Transforming mental health care

COMPASS Pathways plc
February 2022

COMPASS
Navigating Mental Health Pathways

Disclaimer

Cautionary Note Regarding Forward-Looking Statements This presentation includes express and implied "forward-looking statements." In some cases, you can identify forward-looking statements by terms such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "will," "would," or the negative of these terms, and similar expressions intended to identify forward-looking statements. However, not all forward-looking statements contain these identifying words. These statements may relate to our strategic plans or objectives, revenues or earnings projections, or other financial items. By their nature, these statements are subject to numerous uncertainties, including factors beyond our control, that could cause actual results, performance or achievement to differ materially and adversely from those anticipated or implied in the statements. You should not rely upon forward-looking statements as predictions of future events. Although our management believes that the expectations reflected in our statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances described in the forward-looking statements will be achieved or occur. Moreover, neither we, nor any other person, assumes responsibility for the accuracy and completeness of these statements. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date such statements are made and should not be construed as statements of fact. We undertake no obligation to update these forward-looking statements to reflect events or circumstances after the date hereof, or to reflect the occurrence of unanticipated events.

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Pioneering the development of a new model of psilocybin therapy

2021 Key achievements

- ✓ Progressed COMP360 development program with positive phase IIb clinical trial results – 25mg dose selected for phase III program; program has Breakthrough Therapy designation
- ✓ SSRI combination study supports potential adjunctive use of COMP360
- ✓ Full pipeline of COMP360 trials underway in multiple IISs exploring range of indications
- ✓ New patents awarded bringing total granted to 10 – numerous additional patents under review
- ✓ Experienced leadership team, board of directors, scientific advisory network
- ✓ COMP360 phase II study launched in PTSD
- ✓ Aquilino Cancer Center completes positive COMP360 psilocybin therapy study with simultaneous administration and 1:1 therapist support
- ✓ Data published in *The New England Journal of Medicine* on COMP360 in MDD from Imperial College London
- ✓ Advanced preclinical studies in new indications; Discovery Center expanded
- ✓ Established first Centre of Excellence
- ✓ COMPASS well capitalized from successful IPO and follow-on financings

Note: TRD = treatment-resistant depression; PTSD = post traumatic stress disorder


Everyone has a
S T O R Y

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 purified psilocybin formulation designated a FDA Breakthrough Therapy for TRD
- Completed phase I healthy volunteers trial
- Completed phase IIb – world's largest psilocybin therapy clinical trial
- Completed SSRI as adjunct to COMP360 open-label study
- Planned expansion into additional indications

