Incannex psychedelic therapies

A subsidiary of Incannex Healthcare Ltd

ASX: IHL

Psi-GAD clinical development overview
August 2021

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Psilocybin-assisted psychotherapy for Generalised Anxiety Disorder: a world-first clinical trial program

Unmet need in the treatment of Generalised Anxiety Disorder

- Around 300M people globally are estimated to have an anxiety disorder
- Generalised Anxiety Disorder (GAD) is often more severe and intractable than other anxiety disorders
- GAD is characterised by persistent and excessive worry, nervousness, irritability, and physical manifestations, including difficulty sleeping, fatigue, muscle tension, and nausea
- Treatment of GAD remains inadequate, with less than half of patients achieving remission following evidence-based treatment, alongside high relapse rates, and substantial treatment side-effects.

Promising signs in early psilocybin trials

- Evidence from academic studies has shown that psilocybin-assisted psychotherapy can produce large, rapid and sustained clinical benefits for patients suffering with anxiety and depression symptoms
- Psilocybin-assisted therapy has US FDA 'Breakthrough Therapy' designation in the treatment of Major Depressive Disorder and Treatment Resistant Depression.

Developing "Psi-GAD" psilocybin therapy for Generalised Anxiety Disorder

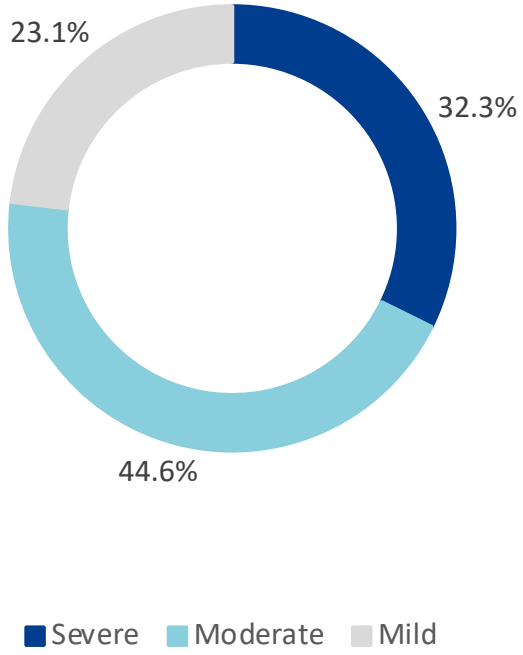
- Research proposal for Phase 2a clinical trial submitted to Human Research Ethics Committee (HREC) in Australia
- Pre-IND information package and meeting request submitted to US FDA regarding phase 2b clinical trial
- Clinical trial protocols, including therapy protocols, have been developed by experts in the fields of psychology, psychiatry, and psychedelic medicine.

Current treatments for Generalised Anxiety Disorder are inadequate

An estimated 7M people in the US and 1M in Australia have moderate to severe GAD, experiencing intense, persistent, and often debilitating anxiety

- GAD is diffuse, excessive, uncontrollable anxiety that is not restricted to any specific environmental circumstances and occurs more days than not for at least 6 months (American Psychiatric Association, 2013)
- About 3% of the adult population in the USA and Australia are estimated to have GAD in any 12 month period
- First line treatment options for GAD include Cognitive Behavioural Therapy, anti-depressants (SSRIs, SNRIs) and pregabalin, with benzodiazepines (e.g. Diazepam) as a second-line short-term option
- Existing treatments show limited efficacy, with less than 50% of patients achieving remission, alongside high relapse rates
- Treatment limitations expose significant patient unmet need.

Severity of GAD among Adults in the United States



Psi-GAD scientific leadership team

Deep and relevant experience

MONASH University

DR PAUL LIKNAITZKY

PRINCIPAL INVESTIGATOR
MONASH UNIVERSITY

Dr Liknaitzky is Head of the Clinical Psychedelic Research Lab within the Turner Institute and the Dept of Psychiatry, Monash University – Australia's first clinical psychedelic lab. He coordinates Australia's first applied psychedelic training for trial therapists. He is a Research Fellow at Monash University, and has Adjunct or Honorary appointments at St Vincent's Hospital, Macquarie University, Deakin University, and the University of Melbourne. He earned an Honours in Neuroscience and a PhD in Psychology from the University of Melbourne.

PROFESSOR MURAT YÜCEL

CO-INVESTIGATOR
MONASH UNIVERSITY

Professor Yücel is a clinical neuropsychologist who heads the Addiction and Mental Health research program at Monash, working at the interface between clinical neuropsychology, psychiatry, neuroscience and technology. He is the founding Director of BrainPark - a world-first neuroscience research clinic designed to bring the latest neuroscience with diagnostic or therapeutic benefit to the community in an accessible and inspiring way. He is a Co-Investigator within the Clinical Psychedelic Research Lab.

