Transforming mental health care

COMPASS Pathways plc
November 2021

COMPASSION
Navigating Mental Health Pathways

Disclaimer

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Everyone has a
S T O R Y

Pipeline overview

COMPASS development programmes

COMPASS-owned and sponsored

Programme	Discovery	Preclinical	Ph1	Ph2	Ph3	Reg.
COMP360 for TRD						
COMP360 for PTSD						
Prodrug programme						
Discovery Center						

Investigator-initiated studies

Signal-generating exploratory studies looking at indications in areas of unmet need with COMP360

- 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 bring into our development pipeline

Indication	Institution	CMPS financed	
MDD in cancer patients	Aquilino Cancer Center	✓	*Complete*
MDD	University of Zurich		
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	✓	
Suicidal ideation	Sheppard Pratt	✓	
Autism	King's College London	✓	

COMPASS's broad expertise

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

Guy Goodwin, DPhil
Chief Medical Officer

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

Danielle Schlosser, PhD
Senior Vice President, Clinical Innovation

Charli Sanders
Senior Vice President, Global Regulatory Affairs

Roberta Tucker
Head of Quality, GxP

Stephen Wright, MD
Senior Scientific Advisor

We are a mental health care company

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

- Significant unmet need: 100m people[1] 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
- Completed Phase IIb with 233 patients, largest psilocybin therapy clinical trial to date
- Planned expansion into additional indications

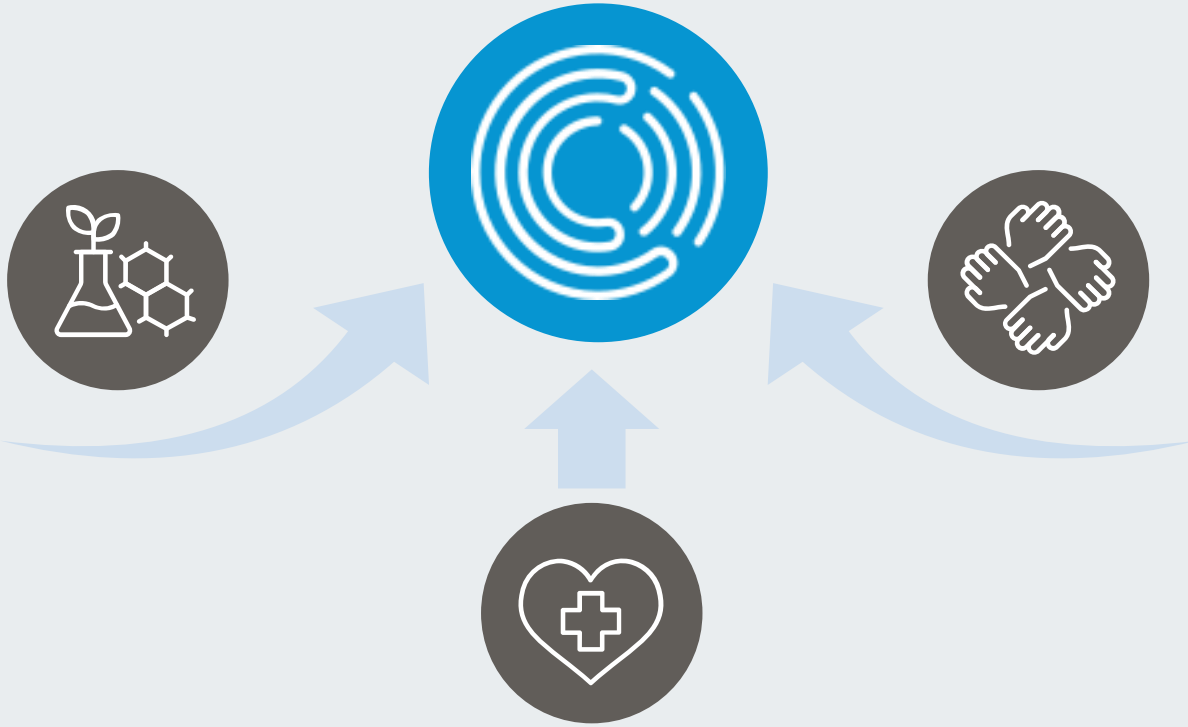
Driven by science and rigour

- COMP360 differentiated mechanism of action, activating the $5HT_{2A}$ receptor[2]
- 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

