhibition of the trypsin activation of PF614. The righthand figure shows the corresponding blood concentrations of the PF614 itself. When administered alone, the majority of PF614 is converted to oxycodone, with little parent prodrug absorbed unchanged (blue line). When in an overdose simulation the nafamostat present prevents activation of the PF614, and more unchanged drug is absorbed (green line). It is important to note that the PF614 when absorbed directly into the blood, is not converted to oxycodone – showing that attempts to abuse PF614 by direct injection will be unsuccessful.

We are very excited with this data as the MPAR combination technology is the first approach that we expect may prevent all four forms of abuse: injecting, chewing, inhaling and oral overdose. Additional data is expected by fourth quarter of this year that will aid design of additional studies for PF614-MPAR in 2023. Along with our current clinical study of PF614, our TAAP opioid with abuse protection, this study of PF614-MPAR with added oral overdose protection will enhance our dual-pronged approach to provide safer solutions to patients and prescribers. The NIDA grant of $2.8 million that we received in 2021 supports this clinical study.

I am very pleased with our progress towards bringing our lead next generation opioids to market. To date, we have successfully hit major milestones for the Company and a major step toward providing safer options for doctors and patients.

I will now turn the call over to Dave Humphrey, Chief Financial Officer, to discuss the financials.

Dave Humphrey

Thank you, Lynn. I am going to touch on our financials at a very high level. A full breakdown is available in our regulatory filings and in the press release that crossed the wire last week on May 12.

Starting with revenues, funding under federal grants was $0.6 million for the first quarter of 2022, up from $0.3 million for the first quarter of 2021. The quarterly increase is attributable to an additional $0.4 million of funding under the MPAR grant, offset by a decrease of $0.1 million under the OUD Grant, due to the timing of research activities eligible for funding.

Now, looking at operating expenses. Our research and development expenses for the first quarter of 2022 increased to $3.1 million from $0.3 million in the 2021 first quarter, primarily the result of increased external research and development costs related to preclinical and clinical programs for PF614 and PF614-MPAR, as Lynn discussed.

General and administrative expenses for the first quarter of 2022 of $2.3 million represents an increase from $0.5 million in the same period of 2021, a result of increased expenses related to operating as a public company, including legal and accounting fees and director and officer insurance expenses.

Shifting to non-operating expenses, total other income/expense for the first quarter of 2022 was $3.9 million of income, compared to $0.4 million of expense in the first quarter of 2021. This increase in other income was primarily related to non-cash valuation adjustments of current obligations of the Company, including convertible notes and related warrants. The 2021 expense primarily reflects non-cash interest expense on notes that were converted into common stock on June 30, 2021.

Overall, our net loss for the first quarter of 2022 totaled $1.0 million compared to net loss of $0.9 million for the comparable year ago period. As we are a clinical stage biotech company, development of our product candidates is expected to continue, resulting in expected losses for the foreseeable future.

Turning to cash, we ended the first quarter of 2022 with $8.4 million in cash and cash equivalents. Cash used in operating activities for the first quarter of 2022 totaled $3.4 million resulting from the clinical advancement of our product candidates and increased costs related to operating as a public company.

In addition to our cash balance, remaining funding from approved federal grants totaled $4.1 million at the end of the first quarter. On July 1st, we also expect to be formally awarded the fourth year of grant funding for the MPAR program, for $2.8 million. These funds would help support the continued clinical development of PF614-MPAR.

As a clinical stage biotech company, we remain committed to investing in our clinical trials and development activities to support our continued path towards regulatory approval and commercialization. As I have previously stated, our management team, along with our Board of Directors, regularly conducts extensive reviews of our operations and development pipeline. We are carefully watching our cash, and we estimate that our cash burn will be approximately $4 million on a quarterly basis. Our plans reflect that our estimated runway of current cash resources takes us into the fourth quarter of this year.

As we execute upon our mission, it is also our intent to align with our shareholders and we remain committed to maximizing the value our shareholders hold as we consider our ongoing capital needs.

I will now turn the call back to Lynn for closing thoughts.

Dr. Lynn Kirkpatrick

Thanks, Dave.