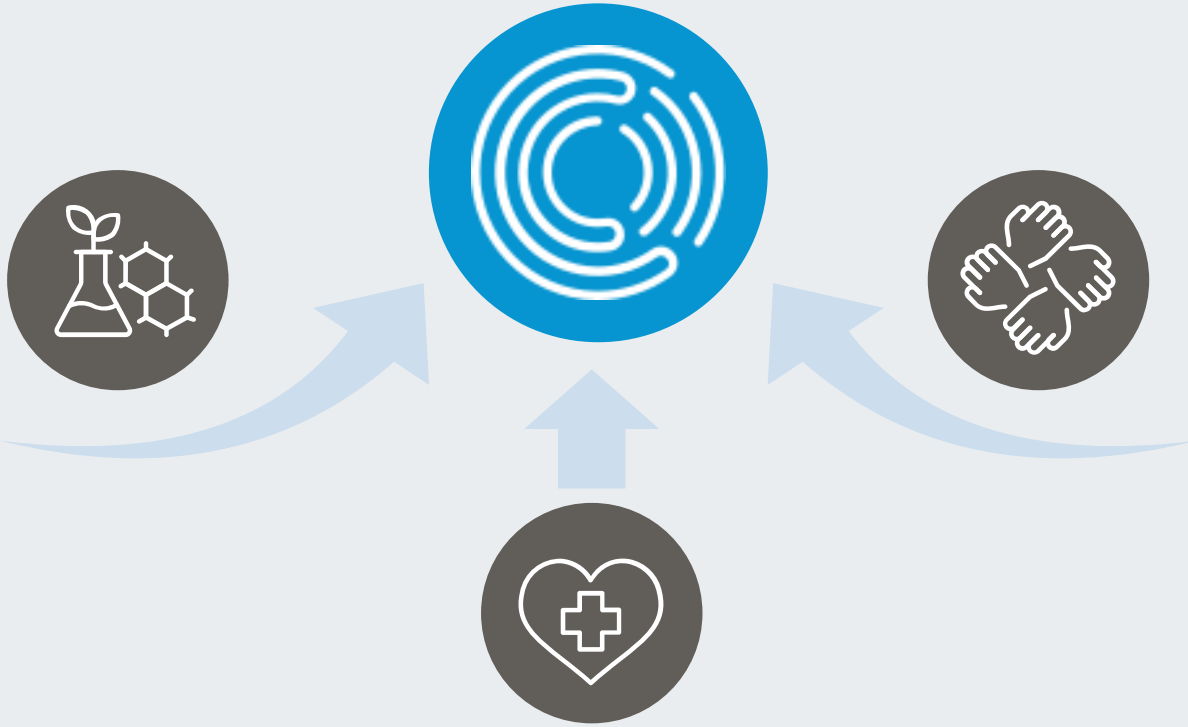
Driven by science and rigour

- 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

Pipeline overview

COMPASS development programmes

COMPASS-owned and sponsored

Programme	Discovery	Preclinical	Phase I	Phase II	Phase III	Approved
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 owns or has a license to new IP generated around COMP360 psilocybin
- 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	✓	

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

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

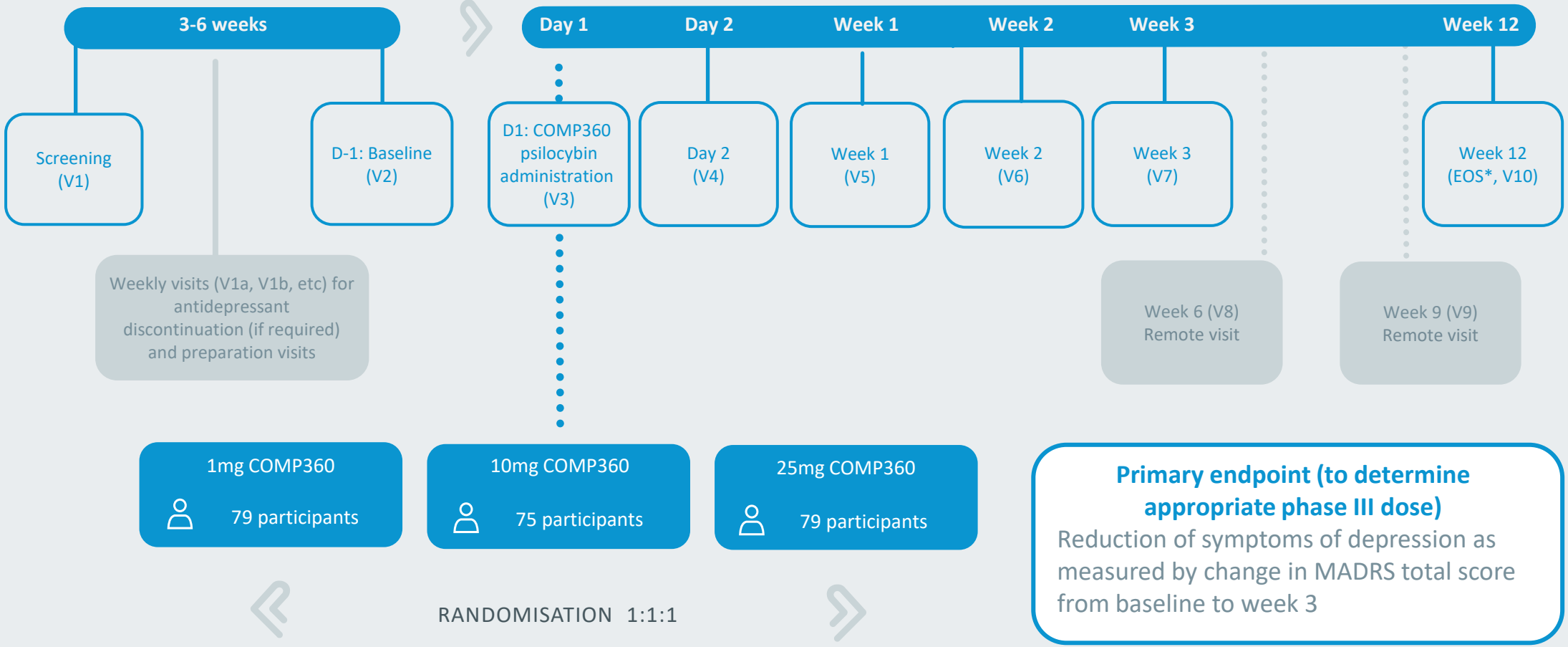
Psilocybin session is preceded by preparation and followed up with integration