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 (n=89)
- Phase IIb trial in TRD completed (n=233)
- Launched phase II study in PTSD

Note: GMP = Good Manufacturing Practice; CMO = Contract manufacturing organisation; MHRA = UK Medical and Healthcare products Regulatory Agency; CMC = chemistry, manufacturing and control

Psilocybin therapy: described by most patients in one study as being among the top five most meaningful experiences of their lives[1]

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

Source: 1.Griffiths et al (2016)

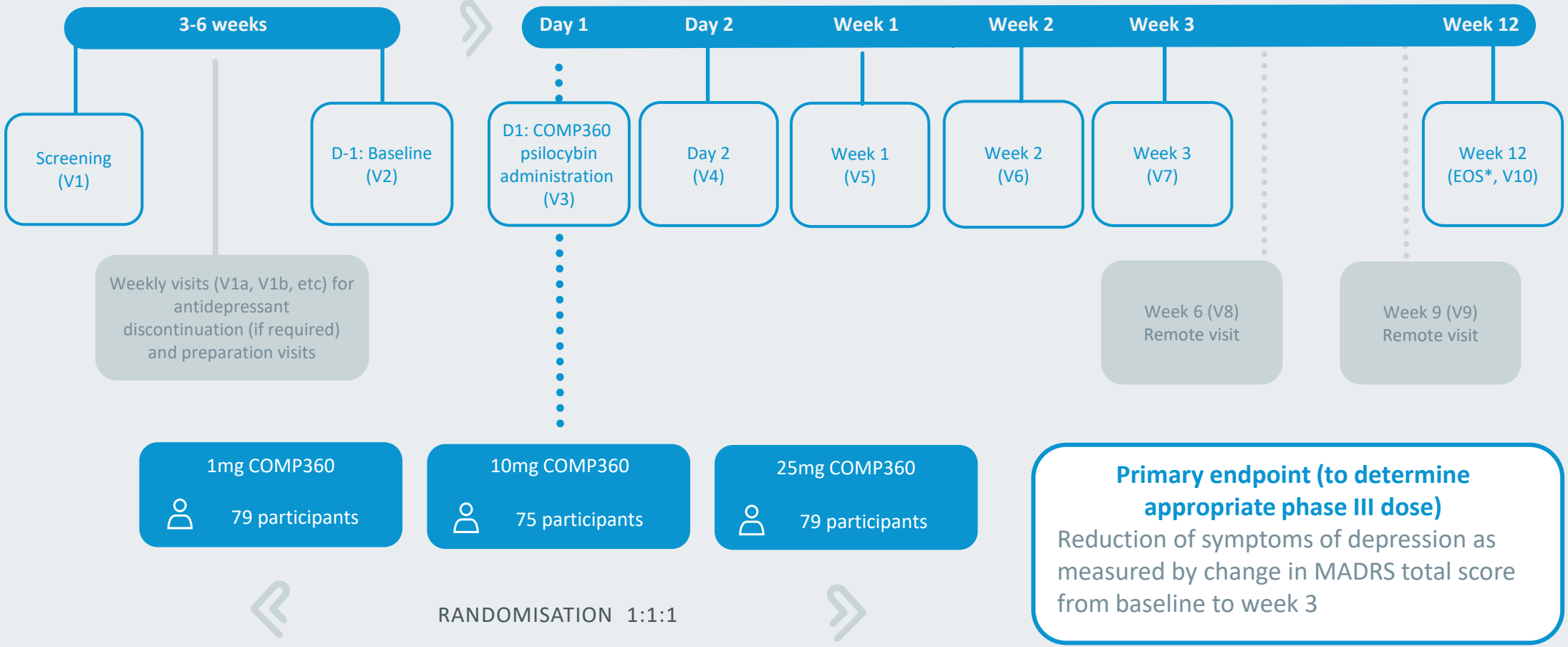
TRD treatment pathway: significant unmet need for 100 million patients

