

Transforming mental health care

COMPASS Pathways plc
July 2021



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Everyone has a
S T O R Y

COMPASS's leadership team



George Goldsmith
Chairman, CEO and Co-founder



Ekaterina Malievskaia, MD
Chief Innovation Officer, Co-founder



Lars Wilde
President, Chief Business Officer, Co-founder



Piers Morgan
Chief Financial Officer



Nate Poulsen
General Counsel and Head of Legal, IP, and Licensing



Marco Mohwinckel
Chief Commercial Officer



Trevor Mill
Chief Development Officer



Tracy Cheung
Chief Communications Officer



Anne Benedict
Chief People Officer



Sue Stansfield, PhD
Senior Vice President, Clinical Operations



Stephen Schultz
Senior Vice President, Investor Relations



Greg Ryslik, PhD
Senior Vice President, Data Science, Machine Learning and Digital Health Research



Gary Gilmour, DPhil
Vice President, Preclinical Research



Steven Levine, MD
Vice President, Patient Access



Dr Stephen Wright
Senior Scientific Advisor



Emilio Arbe, MD
Interim Clinical Sciences Director



We are a mental health care company



Dedicated to accelerating patient access to evidence-based innovation in mental health care

- Significant unmet need: 100m people¹ with treatment-resistant depression (TRD)
- Committed to transforming the patient experience



Developing COMP360 psilocybin therapy for TRD

- COMP360 designated a FDA Breakthrough Therapy for TRD
- Completed Phase I healthy volunteers trial, largest psilocybin therapy clinical trial to date
- Phase IIb ongoing, with 216 patients expected to have completed the trial by late 2021
- Planned expansion into additional indications



Driven by science and rigour

- COMP360 differentiated mechanism of action, activating the 5HT_{2A} receptor²
- Signals from academic studies have shown that psilocybin therapy can improve outcomes for patients
- IP strategy combining patent protection with regulatory and market exclusivity

Source: 1. Depression and Other Common Mental Disorders: Global Health Estimates and Cleare, A. et al - 2015 -Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2008 British Association for Psychopharmacology guidelines. These sources state that 1/3 of those suffering with major depressive disorder (MDD) are estimated to be TRD. Therefore, we approximated 100 million from 320 million people with MDD 2. Halberstadt and Geyer - 2011

Transforming the patient experience in mental health care

Our vision
A world of mental wellbeing

FDA Breakthrough
Therapy designation
for COMP360 in TRD;
New indications and
compounds in
development




Health systems and
payer partnerships
Value-based models,
real-world evidence



Innovative care delivery models
Centres of Excellence,
digital technologies

TRD treatment pathway: significant unmet need for 100 million patients

Treatment pathway stage	New onset depression Major depressive disorder (MDD)	Persistent depression Major depressive disorder (MDD)	Treatment-resistant depression (TRD)
Line of therapy	<div> <div>First line</div> <div>Second line</div> <div>Third line + </div> </div>		
Estimated no of patients (worldwide)	320 million	200 million	100 million (~1 in 3 of total) US healthcare cost approx \$17-25k per patient/year
Available treatments	<ul style="list-style-type: none"> • Antidepressants • Psychological interventions, eg CBT* 	<ul style="list-style-type: none"> • Antidepressants • Antidepressant combinations • Psychological interventions 	<ul style="list-style-type: none"> • Antidepressants • Augmentation therapy (antidepressants, mood stabilisers, anticonvulsants, atypical antipsychotics, esketamine) • Ketamine • Somatic therapy (rTMS*, tDCS*, ECT*, DBS*) • High-intensity psychological interventions
% relapse	60-70%	50-75%	80-90%

Note: *CBT = cognitive behavioural therapy; rTMS = repetitive transcranial magnetic stimulation; tDCS=transcranial direct current stimulation; ECT=electroconvulsive therapy; DBS=deep brain stimulation

Source: Hasler et al, 2004 - Acute psychological and physiological effects of psilocybin in healthy humans: a double-blind, placebo-controlled dose effect study

Our COMP360 psilocybin therapy



COMP360 (GMP drug substance and drug product)

Synthetic, high-purity, polymorphic crystalline psilocybin formulation

1mg, 5mg and 25mg oral capsule formulation (for Phase III and commercialisation)

Stability testing in place with adequate shelf life for clinical trials/commercialisation