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 completed
- 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

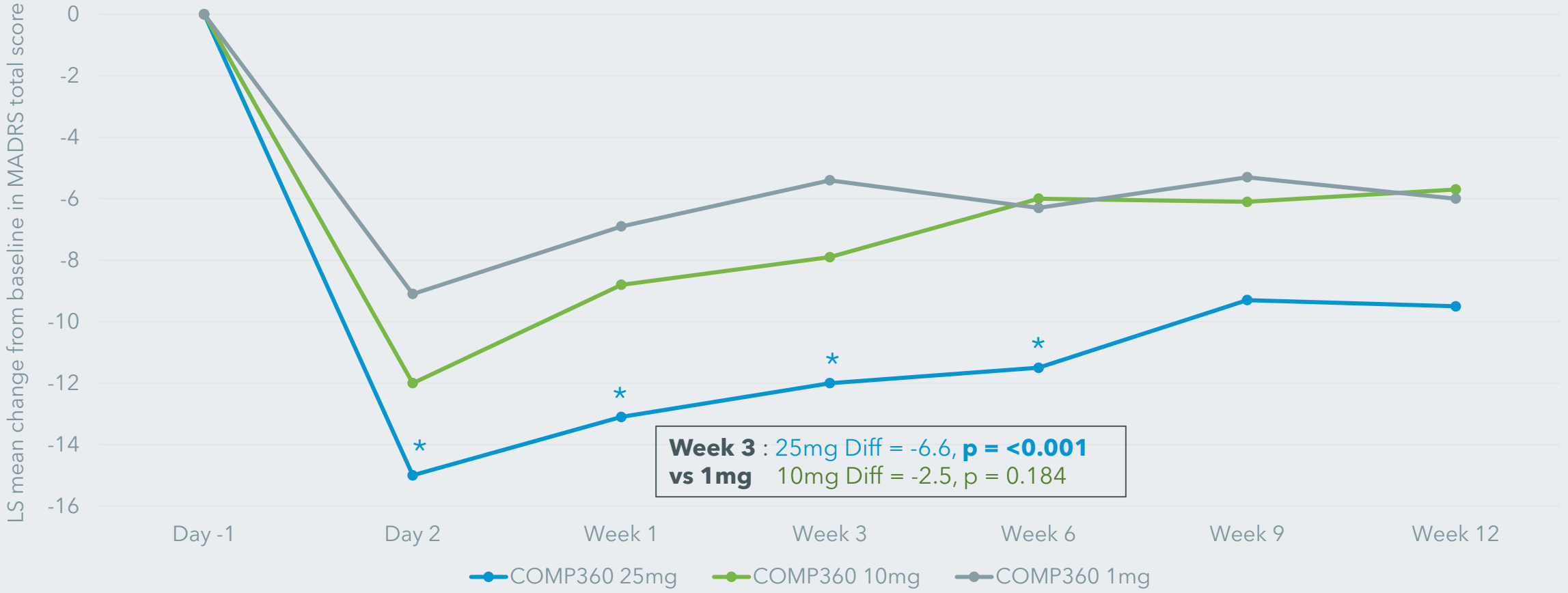
COMP001 study design and endpoints



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

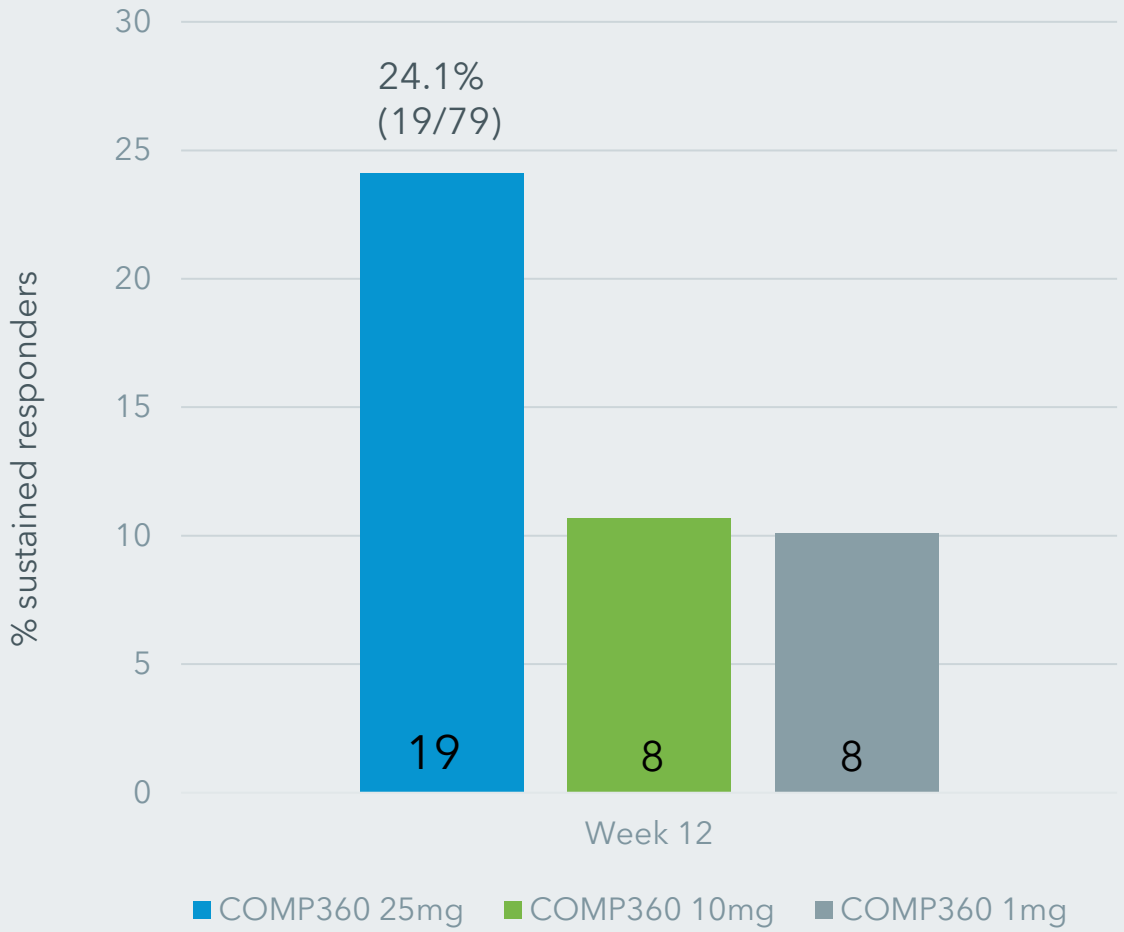


Baseline mean (SD): 25mg (n=79) = 31.9 (5.41); 10mg (n=75) = 33.0 (6.31); 1mg (n=79) = 32.7 (6.24)