Treatment pathway stage	New onset depression Major depressive disorder (MDD)	Persistent depression Major depressive disorder (MDD)	Treatment-resistant depression (TRD)
Line of therapy	**First line**	**Second line**	**Third line +**
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	• Antidepressants • Psychological interventions, eg CBT*	• Antidepressants • Antidepressant combinations • Psychological interventions	• 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

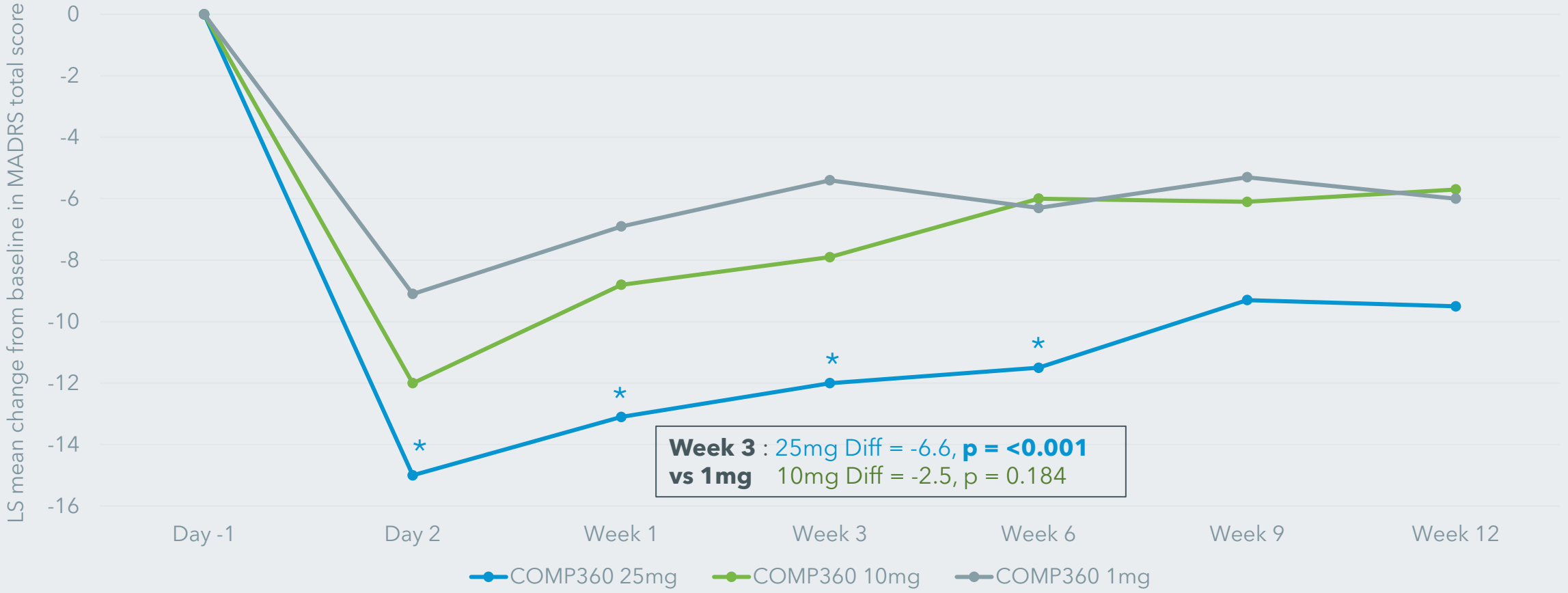
COMP 001 study design and endpoints



Note: MADRS = Montgomery-Åsberg Depression Rating Scale; EOS = end of study; TRD = treatment-resistant depression; D = day; V = visit

Primary endpoint – change from baseline in MADRS total score

Statistically significant primary endpoint (p<0.001) at week 3 (25mg vs 1mg). There was a rapid onset of action and durable effects with treatment differences between the 25mg vs 1mg group apparent from the day after COMP360 psilocybin administration