UK CMO manufacturing at commercial scale



Psychological support

COMP360 is combined with psychological support from specially trained therapists

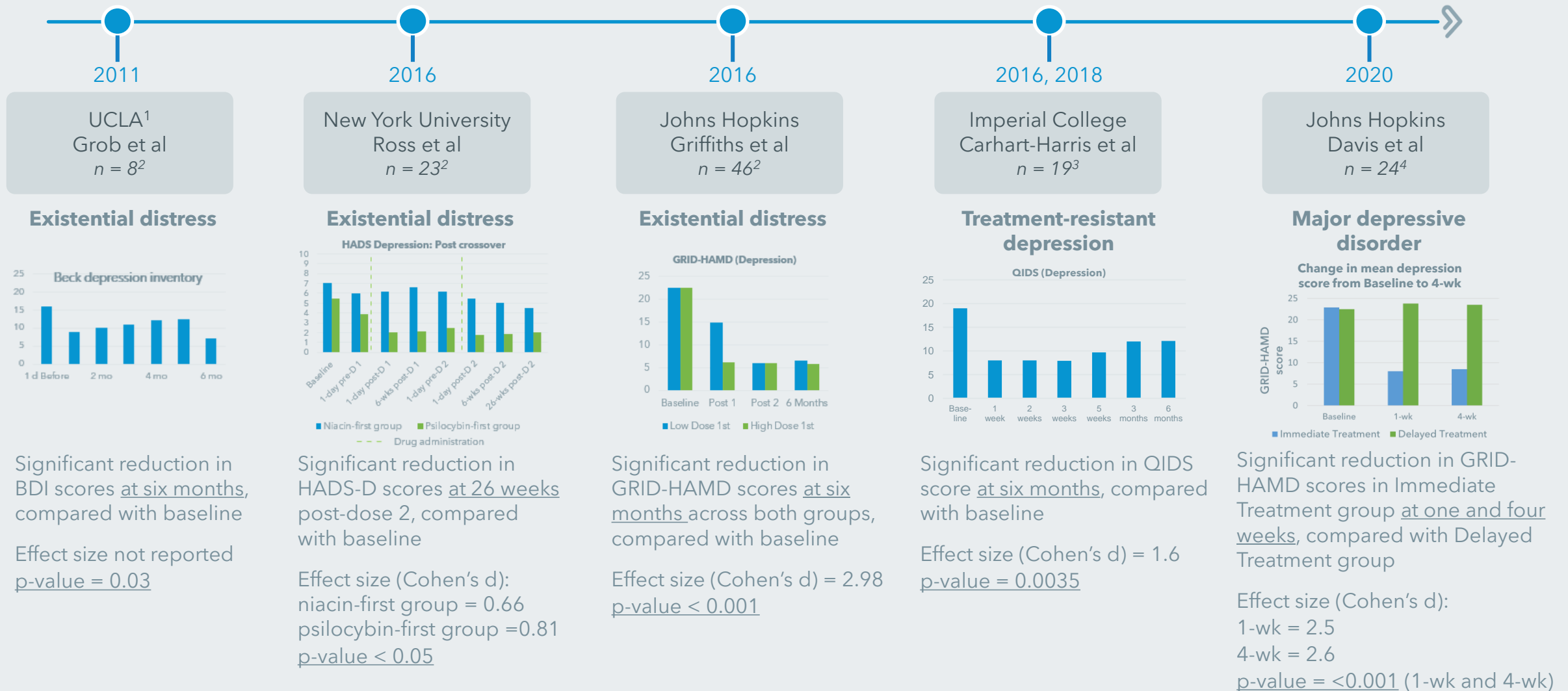
Psilocybin session is preceded by preparation and followed up with integration



COMP360 psilocybin therapy: clinical status

- Designated Breakthrough Therapy for TRD in 2018
- Preclinical genotoxicity and cardiotoxicity studies completed
- Phase I trial completed: COMP360 generally well-tolerated in healthy participants (n=89)
- Phase IIb trial in TRD: underway in 22 sites in 10 countries (n=216)

Clinical signals: early indicators from academic-sponsored trials show rapid reductions in symptoms in TRD and other mental health conditions

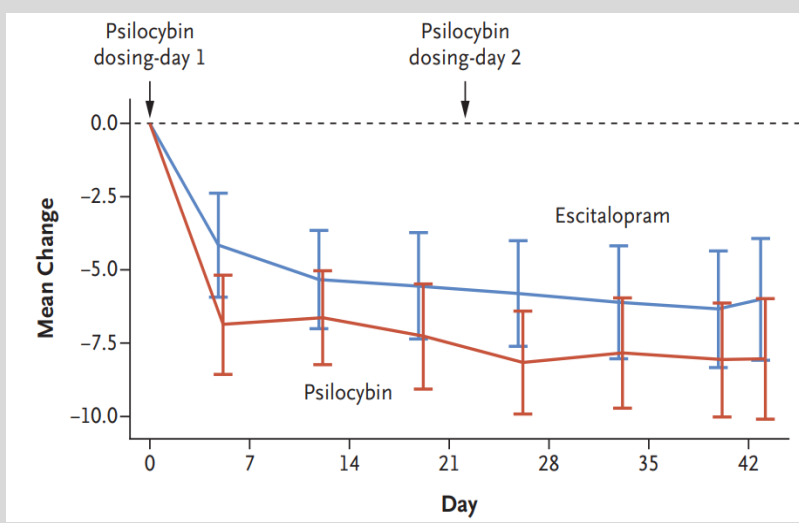


Note: 1. UCLA = University of California, Los Angeles; 2. n denotes the number of patients who completed the relevant disclosed timepoint; 3. Denotes the number of patients for whom data is shown in the bar graph. A total of 19 patients completed six months follow-up; 4. Denotes the number of patients who completed both administration sessions and 1-wk and 4-wk post-session visits.

All charts have been recreated from information provided in relevant papers. None of these studies used COMP360

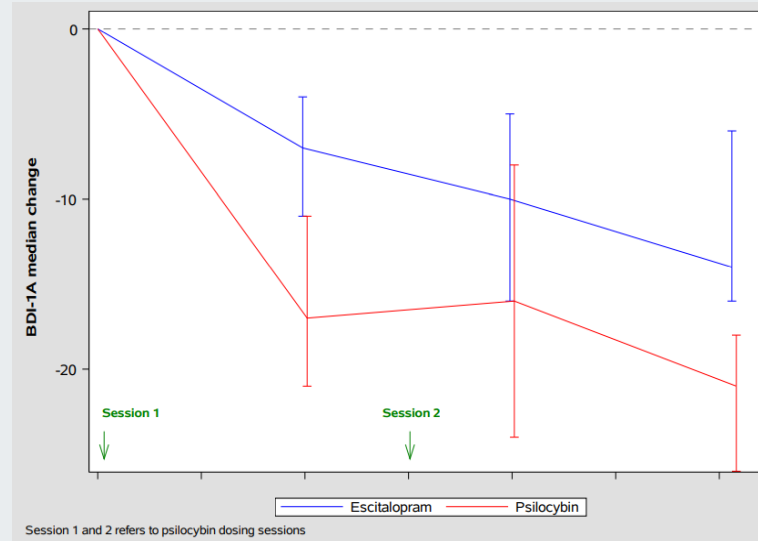
Exploratory study showing signals of psilocybin's positive activity