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

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

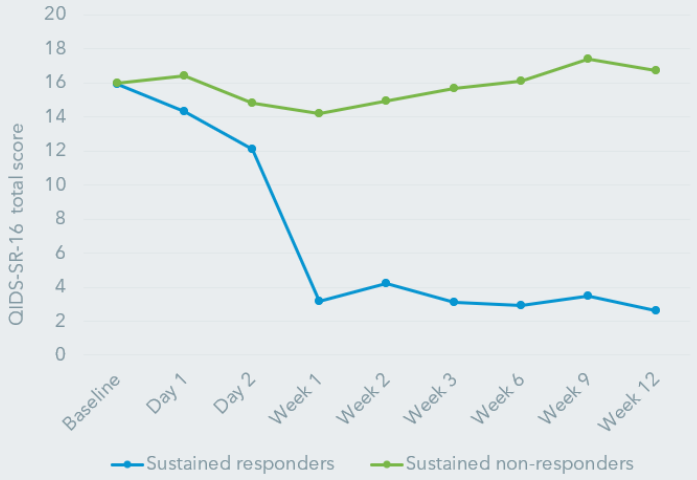
Note: MADRS = Montgomery-Åsberg Depression Rating Scale; number of sustained responders stated in bar

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

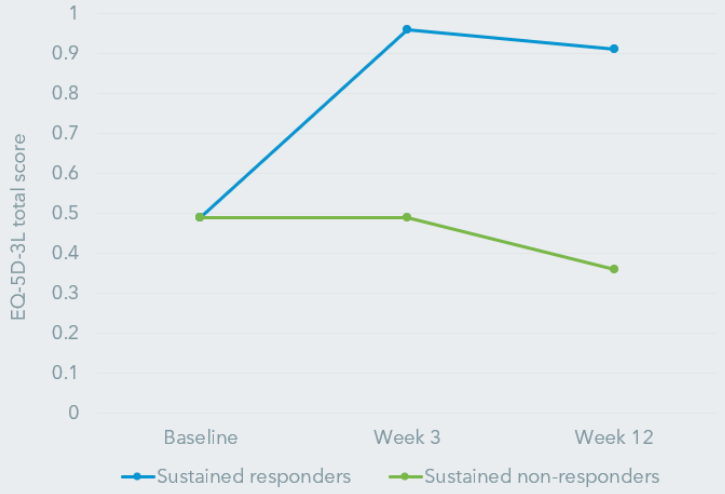
Key secondary endpoints: sustained responders and sustained non-responders for COMP360 25mg