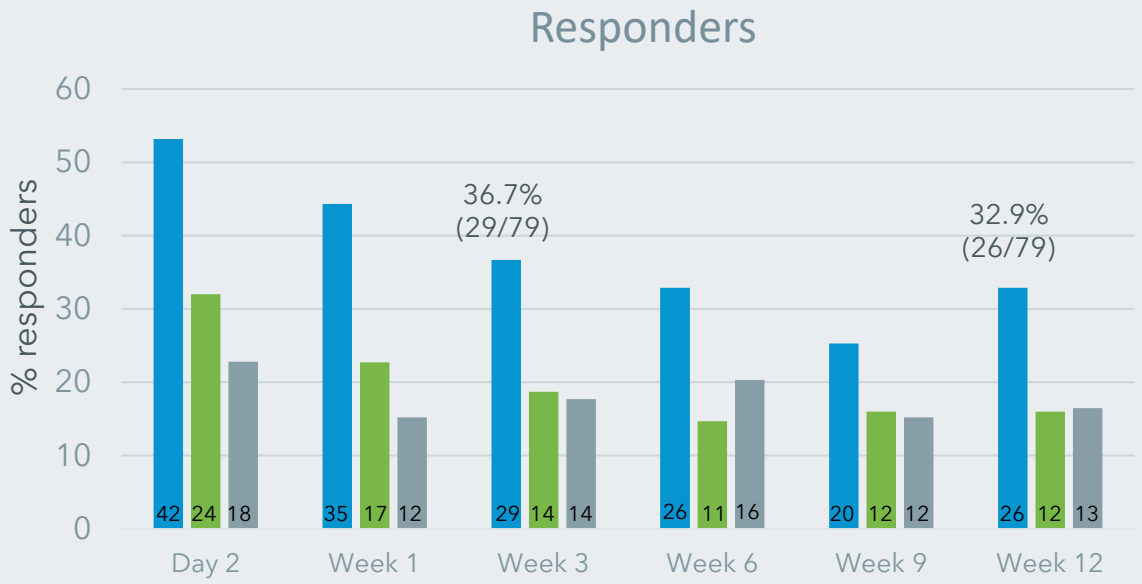


Baseline mean (SD): 25mg (n=79) = 31.9 (5.41); 10mg (n=75) = 33.0 (6.31); 1mg (n=79) = 32.7 (6.24)

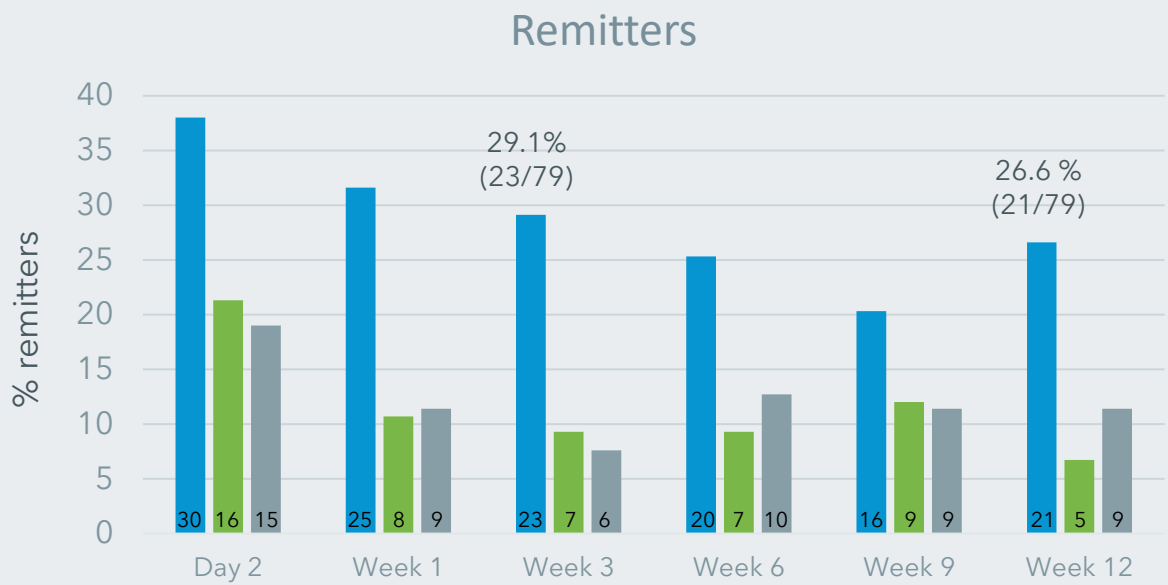
Note: MADRS = Montgomery-Åsberg Depression Rating Scale; n = number observed; SD = standard deviation; LS = least squares; * = statistically significant treatment difference vs 1mg at visit; p = p-value

