5 May 2023

Wholly-owned psychedelics subsidiary, Halucenex Life Sciences Inc. – Phase II Clinical Trial Update

Highlights:

- **Promising early results from Phase II clinical trial to test the efficacy of psilocybin on treatment-resistant Post Traumatic Stress Disorder (PTSD)**
- **Approval secured for a Clinical Trial Amendment to further streamline trial**
- **First 10% of trial patients have experienced total remission from depression and PTSD symptoms after the first macro-dose**
- **Review of initial data has found that two psilocybin doses (one micro dose and one macro dose) spread one week apart leads to a marked decrease of PTSD symptoms in patients with severe treatment-resistant PTSD**
- **Additional early results from initial two-patient cohort immediately post macro dose included:**
  - **Notable improvements in total sleep time**
  - **Reduced cravings and need for THC during day time and for sleep**
  - **Reported reduced cravings for junk food**
  - **Significant improvements in blood pressure readings at follow-up visits (from hypertensive to normal)**
  - **Social improvement with interpersonal relationships**
  - **Symptoms of suicidal ideation were unchanged since neither patient endorsed suicidal ideation**
- **All patients who have completed three months of assessments to date have reported a 95% reduction in symptoms at month one and a 75% reduction in symptoms by month three, with one patient experiencing a total remission of PTSD by month three**
- **Creso continues to progress groundwork for a commercial pathway into the Australian market, following the Therapeutic Goods Administration (TGA) indication that medicines containing psilocybin and MDMA for prescription by specifically authorised psychiatrists for the treatment of certain medical conditions would be permissible from 1 July 2023**

Creso Pharma Limited (ASX:CPH, FRA:1X8) ('Creso Pharma' or 'the Company') is pleased to report that wholly-owned, Canadian based psychedelics company, Halucenex Life Sciences Inc. ("Halucenex") has recorded promising early results for the initial patient cohort participating in the Company's phase II clinical trial on the use of psilocybin in the treatment of PTSD. This has also led to the Company seeking a Clinical Trial Amendment (CTA) to streamline the clinical trial process.

Clinical Trial Amendment:

The Company applied for a clinical trial amendment via Health Canada on 20 March 2023 that was approved on 26 April 2023. Amendments include a larger window for pre-screening, approval for Halucenex's Chief Science Officer to prepare doses without the need for a compounding pharmacist, and the ability to spread each patient's seventh visit over 1-3 days. The key amendments will help streamline the trial, de-risking attrition rates and mitigating scheduling stressors for participants.

Clinical trial background and promising early results:

The trial is a single-arm, open-lab trial to test the efficacy of psilocybin on PTSD symptoms. The trial utilises Halucenex's 100%-owned and formulated synthetic psilocybin aqueous solution Lucenex, in both 10mg and 25mg formats which is being delivered to 20 respective patients on separate occasions in a micro dose and macro dose format (*refer ASX release 6 October 2022*). Of the 20 trial participants, only two patients to-date have received an initial dosing, which took place in December 2022 (*refer ASX release 7 December 2022*).

All psychiatric disorders were confirmed and diagnosed at the baseline assessment using the Structured Clinical Interview for DSM-5 (SCID-5). Symptoms of PTSD were assessed at each visit using the Clinician-Administered PTSD Scale for *DSM-5* (CAPS-5), the gold standard tool in assessment of PTSD. Participants were enrolled if they had a score of ≥40, indicating severe symptoms of PTSD. Remission of PTSD was defined as a score of ≤ 20 on the CAPS-5.

Depressive symptoms were assessed using two standardised measures for Major Depressive Disorder — The Quick Inventory of Depressive Symptomatology (QIDS-16) and the Beck Depression Inventory (BDI). Remission was defined as a score of ≥5 on the QIDS and a 50% reduction in overall score on the BDI.

We assessed for anxiety using the Beck Anxiety Inventory (BDI). Remission was defined as a 50% reduction in scores from baseline on the BAI. Scores on the BAI are assessed as minimal anxiety (0 to 7), mild anxiety (8 to 15), moderate anxiety (16 to 25), and severe anxiety (30 to 63).

Other outcomes measures included sleep time on actigraphy device, addiction severity (Addiction Severity Index), suicidal ideation (Columbia Suicide Severity Scale), general psychological symptoms such as pain and interpersonal relationships on the Symptom Checklist 90-R (SC90-R), overall functioning on the Clinical Global Impression scale, work capacity on the Sheehan Disability Scale, and physiological measures such as weight and blood pressure.

The first two patients were administered with both 10mg and 25mg doses of Halucenex's 100%-owned and formulated Lucenex branded synthetic psilocybin, with no adverse effects.

The review of data from these first two patients have highlighted particularly promising results, showing that two doses of psilocybin spread one week apart leads to a marked decrease in symptoms of PTSD in patients with severe treatment-resistant PTSD. The mean score on the CAPS-5 was 51, indicating severe PTSD symptoms at the start of the study.

After the initial low dose, there was nearly 40% reduction in PTSD symptoms. The macro dose given one week later resulted in immediate decrease in symptoms associated with PTSD with both participants endorsing zero symptoms of PTSD at one month post-macro dose, indicating a drop of 51 points on the CAPS-5.