In summary, we are very pleased with the results of our recently concluded clinical studies, positioning us closer to commercialization. 2022 is capitalizing on the momentum achieved in 2021 in which we made significant advances for our TAAP and MPAR platforms. Our revolutionary abuse resistant opioids are designed to combat prescription drug abuse, a problem that continues to be a major concern in the U.S.

Although we feel we have made significant strides to date, there is much work to be done. As I laid out in my presentation, the near-term path ahead consists of the human abuse liability studies to determine labeling claims for PF614, scheduled to initiate in the second quarter. We expect to report data from the nasal study by the end of the third quarter and the oral study in the first quarter of 2023. We expect to report on the safety and additional pharmacokinetic data from the Phase 1 study of PF614-MPAR in the fourth quarter of this year.

I look forward to providing our shareholders with further updates in the near term as we move towards commercialization.

I thank you all for attending. I now would like to hand the call over to the Operator to begin our question-and-answer session. Operator?

Operator

Thank you.

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

Thomas Flaten

Hey, good morning. I appreciate you guys taking the questions. Lynn, with respect to the five day AUC, you noted there was a gap between PF614 and OxyContin. Is there an upper limit there that kind of keeps you under the radar? I'm just trying to think about how the regulators will look at that AUC differential based on the half-life. Can you just talk about your thoughts on that?

Dr. Lynn Kirkpatrick

Yes, we believe we are on steady state. We're still evaluating that, Thomas. We're really, with the few number of subjects, obviously only two in the OxyContin arm, we will evaluate and certainly I don't believe we are going to see much more in the accumulation based on the fact that we should be at steady state by this Day 5 data. But we will be evaluating this in, obviously, our larger trials.

Thomas Flaten

Then switching gears a little bit, with respect to FDA, obviously, you still need to clarify the 505(b)(2) question, but from an FDA meeting engagement, will that be post the second Human Abuse Liability study, so maybe second or third quarter of next year, or how should we think about timing and content of that meeting and potential outcomes as well?

Dr. Lynn Kirkpatrick

Yes. We really do believe we will be in front of the FDA in 2023 really for what we refer to as the end of Phase 2 study. We're hoping in the first half, it depends on delays with the agency, with that we'll be discussing the path, but the comments that we have had from the agency have indicated if we do not reach bioequivalence we're still only required to do one Phase 3 study. We're in discussions with what that study will look like, and anticipate we will be able to initiate that starting in 2023.

Thomas Flaten

Got it. Then Dave, it looks like some of the converts converted given the share count increase. Is the expectation that the remainder of those notes will convert in the near term?

Dave Humphrey

Yes, we did have a fair amount of the notes converted in the first quarter. As you'll recall from the terms of the convertible notes, there are monthly redemptions, so each month additional parts of the note are converting into common stock, and we expect that to continue and to complete in the near term.

Thomas Flaten

Got it. Then just a quick clarification. The oral Human Abuse Liability study, it looks like it spans two quarters versus the intranasal one quarter. Is that just months or is there is some reason that one would take longer than the other?

Dr. Lynn Kirkpatrick

It's just really the starting of the timing. The nasal study is evaluating three different groups; one dose of PF614, one dose of a comparator and a placebo. The oral study is comparing five different groups. So it will take longer. We're anticipating (audio interference). So, the number of subjects may be different, although that is just being looked at right now with our stats group. So, I'm not entirely sure of the subject number, but it is mainly the difference in the number of subject groups. So, all of the subjects will be evaluating three different conditions in the nasal study versus five conditions in the oral study.

Thomas Flaten

Got it. Appreciate it. Thanks for taking the questions.

Dr. Lynn Kirkpatrick

Thanks Thomas.

Operator

We have reached the end of the question-and-answer session. I'll now turn the call back over to Dr. Lynn Kirkpatrick for closing remarks.

Dr. Lynn Kirkpatrick

Thank you Operator and thank you for joining us today. I look forward to updating you as we progress on our clinical trials and have additional data to review. In the interim, if we are unable to answer any of your questions, please reach out to our IR firm, MZ Group, who would be more than happy to assist.

Operator

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