Key secondary endpoints - MADRS responders & remitters

25mg group demonstrated rapid response, with treatment differences from day 2 to week 3 compared with the 1mg group



Responder: ≥50% decrease in MADRS total score from baseline



Remitter: MADRS total score ≤ 10

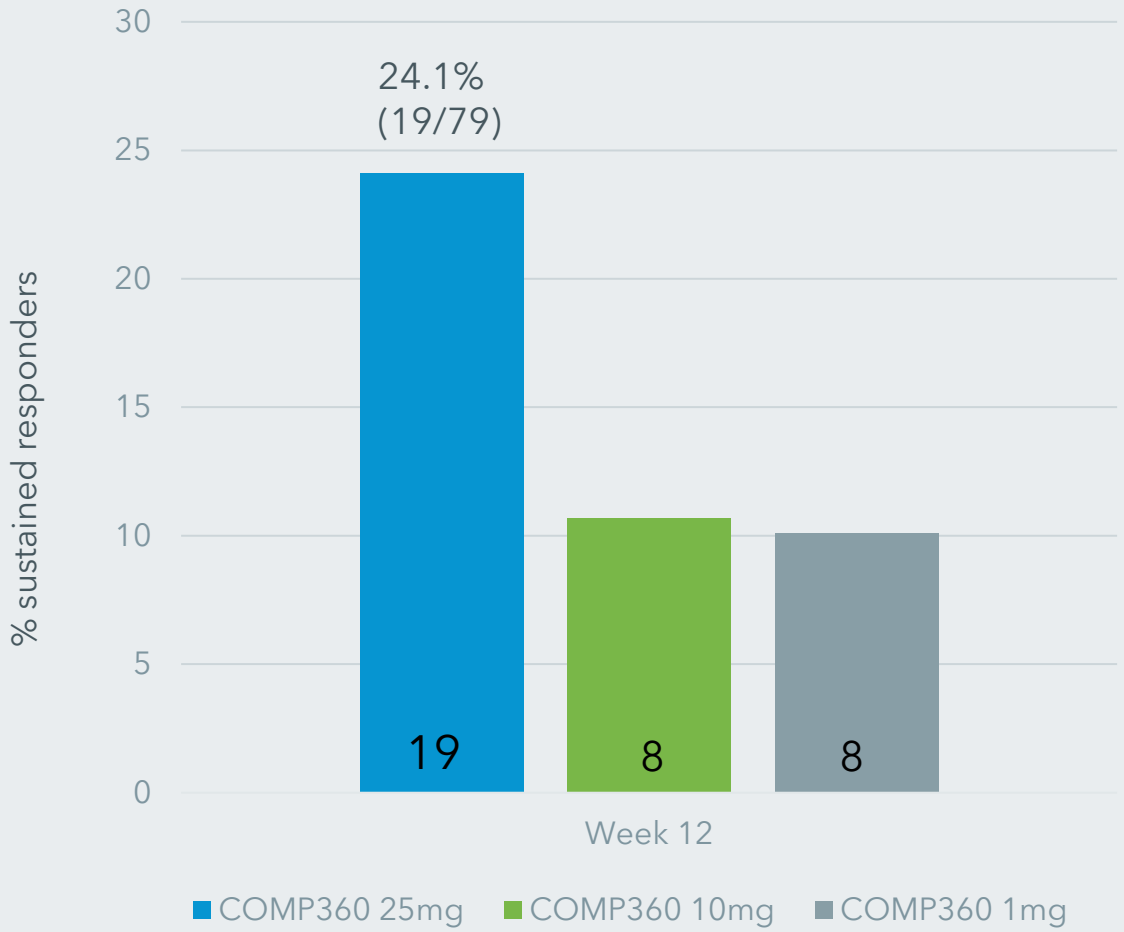
COMP360 25mg COMP360 10mg COMP360 1mg

Note: MADRS = Montgomery-Åsberg Depression Rating Scale; number of responders stated in bar