At three-months post-macro dose, there was a 75% reduction in symptoms of PTSD on the CAPS-5. The two patients continued to experience significant reductions in PTSD at three months, with one patient maintaining a total remission of all PTSD symptoms at month-three (CAPS-5=0).

Both participants endorsed ratings of severe depression on the BDI (mean score=45) and the QIDS (mean score=18). After the macro dose, participants experienced remission of depressive symptoms which was sustained into month three with a mean score of 5 on the BDI and 6 on the QIDS. One participant experienced total remission of depressive symptoms into month three (BDI=1; QIDS=1).

The mean score on the BAI at baseline was 28, indicating severe anxiety. Anxiety scores on the BAI were reduced 50% in one participant immediately after macro dose and 100% in the other participant. By month 3 there was a mean decrease of 22 points on the BAI bringing participants mean scores on the BAI from the severe anxiety range into minimal, or remission.

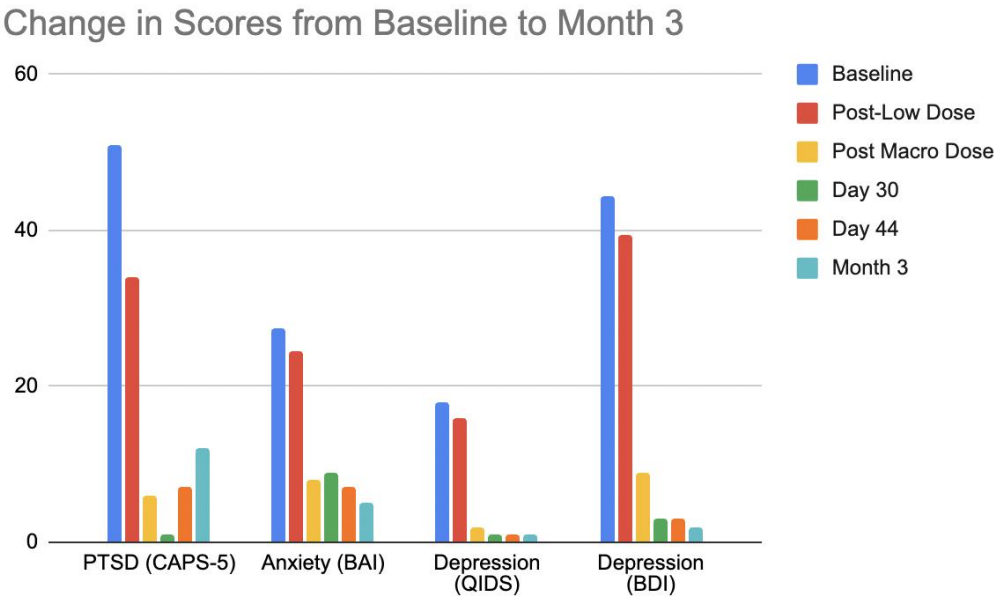

Chart: % decline in PTSD symptoms from application of Lucenex branded psilocybin treatment

Results for the initial 2-patient cohort showed a material improvement for the following symptoms of PTSD, immediately post-macrodose and into month 3:

- Notable improvements in total sleep time
- Reduced cravings and need for THC during day time and for sleep
- Reported reduced cravings for junk food
- Significant improvements in blood pressure readings at follow-up visits (from hypertensive to normal)
- Social improvement with interpersonal relationships
- Symptoms of suicidal ideation were unchanged since neither patient endorsed suicidal ideation

All of the above changes remain at 3 months post macrodose session.

Whilst Creso is encouraged by the early results of the trial, the Company notes that these are preliminary only, and based on data derived from only the first 10% of patients enrolled in the trial. Investors should await the full and complete results (anticipated in Q3 2023) before making an assessment on the success (or otherwise) of the trial.

Following the initial administering of its unique psilocybin formulation, Halucenex has continued to work with regulators after making the strategic decision to seek an amendment to its clinical trial with Health Canada to investigate sleep disruption, which is seen as one of the most impactful PTSD symptoms.

Pending the outcome of that amendment, Halucenex still intends to administer its synthetic psilocybin to an average of two patients per week and is targeting completion of the trial in Q3 CY2023.

Early results follow a key regulatory update in February 2023, when the Australian Therapeutic Goods Administration (TGA) approved medicines containing psilocybin and MDMA for prescription by specifically authorised psychiatrists for the treatment of certain medical conditions from 1 July 2023.

Management commentary:

CEO and Managing Director, Mr William Lay said: *"We are pleased to report the initial results from our Phase II clinical trial, which clearly indicate the early promise of the Lucenex branded synthetic psilocybin product as a viable treatment option for patients suffering from treatment-resistant PTSD symptoms."*

"As the trial continues, we look forward to providing more details on patient results and our ongoing dialogue with regulators. Amid broader regulatory tailwinds for the psilocybin products, we are confident the current phase II trial will continue to establish a strong platform for the future commercial application of our products."

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Authority and Contact Details

This announcement has been authorised for release by the Disclosure Committee of Creso Pharma Limited.

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About Creso Pharma

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