**Primary endpoint:
Change from baseline on the QIDS-SR-16**



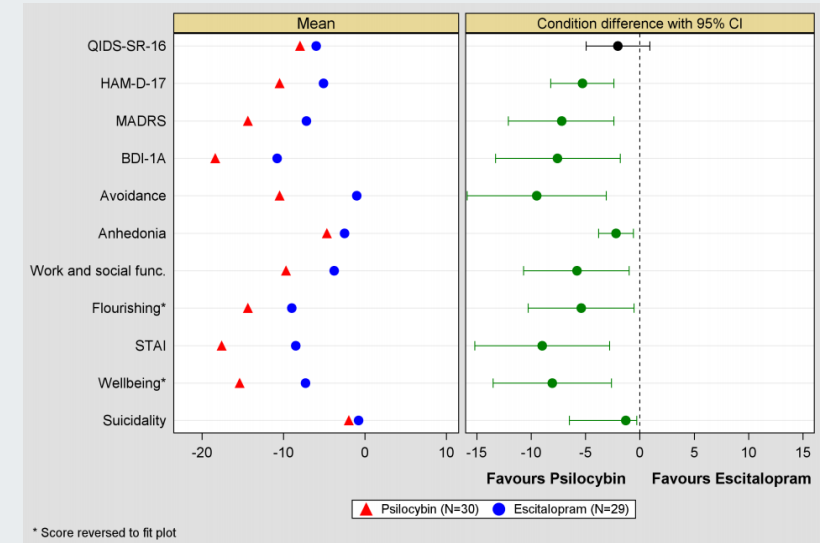
- Primary efficacy measure: the change from baseline in QIDS-SR-16 total score at six weeks showed a two point difference favouring psilocybin compared with escitalopram

**Key secondary endpoint:
BDI-1A scores vs time (Median values and 95% CI)**



- Secondary measures: positive effects of both psilocybin and escitalopram, with psilocybin showing numerical benefits compared with the SSRI
- Change from baseline at week six on MADRS showed a 7.2 point treatment difference favouring psilocybin; HAM-D-17 showed a 5.3 point treatment difference favouring psilocybin
- Response rates (a 50% or greater reduction on the QIDS-SR-16 total score from baseline) at week six were 70.2% for the psilocybin arm compared with 48.0% for the escitalopram arm, and remission rates (defined as a QIDS-SR-16 total score ≤ 5) at week six were 57.1% and 29.1%, respectively

All efficacy outcomes at week six



- Phase II, double-blind, randomised, controlled trial involving patients with major depressive disorder (MDD)
- N=59; comparing psilocybin with escitalopram (1:1 randomisation) over a 6-week period
- Psilocybin arm received two doses of 25mg psilocybin three weeks apart with psychological support
- The study was not powered to detect superiority between psilocybin or escitalopram for the primary endpoint
- COMP360 psilocybin was generally well-tolerated with no serious adverse events
- Study concludes that psilocybin findings should be explored further in larger studies

Psilocybin therapy: potential benefits for patients, clinicians and payers

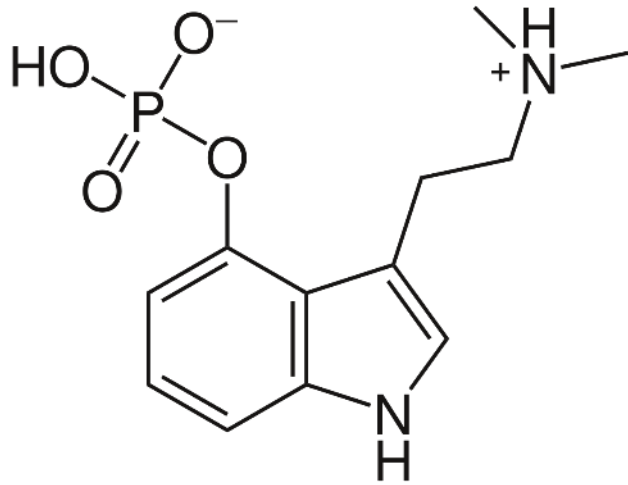
Potential patient benefits

- Rapid and sustained relief
- A meaningful patient experience
- A sense of agency and empowerment

Potential economic benefits

- Reduction in total cost of care
- Lower healthcare resource utilisation
- Increased productivity, reduced absenteeism