Participants who started new treatment for depression were assumed to be a non-responder hence decreasing numbers reflecting antidepressant use over time

MADRS sustained responders at week 12

Higher proportion of sustained responders found in the 25mg vs 1mg arm



Sustained responder – patients meeting the MADRS response criteria at any visit up to and including week 3 and also at week 12 and at least one visit out of week 6 and week 9, and who did not start any new treatments for depression

Note: MADRS = Montgomery-Åsberg Depression Rating Scale; number of sustained responders stated in bar

Statistical significance cannot be claimed on secondary endpoints due to hierarchical testing being broken for the 10mg vs 1mg dose on the primary endpoint

Participants who started new treatment for depression were assumed to be a non-responder hence decreasing numbers reflecting antidepressant use over time

Safety – treatment emergent adverse events (TEAEs) overview

- The vast majority of TEAEs (over 90%) were of mild or moderate severity
- The proportion of patients reporting a serious TEAE was comparable between the 25mg and 10mg groups:
  - 5 (6.3%) patients in the 25mg COMP360 arm
  - 6 (8.0%) patients in the 10mg COMP360 arm
  - 1 (1.3%) patient in the 1mg COMP360 arm
  - 19 TESAEs were reported in total, experienced by 12 patients (note: two patients had the same TESAE twice)
  - All suicidal behaviours were experienced at least one month after COMP360 administration
- TEAE incidence was slightly higher in the 25mg group than in the 10mg and 1mg groups
- Further analysis on the onset and duration of TEAEs is underway
- TEAE incidence includes all events, including those thought to be related to the psychedelic experience on the day of COMP360 psilocybin administration in the therapeutic setting

Note: TEAE = treatment emergent adverse event

Most frequent TEAEs ordered by the 25mg arm (at least 5% in any treatment group)