Sustained responders were found to have clinically meaningful reductions on the QIDS-SR-16 from baseline at week 1 through to week 12 with mean scores moving from the moderate/severe range at baseline to subthreshold at week 1 onwards



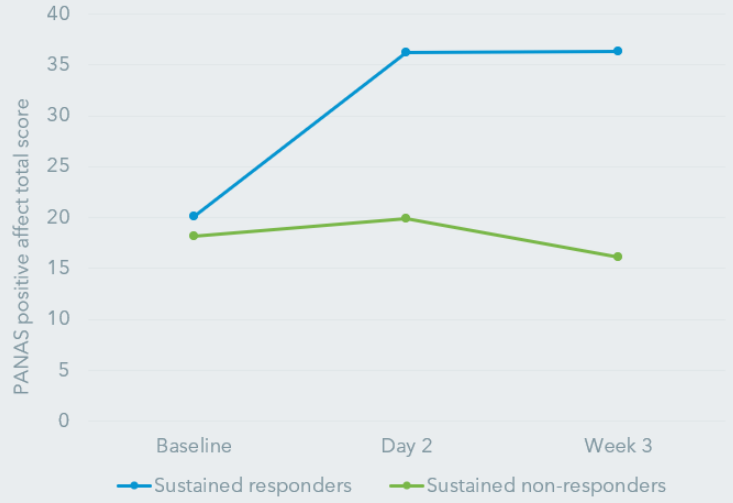
Baseline mean (SD): Sustained responders 25mg (n=19) = 15.9 (3.48); sustained non-responders 25mg (n=21) = 16.0 (4.77)

Sustained responders were found to have clinically meaningful increases in quality of life from baseline at week 3 and week 12 with scores in the normal range after treatment



Baseline mean (SD): Sustained responders 25mg (n=19) = 0.49 (0.249); sustained non-responders 25mg (n=21) = 0.49 (0.223)

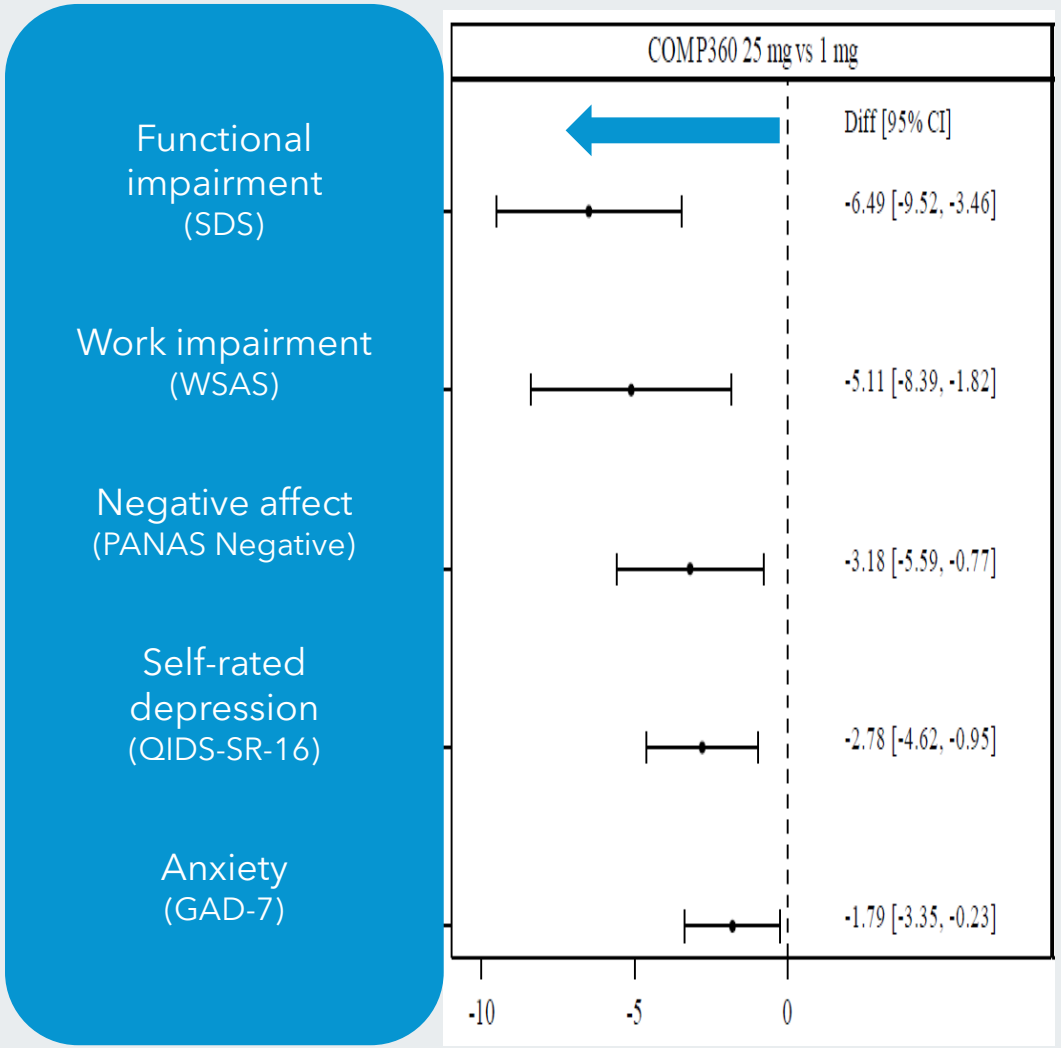
Sustained responders were found to have clinically meaningful increases in positive affect from baseline at day 2 and week 3