PROFESSOR SURESH SUNDRAM

CO-INVESTIGATOR
MONASH UNIVERSITY

Professor Sundram is a psychiatrist, and Head of Department of Psychiatry at Monash University. He has a distinguished career as a clinician and researcher, and is Head of both the Translational Molecular Psychiatry and the Asylum Seeker and Refugee Mental Health research groups at Monash. He is an external expert advisor to the UN Human Rights Council, consultant to the Australian Human Rights Commission, the Australian Department of Home Affairs, and non-government organisations. He is a Co-Investigator within the Clinical Psychedelic Research Lab.

Academic-led clinical trial programs: Monash University and BrainPark

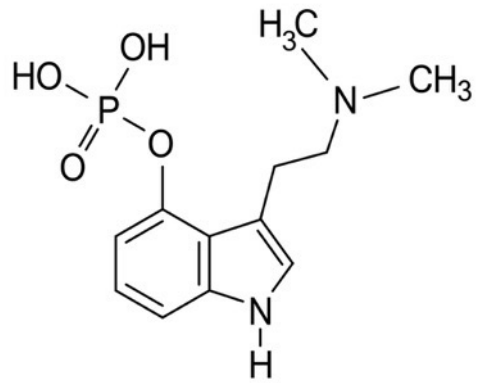
- Phase 2a clinical trial treatment will be delivered at BrainPark; a state-of-the-art research platform and collaboration between the Monash School of Psychological Sciences and the Department of Psychiatry
- Monash University consistently ranks among the world's top 100; ranking #55 out of 1604 university institutions and #35 in the world for life sciences and Medicine (QS World University Rankings)
- Strong academic partnerships ensure scientific independence and rigour for the best possible patient outcomes.

MONASH University

BrainPark
DAVID W. TURNER RESEARCH CLINIC

Psilocybin-assisted psychotherapy: a new mental health treatment paradigm

Early studies indicate clinical benefits may be two to four times greater than front-line treatments.



Psilocybin molecule

Psilocybin is a naturally-occurring psychedelic molecule produced by more than 100 species of mushrooms. It is a well-tolerated serotonergic psychedelic that produces therapeutically useful **altered states of consciousness**, and possibly greater **neuroplasticity,** providing a "window of opportunity" for more successful psychotherapy.

Promising evidence for **rapid, large, and lasting** benefit for psilocybin-assisted psychotherapy in treating major depression, depression and anxiety symptoms associated with physical illness, and substance misuse.

Psilocybin-assisted psychotherapy does not work by supressing or managing symptoms, but by facilitating access to more fundamental causes of anxiety, and providing a remarkable opportunity for patients to make **real and lasting changes.**

A year after treatment, clinical psilocybin sessions have been described as amongst the **top 5 personally meaningful experienced of lifetime** by more than 50% of participants.

Compass Pathways and Usona Institute have received **FDA Breakthrough Designation** for psilocybin-assisted psychotherapy in its use for depressive disorders, due to highly promising clinical evidence and substantial unmet need.

Clinical signals: early indications from academic-sponsored clinical trials

New York University, Ross et al 2016 (n=29)

Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial. Psilocybin produced immediate, substantial, and sustained improvements in anxiety and depression, as well as decreases in cancer-related demoralization and hopelessness, improved spiritual wellbeing, and increased quality of life.

Imperial College London, Carhart-Harris et al 2018 (n=20)

Psilocybin with psychological support for treatment-resistant depression: six-month follow-up. Tolerability was good, effect sizes large and symptom improvements appeared rapidly after just two psilocybin treatment sessions, and remained significant 6 months post-treatment in a treatment-resistant cohort.

University of California, Los Angeles, Grob et al 2011 (n=12)

Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. The State-Trait Anxiety Inventory anxiety subscale demonstrated a significant reduction in anxiety at 1 and 3 months after treatment. There were no clinically significant adverse events with psilocybin.

John Hopkins University, Griffiths et al 2017 (n=51)

Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: a randomized double-blind trial. Large and significant decreases in clinician-rated and self-rated measures of depression, anxiety or mood disturbance, and increase measures of quality of life, life meaning, death acceptance, and optimism.

Psilocybin + psychotherapeutic support for GAD
Psi-GAD

THE PSI-GAD TREATMENT APPROACH USES MULTIPLE HIGH DOSE PSILOCYBIN SESSIONS ALONGSIDE SPECIALISED PSYCHOTHERAPEUTIC SUPPORT WITH MENTAL HEALTH PROFESSIONALS WHO HAVE UNDERGONE A SPECIALISED THERAPIST TRAINING PROGRAM ALONGSIDE SUPERVISED PRACTICE. THE TREATMENT IS DESIGNED TO OPTIMISE PATIENT SAFETY AND THERAPEUTIC OUTCOMES IN GAD WITH SPECIFIC SUPPORT BEFORE, DURING AND AFTER PSILOCYBIN DOSING SESSIONS.

01

Preliminary Psychotherapy:

conducted during the Screening Stage with key focus on clinical formulation, therapeutic alliance, tools to navigate psychedelic experience, and practical preparation for dosing.

02

Preparation Psychotherapy:

conducted following full enrolment and prior to the first dosing session with a key focus on anxiety-specific psychological and practical preparation for dosing.