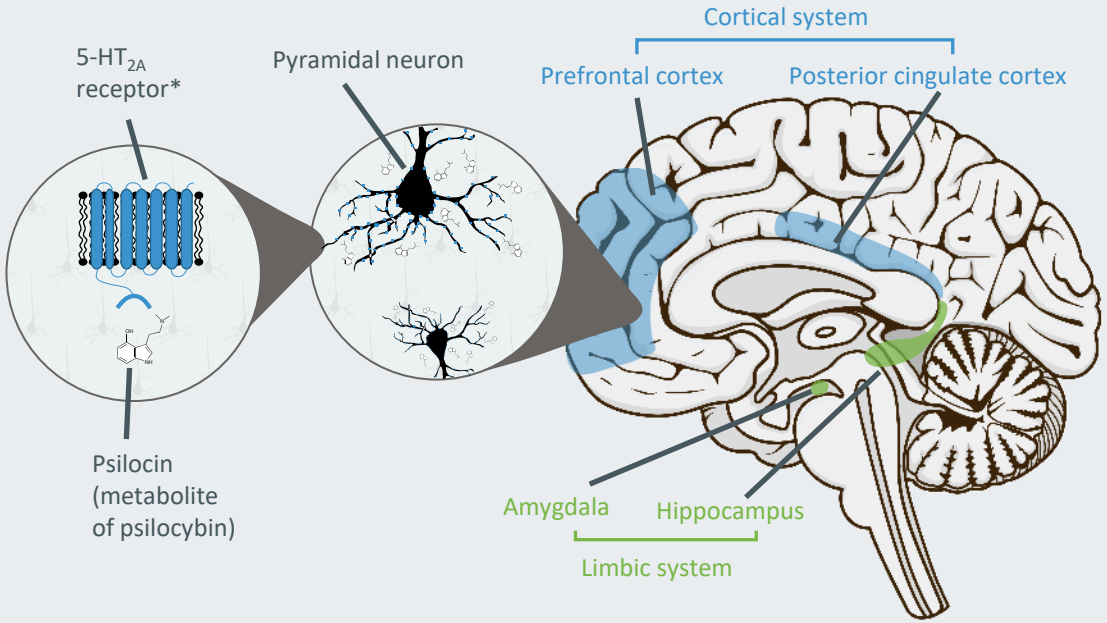
MedDRA TEAE preferred term	COMP360 25mg	**COMP360** 10mg	**COMP360** **1mg**	Overall
	N=79	N=75	N=79	N=233
	n (%)			
Headache	27 (34.2)	16 (21.3)	20 (25.3)	63 (27.0)
Nausea	18 (22.8)	7 (9.3)	4 (5.1)	29 (12.4)
Fatigue	12 (15.2)	5 (6.7)	7 (8.9)	24 (10.3)
Insomnia	8 (10.1)	11 (14.7)	14 (17.7)	33 (14.2)
Anxiety	7 (8.9)	13 (17.3)	3 (3.8)	23 (9.9)
Mood altered	7 (8.9)	3 (4.0)	1 (1.3)	11 (4.7)
Back pain	6 (7.6)	0	3 (3.8)	9 (3.9)
Dizziness	6 (7.6)	1 (1.3)	1 (1.3)	8 (3.4)
Suicidal ideation	5 (6.3)	5 (6.7)	4 (5.1)	14 (6.0)
Myalgia	5 (6.3)	2 (2.7)	1 (1.3)	8 (3.4)
Euphoric mood	4 (5.1)	5 (6.7)	4 (5.1)	13 (5.6)
Depression	4 (5.1)	6 (8.0)	5 (6.3)	15 (6.4)
Abdominal pain upper	4 (5.1)	2 (2.7)	1 (1.3)	7 (3.0)
Irritability	4 (5.1)	2 (2.7)	1 (1.3)	7 (3.0)
Panic reaction	4 (5.1)	1 (1.3)	1 (1.3)	6 (2.6)
Depressed mood	3 (3.8)	5 (6.7)	4 (5.1)	12 (5.2)
Paraesthesia	3 (3.8)	4 (5.3)	1 (1.3)	8 (3.4)
Thinking abnormal	0	4 (5.3)	0	4 (1.7)

TEAE incidence is higher in the 25mg group overall

Key mood-related TEAEs (euphoric mood, depression, depressed mood, suicidal ideation) do not have a higher incidence in the 25mg arm

Note: MedDRA = Medical Dictionary for Regulatory Activities; TEAE = treatment emergent adverse event; N = number of participants in the population; n = number observed

COMP360 mechanism of action



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

1. Stimulation of 5-HT_{2A} receptors[1] results in downstream cascades via G-protein signalling[2]

2. Altered extracellular release of dopamine[3,4] and leading to enhanced positive mood

3. Downregulation of the default mode network, or DMN*[5], and de-synchronisation of cortical activity as well as the emergence of new patterns of functional connectivity across the brain[6]

4. Sustained cellular changes leading to neuroplasticity[7] and "window of opportunity" for therapy

Note: *5-HT_{2A} = 5-hydroxytyryptamine 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