Psilocybin is a psychoactive substance



Psilocybin molecule



An active ingredient in some species of mushrooms

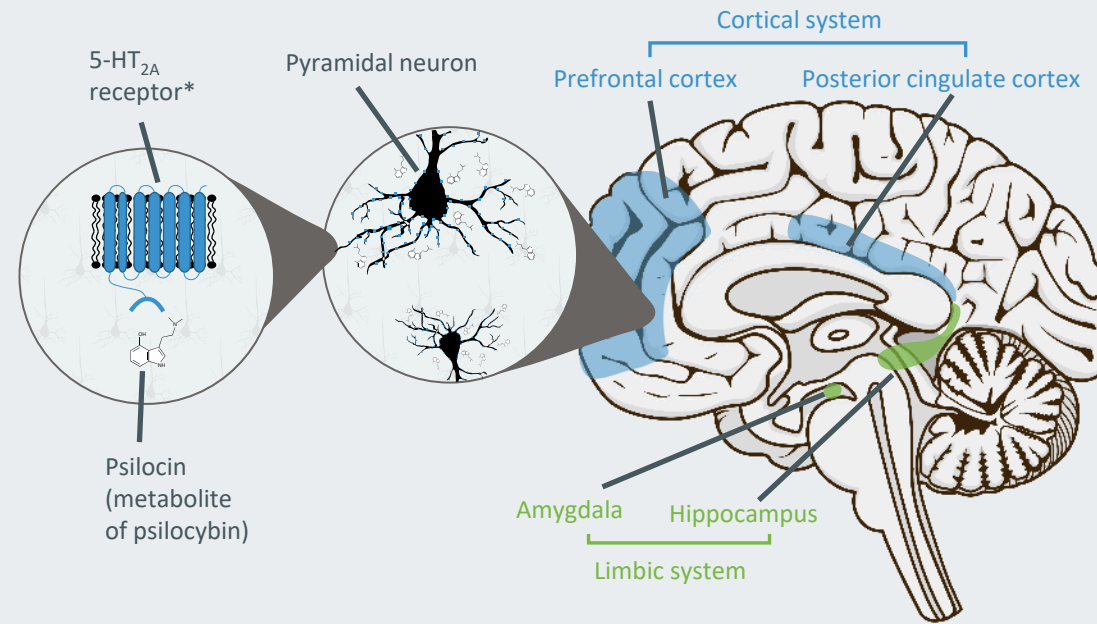


Established knowledge of subjective effects



A generally well-tolerated serotonergic psychedelic

COMP360 mechanism of action



Modulation of cortical and limbic systems via 5-HT_{2A} receptors

1. Stimulation of 5-HT_{2A} receptors¹ results in downstream cascades via G-protein signalling²

2. Altered extracellular release of dopamine^{3,4} and leading to enhanced positive mood

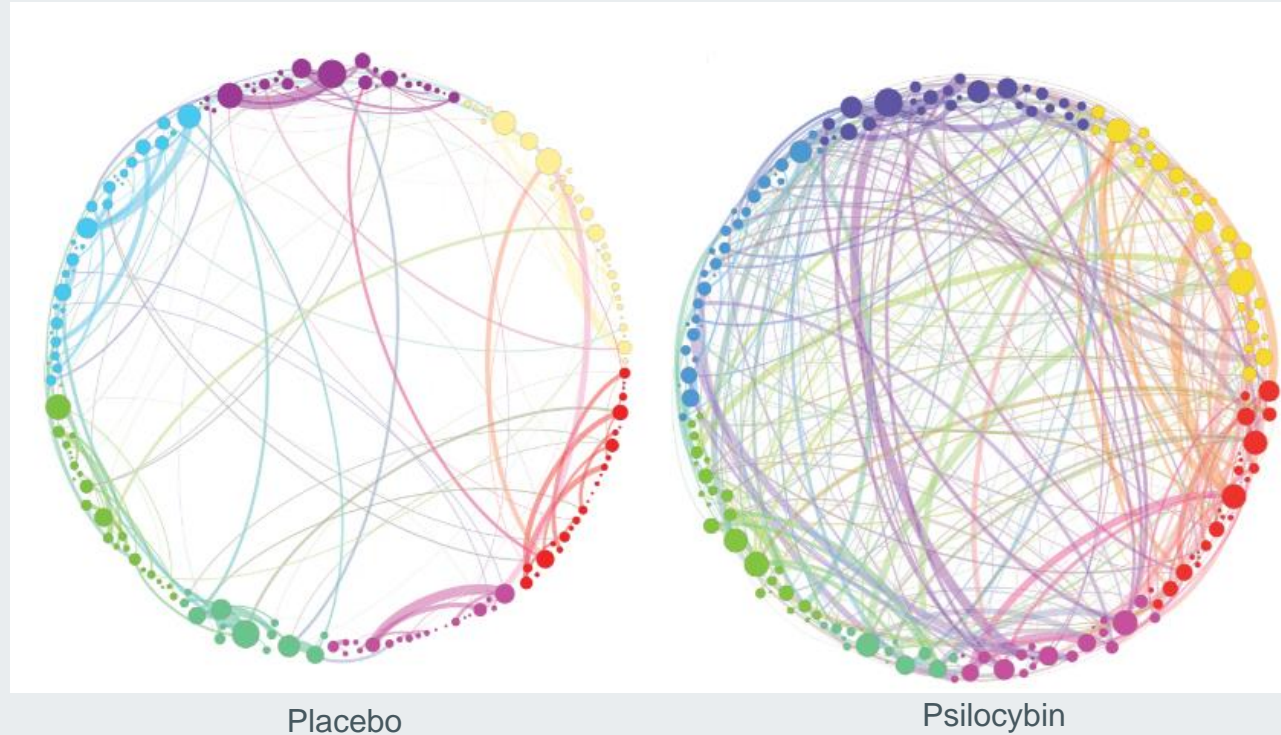
3. Downregulation of the default mode network, or DMN⁵, and de-synchronisation of cortical activity as well as the emergence of new patterns of functional connectivity across the brain⁶

4. Sustained cellular changes leading to neuroplasticity⁷ and “window of opportunity” for therapy

Note: *5-HT_{2A} = 5-hydroxytryptamine 2A; DMN = default mode network; mPFC = medial prefrontal cortex

Source: 1. Halberstadt et al (2011); 2. Lopez-Gimenez et al (2018); 3. Vollenweider et al (1999); 4. Sakashita et al (2015); 5. Carhart-Harris et al (2012a); 6. Petri (2014); 7. Ly et al (2018)

Simplified visualisation of the acute changes in brain network connectivity



Brain network alterations may indicate the emergence of novel patterns of connectivity, following downregulation of the DMN

Note: Figure adapted from *Petri et al, 2014*; study analysed fMRI (functional magnetic resonance imaging) data from healthy volunteers to compare resting-state functional brain connectivity after intravenous infusion of placebo and psilocybin