03

Dosing Support:

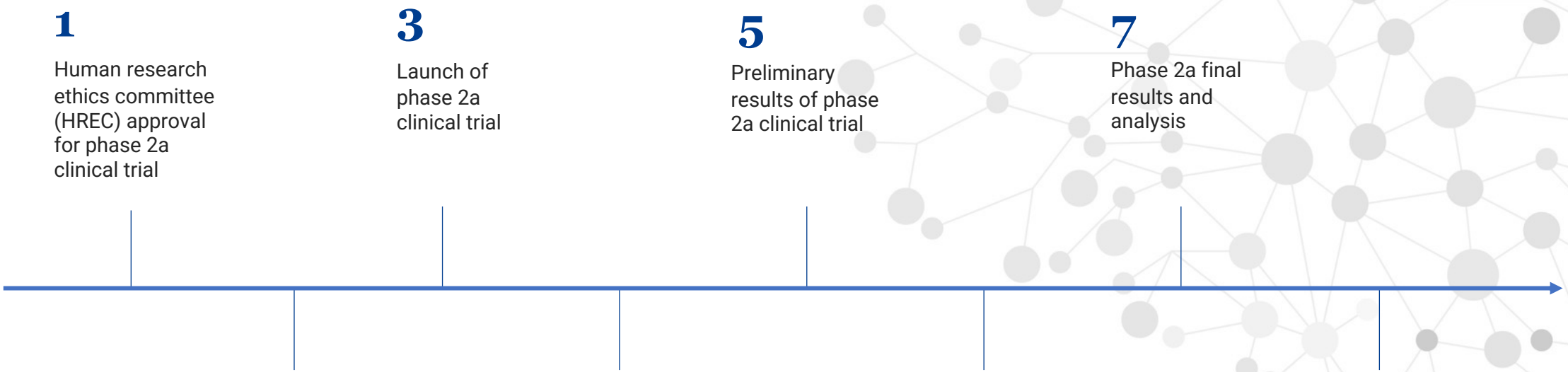
conducted soon after the Preparation session with key focus on trust, suitable mindset, conducive physical setting, and participant-led support.

04

Integration Psychotherapy:

conducted following the Dosing sessions, including the day after each Dosing session, with a key focus on sustaining benefits through re-engagement with past psychedelic experience, meaning-centred support, and contextual changes to support outcomes.

Psi-GAD immediate development plan



1 Human research ethics committee (HREC) approval for phase 2a clinical trial

2 Completion of therapist training

3 Launch of phase 2a clinical trial

4 Pre-IND meeting for “pivotal” phase 2b clinical trial

5 Preliminary results of phase 2a clinical trial

6 Open of FDA Investigational New Drug Application (IND)

7 Phase 2a final results and analysis

8 Commence phase 2b clinical trial.

Phase 2a trial design

World-first clinical trial prioritising scientific independence and rigour for the best patient outcomes

THE STUDY

A phase 2 randomised triple-blind active-placebo-controlled clinical trial

SAFETY AND EFFICACY

The safety, efficacy and tolerability of psilocybin-assisted psychotherapy

PARTICIPANTS

72 participants that will experience two psilocybin or active-placebo dosing sessions

PSYCHOTHERAPY

Up to 11 non-drug, specialist psychotherapy sessions over a period of 10 weeks

PRIMARY OUTCOMES

Reduction in anxiety as measured using the Hamilton Anxiety Rating Scale

SECONDARY OUTCOMES

Quality of life, functional impairment, and comorbidities

ANALYSIS

A preliminary analysis of patient data will be conducted after 30 patients, full analysis at 72 patients

2B PLANNING

Preliminary analysis will inform the second part of the trial (n=42) and/or facilitate commencement of the phase 2b pivotal clinical trial

Comparative clinical programs working towards FDA approved therapies

Company Name	Psychedelic Drug	Lead Project Indication	Clinical Trial Phase	Progress	Stock Exchange
MAPS	MDMA	Post-traumatic stress disorder (PTSD)	Phase 3	Underway	Non-profit organisation
Compass Pathways	Crystalline Psilocybin	Treatment-resistant depression (TRD)	Phase 2	Underway	Nasdaq
Usona Institute	Psilocybin	Major Depressive Disorder (MDD)	Phase 2	Underway	Non-profit organisation
Cybin Inc.	Psilocybin	Major Depressive Disorder (MDD)	Phase 2a	Planning	NEO exchange
Mindmed	LSD	Anxiety	Phase 2	Planning	Nasdaq
Incannex Psychedelic Therapies	**Psilocybin**	**Generalised Anxiety Disorder**	**Phase 2a**	**Planned - awaiting HREC approval**	**ASX**

Summary

Experienced scientific team, with deep and relevant experience in Anxiety disorders

Australian **HREC research proposal** and FDA pre-IND meeting request submitted

Phase 2a clinical trial to commence 2021 and Phase 2b in 2022

Intellectual property and market exclusivity strategies

Advancing a potential **second** novel psychedelic opportunity

Incannex psychedelic therapies

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