Placebo

Psilocybin

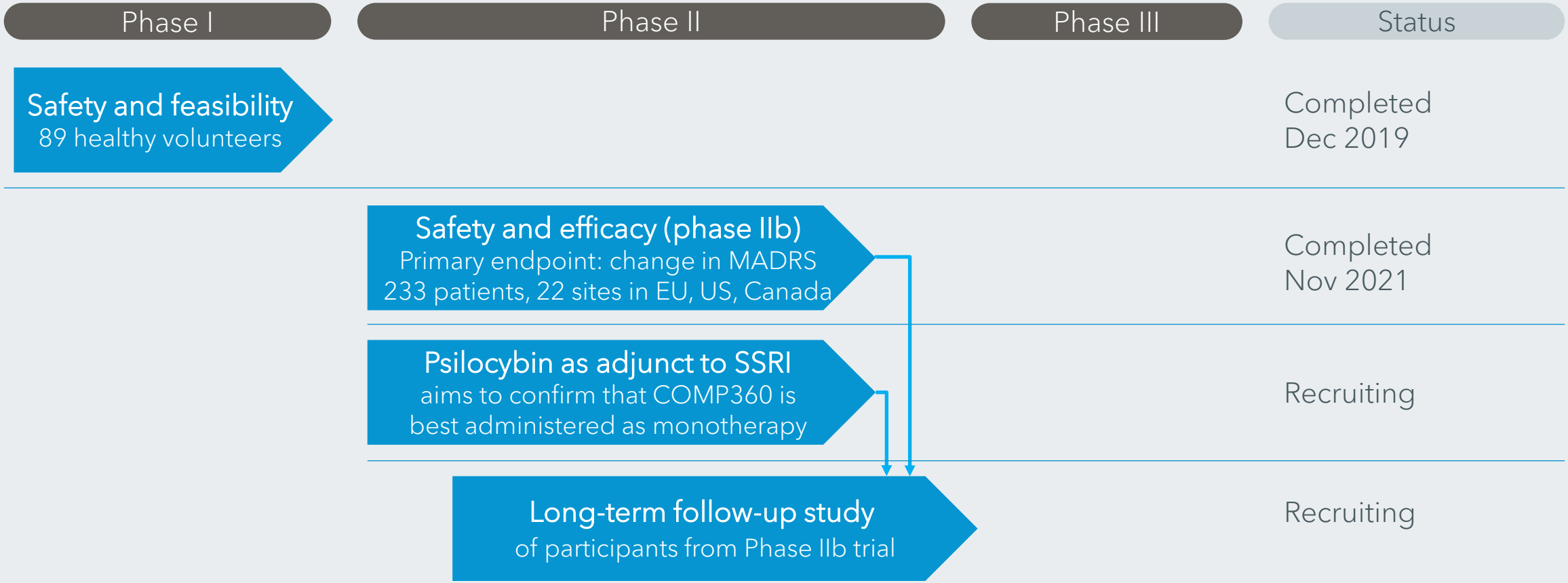
Brain network alterations may indicate the emergence of novel patterns of connectivity, following downregulation of the DMN

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

Our clinical development programme for COMP360 psilocybin therapy in TRD

Getting ready for Phase III



Note: SSRI = Selective serotonin reuptake inhibitors; TRD = treatment-resistant depression

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

Note: AI = augmented intelligence

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

Note: *HTAb = Health Technology Assessment bodies; Centre of Excellence prototype designs by Gensler (architecture, design, planning and consulting firm)

COMP360 commercial exclusivity strategy

Regulatory 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

+ Patent strategy

Four 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
- 4th US patent (October 2021), composition claims to an alternative crystalline 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

Note: *NCE = new chemical entity; NAS = new active substance; ADHD = attention deficit hyperactivity disorder; ALS = amyotrophic lateral sclerosis

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)

IP portfolio of novel psychedelic compounds and prodrugs developed together with inventor Matthias Grill PhD, who will be working with COMPASS on an exclusive research project to develop new product candidates

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

Note: MDD = major depressive disorder; IIS = investigator-initiated study

Financial overview

Cash and cash equivalents at 30 September 2021
- $294.0 million

Issued shares
- 41.7 million[1]

Covering analysts
- Esther Hong, Berenberg
- Robert (Bert) Hazlett, BTIG
- Sumant Kulkarni, Canaccord Genuity
- Charles Duncan, Cantor Fitzgerald
- Neena Bitritto-Garg, CITI
- Ritu Baral, Cowen
- Josh Schimmer, EvercoreISI
- Patrick Trucchio, HC Wainwright & Co
- Jason McCarthy, Maxim Group
- Francois Brisebois, Oppenheimer
- Elemer Piros, ROTH

Notes:
1. As at Sept 30, 2021

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
  - ✓ Imperial College London in MDD (published in The New England Journal of Medicine)
  - ✓ Maryland Oncology Hematology at the Aquilino Cancer Center in MDD
- ✓ Expand current IP portfolio with additional patent grants
- ✓ Further senior appointments
- ✓ Phase IIb trial: data
- ✓ Further partnerships and collaborations
- ➤ Evolve data and technology strategy

Note: TRD = treatment-resistant depression

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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