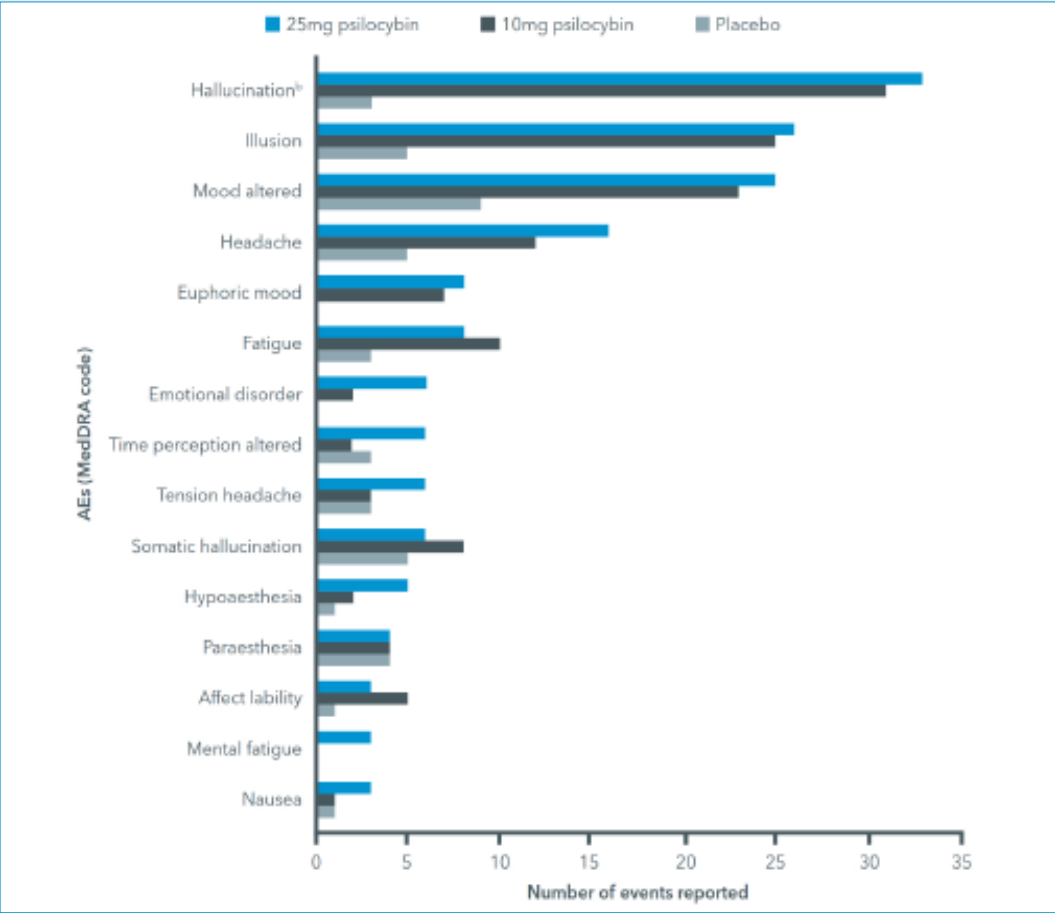
Source: Petri, 2014 - Homological scaffolds of brain functional networks

Phase I safety and feasibility trial – data published in December 2019

- Largest randomised controlled study of psilocybin completed, in 89 healthy volunteers
- COMP360 psilocybin was generally well-tolerated with no serious adverse events
- No clinically-relevant negative effects on cognitive and emotional functioning
- Feasibility of simultaneous administration to up to six people, with 1:1 support
- Clinical training for phase IIb trial therapists

COMP360 induced psychedelic experiences that correlate with therapeutic effect

Most frequently reported AEs* (MedDRA Code)^a in our Phase I trial with healthy volunteers



a. Ranked by incidence in the 25mg psilocybin group

b. Includes auditory, gustatory, olfactory, tactile and visual hallucinations

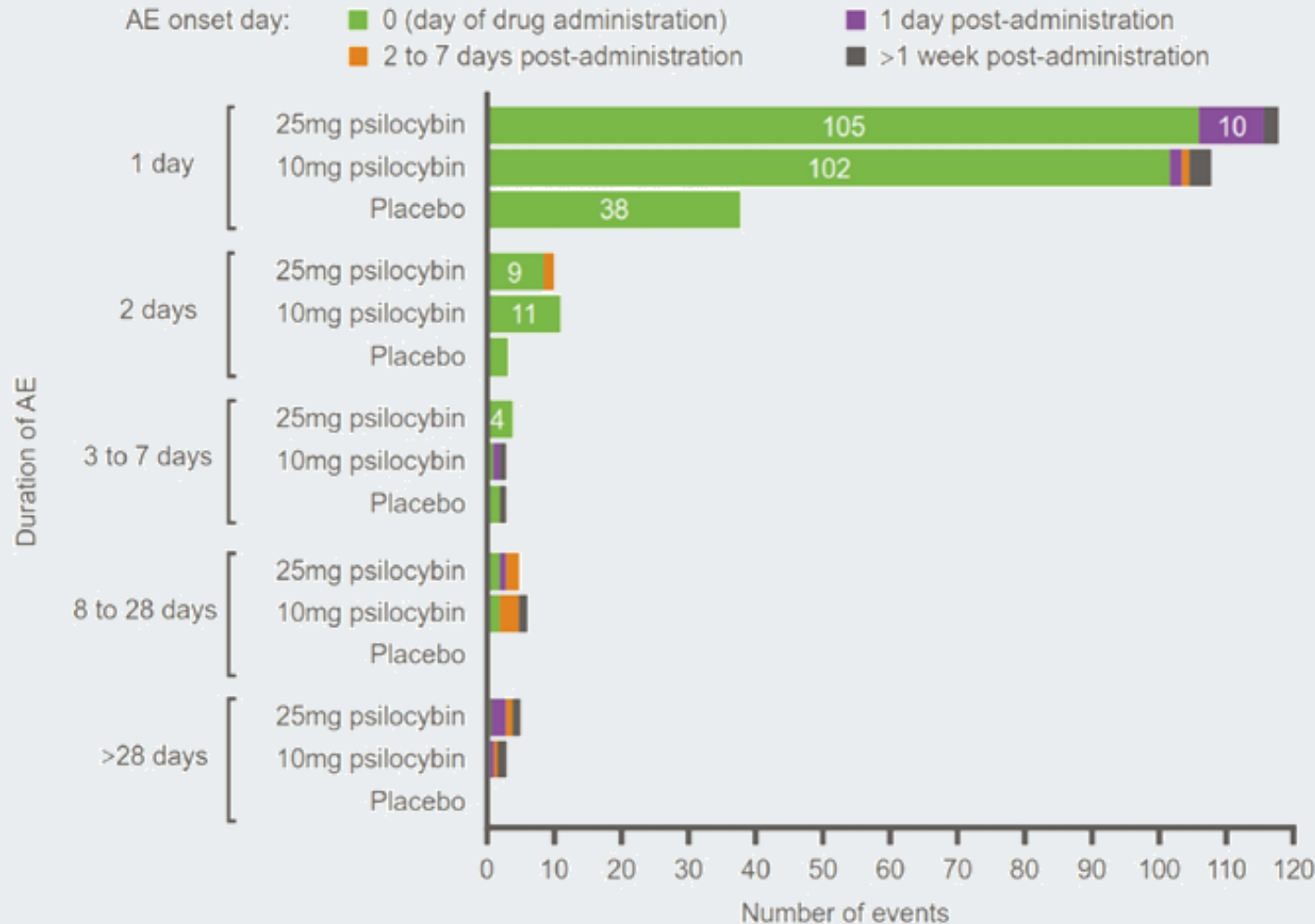
Mood altered AEs ranked by incidence in the 25mg psilocybin group