Baseline mean (SD): Sustained responder 25mg (n=19) = 20.1 (7.53); Sustained non-responder 25mg (n=21) = 18.2 (4.77)

Note: QIDS-SR-16= 16-item Quick Inventory of Depressive Symptomatology – Self Report; n = number observed; EQ-5D-3L= EuroQoL 5-Dimensions 3-Levels; PANAS= Positive and Negative Affect Schedule; n = number observed; n = number observed; SD = standard deviation. 12 sustained non-responders in 25mg arm took treatment for depression at some point in the study. Sustained responders are defined as participants who responded (≥50% change in MADRS total score from baseline) at weeks 3 and 12, and at least one visit at week 6 or 9 who did not start new treatments for depression. Sustained non-responders are defined as participants who did not respond (<25% change in MADRS total score from baseline) at weeks 3 and 12, and at least one visit at week 6 or 9.

Indications of important improvements in quality of life



25mg v 1mg – average trends seen in favor of the 25mg group when compared to 1mg group in exploratory measures at week 3 and reductions in impairment and distress

Note: SDS = Sheehan Disability Scale; WSAS = Work and Social Adjustment Scale; PANAS = Positive and Negative Affect Scale; QIDS-SR-16 = Quick Inventory of Depressive Symptomatology – Self-Rated; GAD-7 = Generalised Anxiety Disorder 7-item; CI = confidence interval

Safety

- **COMP360 was generally well tolerated, with more than 90% of treatment-emergent adverse events (TEAEs) being mild or moderate in severity**
- Further analysis showed that there were no concerns with vital signs, ECG or clinical laboratory data in any of the treatment groups
- The majority of treatment-emergent adverse events (TEAEs) occurring on the day of COMP360 administration resolved on the same day or the day after (77.4%); most were mild or moderate in nature, eg headache, nausea, fatigue
- All TEAEs involving hallucination (which only occurred in the 25mg and 10mg groups) and illusion (which occurred in all groups) started on the day of administration and resolved on the same day. No events of this nature continued past the administration day
- TEAEs of suicidal ideation, suicidal behaviour and intentional self-injury were seen in all groups, as is regularly observed in a TRD population
- Two thirds of the patients had previous thoughts of wishing to be dead, as assessed by a suicidality scale completed during patient screening; this included all patients reporting one of these adverse events, so all patients who experienced these events during the trial had said in patient screening that they had had suicidal thoughts prior to the trial
- Case-by-case analysis of safety data found no evidence to suggest, at this time, a causal relationship between these reported adverse events and administration of COMP360. The events occurred in all treatment groups and at a range of onset times and durations; the majority occurred more than a week after the psilocybin session

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)