	25mg COMP360 (n=30)	10mg COMP360 (n=30)	Placebo (n=29)
Any "mood altered" AE	15 (50.0)	13 (43.3)	6 (20.7)
Introspection	7 (23.3)	5 (6.7)	1 (3.4)
Reflections	3 (10.0)	2 (6.7)	2 (6.9)
Increased empathy	2 (6.7)	3 (10.0)	0
Sense of oneness	1 (3.3)	4 (13.3)	0
Introspection/reflection	1 (3.3)	1 (3.3)	1 (3.4)
Laughter	1 (3.3)	1 (3.3)	0
New perspective	1 (3.3)	1 (3.3)	0
Awareness of importance of considering others	1 (3.3)	0	0
Clarity of thought	1 (3.3)	0	0
Contemplative state	1 (3.3)	0	1 (3.4)
Increased compassion	1 (3.3)	0	0
Increased creativity	1 (3.3)	0	0
Increased sense of connectedness	1 (3.3)	0	0
More socially upbeat	1 (3.3)	0	0
Reflections and new perspectives	1 (3.3)	0	0
Sense of oneness and connectedness	1 (3.3)	0	0
Being less judgmental	0	1 (3.3)	0
Feeling more moody/sensitive	0	1 (3.3)	0
Feeling rested	0	1 (3.3)	0
Increased wit	0	1 (3.3)	0
Reflections and new perspective on relationships and society	0	1 (3.3)	0
Sense of oneness	0	1 (3.3)	0
Calm	0	0	1 (3.4)
Feeling of adrenaline release	0	0	1 (3.4)
Negative mood	0	0	1 (3.4)
Unusual appreciation of music	0	0	1 (3.4)

Note: *AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities

Majority of adverse events resolved on day of administration, with a median duration of one day

Most frequent AEs: onset and duration by treatment arm in our Phase I trial



✓ Of all AEs, 68% reported as starting and resolving on the day of administration

✓ The median duration of AEs in all treatment arms across the 12-week trial was one day

Psilocybin therapy: described by most patients in one study as being among the top five most meaningful experiences of their lives¹



Preparation

- Establish therapeutic alliance
- Demonstrate and practise self-directed inquiry and experiential processing
- Online preparation platform to remind patients what to expect and how to prepare



Psilocybin session

- Supported by therapist and assisting therapist throughout 6-8 hour session
- Room designed for non-clinical, calming atmosphere
- Specially-designed music playlist, eyeshades to help focus internally
- Patients often experience sense of connectedness, emotional breakthrough and acceptance



Integration

- Therapists help patients process the emotional and physical experiences facilitated by psilocybin
- Generate insights that can lead to cognitive and behavioural changes
- Patients often experience a sense of agency and a separation from their symptoms, and report feeling empowered to make changes in their lives

technology application solutions



Developing and researching technology applications to improve the safety, efficacy and accessibility of our therapy

COMPASS solutions in development

Patient preparation platform

Online therapist training and learning platform

AI-assisted therapist feedback and monitoring

Research

Analyse digital biomarker data with the goal of predicting relapse and modelling disease course

Develop technologies to augment or complement our therapies

Building a strong in-house team



Greg Ryslik - SVP Data Science, Machine Learning and Digital Health Research

- Former Chief Data Officer at Celsius Therapeutics; VP of Data Science at Mindstrong Health; Service Data Science Lead at Tesla Motors



Bob Dougherty - VP, Digital Health Research

- Former VP of Research at Mindstrong Health; Research Director at the Stanford Center for Neurobiological Imaging
- Published 50+ peer-reviewed articles in psychology and neuroscience