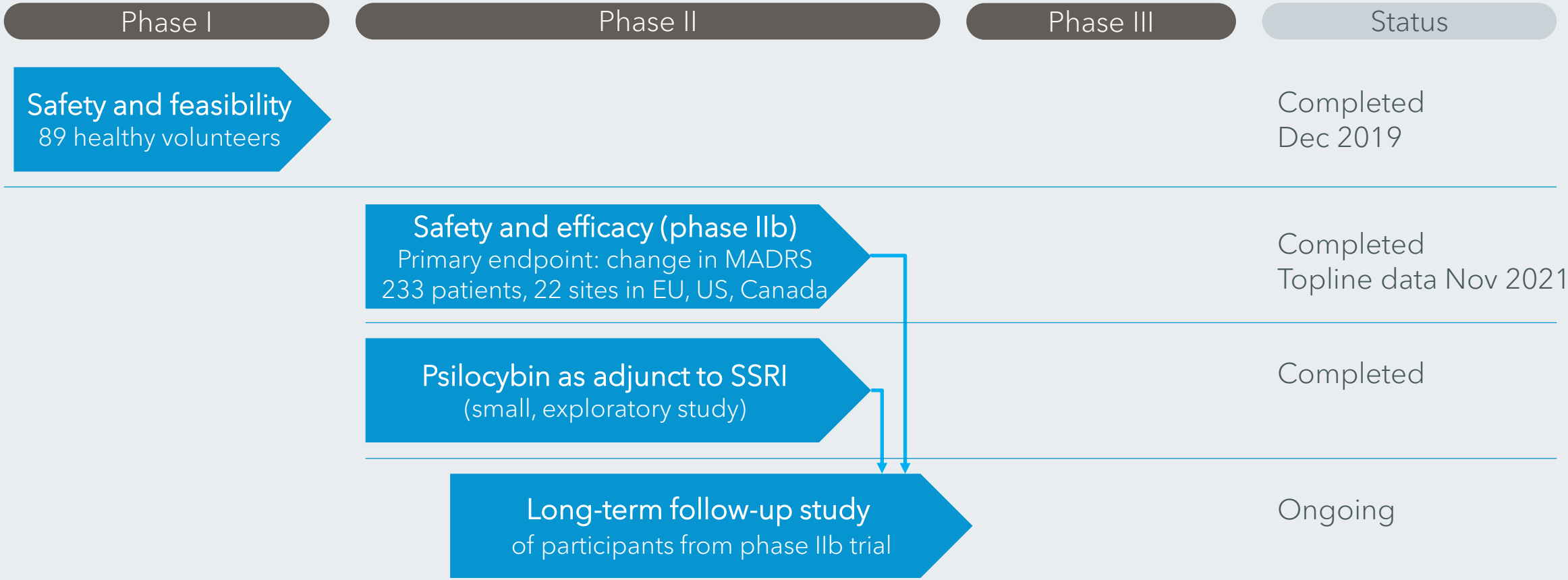
TEAE incidence is higher in the 25mg group overall

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

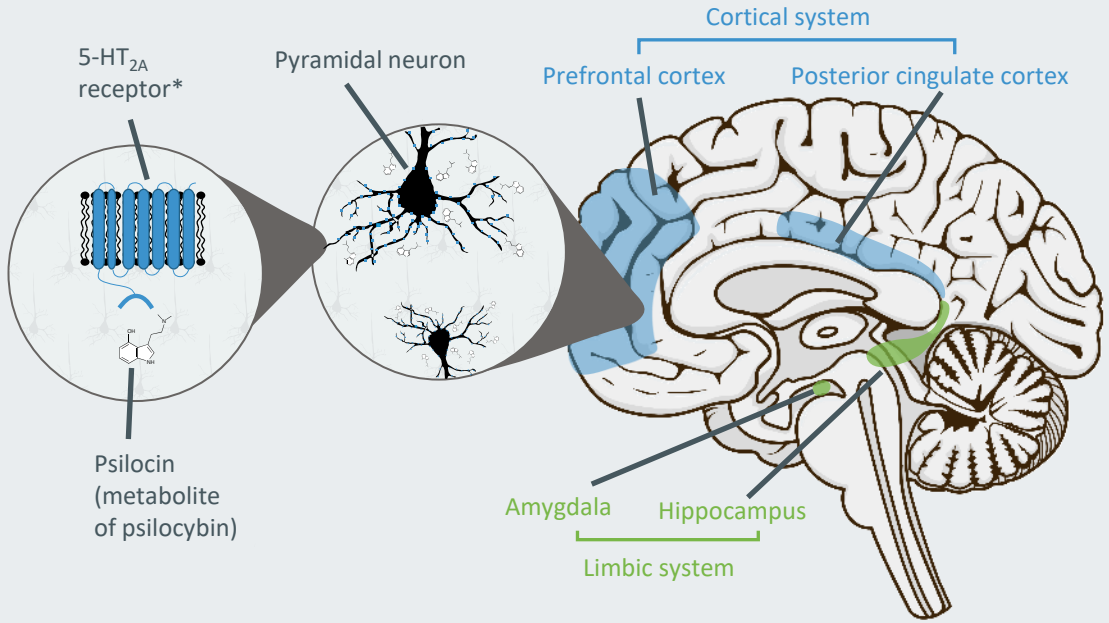
Our clinical development programme for COMP360 psilocybin therapy in TRD