Phase IIb clinical trial: COMP360 psilocybin therapy for TRD

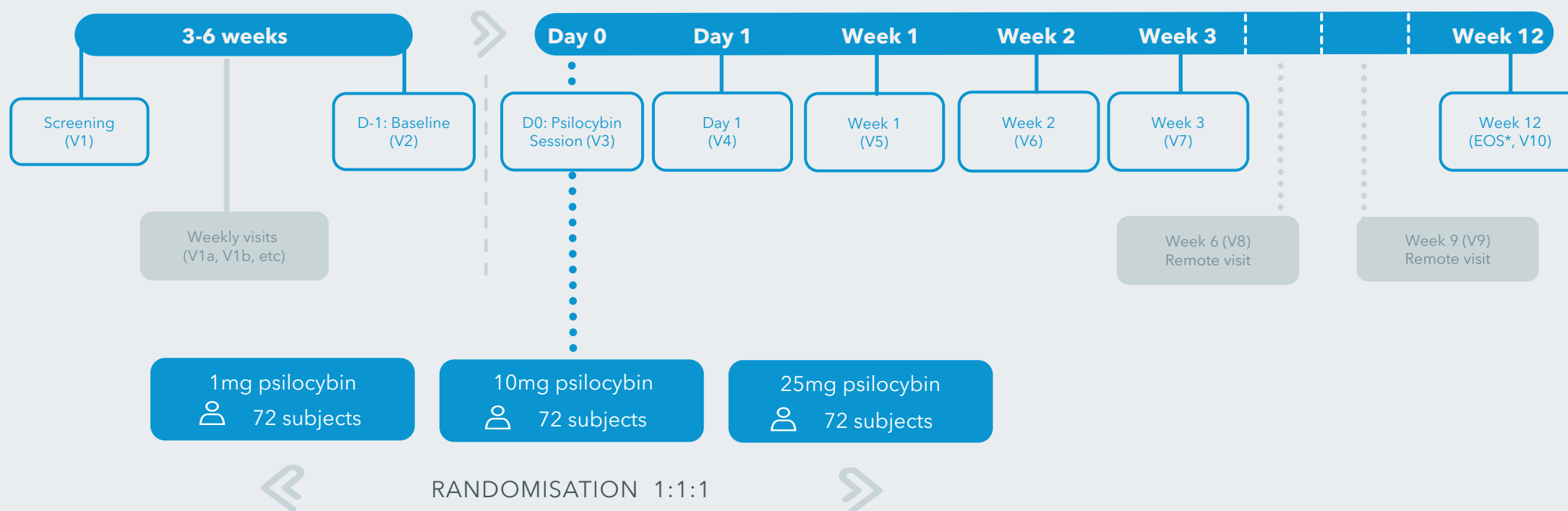
Target enrolment of 216 patients achieved; data expected late 2021

Primary endpoint

✧ Reduction of symptoms of depression as measured by MADRS* from Baseline to 3 weeks

Secondary endpoint

✧ Proportion of responders who maintained $\geq 50\%$ improvement in MADRS up to week 12



Note: *MADRS = Montgomery-Åsberg depression rating scale; EOS = end of study; TRD = treatment-resistant depression

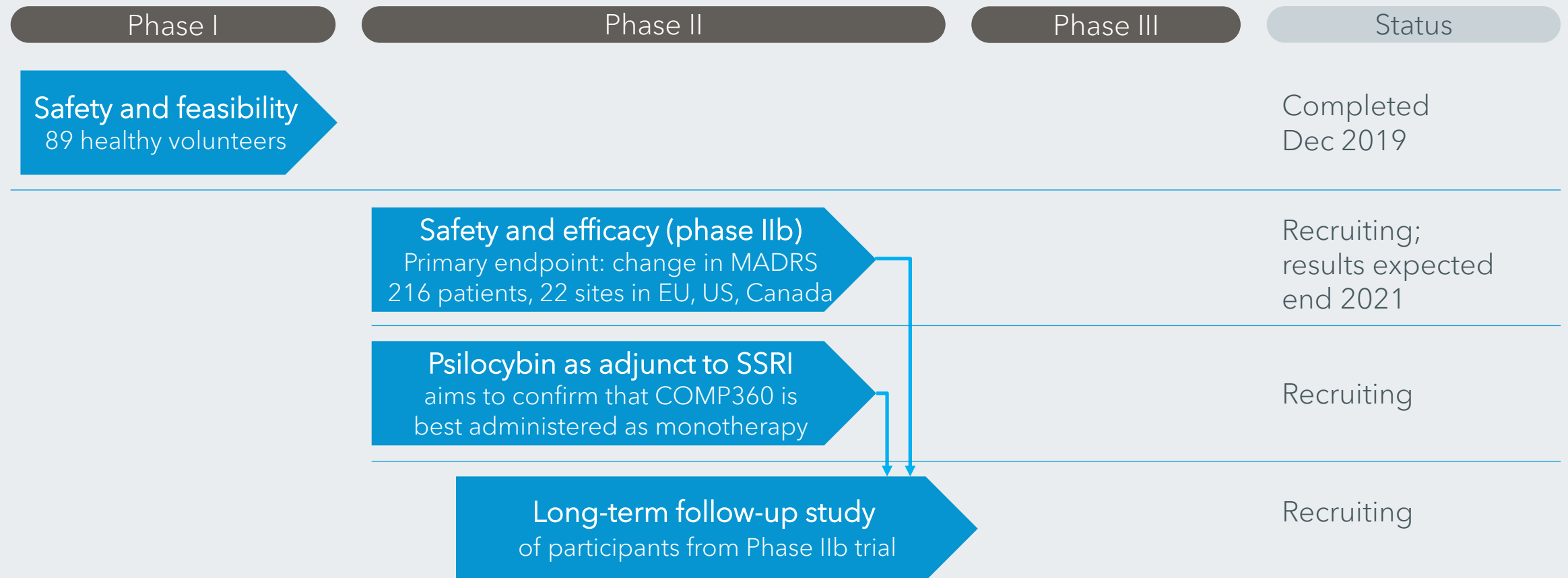
To date, four patients have experienced suspected, unexpected serious adverse reactions (SUSARs) in our Phase IIb trial for TRD patients

Sites engaged for phase IIb TRD study are well established and have access to significant patient populations



Our clinical development programme for COMP360 psilocybin therapy in TRD

Getting ready for Phase III



Achieving broad patient access



Comprehensive and payer-relevant evidence generation plan

- Early scientific advice with key payer-experts and HTAb*
- US reimbursement and coding strategy
- Real-world evidence - data access agreements



Differentiated and modular commercial offering

- Therapist training services and partnerships
- Treatment centre activation services
- Digital solutions – companion apps for prediction and prevention



Strategic partnerships with payers, health systems and clinic networks

- Centres of Excellence
- Prospective payer-focused trials
- Potential franchise model

Prototype design Centre of Excellence treatment room



Prototype design Centre of Excellence post-treatment space



COMP360 commercial exclusivity strategy

Regulatory strategy



Patent strategy

COMP360 can be registered as NCE*/NAS*

- Possibility of full patent and regulatory exclusivity
- Data protection, up to
 - 8-11 years (EU)
 - 5-7.5 years (US)

Reschedule COMP360 psilocybin

- Upon approval by FDA, COMP360 psilocybin could be rescheduled by DEA

Three US patents granted

- 1st US patent (Dec 2019): includes claims to methods of treating drug-resistant depression with high-purity polymorphic crystalline psilocybin formulations
 - Petition for Post Grant Review was dismissed on merits in August 2020
- 2nd US patent (March 2021): includes claims to oral dosage forms of psilocybin and methods of treating major depressive disorder (MDD) with those forms
- 3rd US patent (March 2021): includes claims to high-purity crystalline psilocybin (including the form used in COMP360), formulations of psilocybin and methods of treating MDD with psilocybin

European & Asian patents granted/registered

- German utility model (March 2020): includes claims to forms of crystalline psilocybin, use in medicine and methods of synthesis
- First UK patent (May 2020): includes claims to manufacturing methods, product-by-process and formulations
- Second UK patent (July 2020): includes claims covering crystalline psilocybin, pharmaceutical formulations, medical uses and manufacturing methods
- Two Hong Kong patents granted (Feb 2021) covering crystalline psilocybin compositions, formulations and manufacturing methods (corresponds to above UK patents)

Multiple related applications pending

- Pursue additional claim scope and extend coverage in over 20 additional countries/regions












Three PCT applications and Taiwanese application pending

- Additional formulations, methods of administration, therapeutic and digital supports, combination treatments, methods of treatment for a variety of additional indications

COMP360 in psilocybin therapy research

IISs using COMP360: signal-generating, exploratory studies looking at indications in areas of unmet need

- COMPASS has pending patent applications that include the indications listed
- COMPASS owns or has a license to new IP generated
- Studies may provide signals that we can explore further and expand in a portfolio approach to different indications

MDD comparative mechanism of action	Imperial College London	
MDD	University of Zurich	
	Aquilino Cancer Center	
Chronic cluster headache	University of Copenhagen	
Severe TRD	Sheppard Pratt	
Bipolar disorder II	Sheppard Pratt	
Body dysmorphic disorder	Columbia University	
Anorexia nervosa	UC San Diego	
TRD	King's College London	
Suicidal ideation	Sheppard Pratt	
Autism	King's College London	

Note: IIS = investigator-initiated studies, MDD = major depressive disorder, TRD = treatment-resistant depression

We do not sponsor investigator-initiated studies, some of which use their own protocols and study design. We encourage the open publication of all associated findings from any study or trial using COMP360

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Working in partnership



COMPASS's first
Centre of Excellence, at
Sheppard Pratt,
Baltimore, US



COMPASS Discovery Center
with University of the Sciences,
Philadelphia,
UC San Diego, School of
Medicine, and Medical
College of Wisconsin (MCW)



COMP360 psilocybin therapy
study of MDD in cancer, at the
Aquilino Cancer Center, Rockville,
Maryland, US



IIS signal-generating studies
in new indications for
psilocybin therapy using
COMP360

Comprehensive preclinical program - COMP360 psilocybin in a broad range of indications with pending patent applications

Preclinical research has been conducted in the following indication areas:

Alzheimer's disease

Autistic spectrum disorder

Chronic pain

Epilepsy

Inflammation

Parkinson's disease

Attention deficit hyperactivity disorder

Binge eating disorder

Cluster headache

Generalised anxiety disorder

Obsessive-compulsive disorder

Sleep wake disorders

We believe the data from the above programme of research is supportive of performing preclinical research into the following additional indications:

Anorexia nervosa

Bulimia nervosa

Inflammatory bowel disease

Panic disorder

Post-traumatic stress disorder

Stroke

Body dysmorphic disorder

Fibromyalgia

Migraine

Post-partum depression

Social anxiety disorder

Traumatic brain injury

Financial overview

Cash and cash equivalents at 31 March 2020

- \$179.5 million

April 2021 raise

- \$165.6 million¹

Issued shares

- 41.6 million²

Covering analysts

- Esther Hong, Berenberg
- Robert (Bert) Hazlett, BTIG
- Sumant Kulkarni, Canaccord Genuity
- Charles Duncan, Cantor Fitzgerald
- Ritu Baral, Cowen
- Josh Schimmer, Evercore
- Patrick Trucchio, HC Wainwright & Co
- Elemer Piros, ROTH

Notes:

1. Follow-on raise, includes full over-allotment ("Green shoe")
2. As at May 24, 2021, including 4.6 million shares from recent financing – 100% of greenshoe exercised

Pioneering the development of a new model of psilocybin therapy

Key achievements

- ✓ \$146.6m raised in September IPO; \$80m raised in Series B
- ✓ Breakthrough Therapy designation for COMP360 in TRD
- ✓ Phase I healthy volunteers trial completed
- ✓ Phase IIb clinical trial making steady progress
- ✓ Patent awards in US, UK, Germany
- ✓ Experienced leadership team, board of directors, scientific advisory board; leadership team and board strengthened with recent hires
- ✓ Preclinical studies in new indications; Discovery Center launched
- ✓ Additional trials underway in TRD programme
- ✓ COMP360 used in multiple IISs exploring range of indications
- ✓ FDA approved request for 1:1 therapist patient ratio and online therapist training
- ✓ Aquilino Cancer Center launches psilocybin therapy study with simultaneous administration and 1:1 therapist support

2021 Anticipated milestones

- ✓ Establish first Centre of Excellence
- ✓ Expand Board of Directors with Independent director
- ✓ Data published from IISs using COMP360
- ✓ Expand current IP portfolio with additional patent grants
- ✓ Further senior appointments
- Phase IIb trial: data expected late 2021
- Further partnerships and collaborations
- Evolve data and technology strategy

“

*I had such instant relief I could
make up my mind about things ...
it lifted the fog of depression.
The way I felt after, I have not felt
with any medicine or therapy ...
I forgot what depression was.*

”

Quote from participant in Imperial College London psilocybin therapy study conducted by Carhart-Harris et al, 2016; image is representative and not of a patient



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