Getting ready for phase III



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

Psilocybin 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: understood mechanism of action based on studies of psilocybin (not COMP360); *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 (not using COMP360)

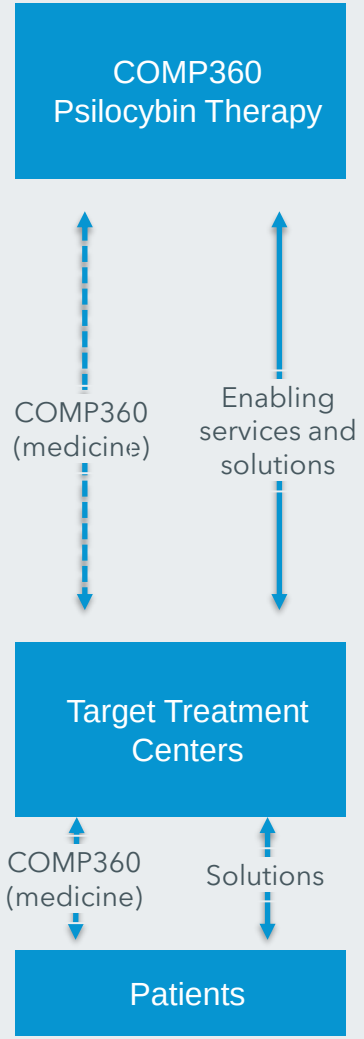
Source: Petri, 2014 - Homological scaffolds of brain functional networks

COMPASS's offering will be a combination of COMP360 (medicine) and enabling services and solutions

- The path to broad and safe patient access to COMP360 psilocybin includes **approval** by the FDA, **rescheduling** by the DEA and individual states; **reimbursement** by commercial and public payers (Medicare / Medicaid); **prescribing and monitoring** by psychiatrists; and **delivery** of supportive therapy before, during and after dosing by licensed and trained therapist.

Prototype design Centre of Excellence treatment room

- Comprehensive reimbursement and coding strategy underway
- Upon approval, COMPASS plans for coverage and formulary inclusion of COMP360 (medicine) with payers
- COMPASS will certify treatment centers and sell COMP360 (medicine) to providers via specialty pharmacies; and offer enabling services and solutions for its safe and effective administration



Targeting multiple channels for COMP360 psilocybin therapy delivery

US target sites of care	#
COMP360 treatment centres at Launch Year 1 to Year 3	200 - 1,000
Academic centres	>400 (~20-30 dosing sites and in phase III; ~70 referring)
Esketamine/SPRAVATO® certified centres	>2,000 – at least 800 actively delivering
Ketamine clinics	>500
TMS centers	>1000
IOPs (intensive outreach) PHPs (partial hospitalisation)	>6,000 IOPs >700 PHPs
CCBHC (certified community behavioral health centers)	>400
Residential treatment facilities	>900
Multidisciplinary/multiservice group psychiatry practices	N/A

Ketamine treatment centre network

COMP360 target centers

- Ketamine clinics are an established channel and preparing to delivery psychedelic therapy
- >2,000 SPRAVATO® certified centers – 800 delivering already
- VC/PE backed channel expansion and consolidation (eg MindPath Care Centers, Lifestance Health, Mindful Health Solutions)

COMP360 target HCPs

- >8,000 SPRAVATO® psychiatrists
- ~50,000 HCPs who can prescribe COM360 (29,000 psychiatrists + 18,000 PMHNPs, physician assistants)
- ~500,000 HCPs who can deliver COMP360 psilocybin therapy (all above + 100,000-150,000 psychologists, >300,000 master-level accredited therapists/counsellors)

Note: TMS = Transcranial Magnetic Stimulation

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

COMP360 commercial exclusivity strategy

Regulatory

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

+ Intellectual Property Coverage

Five 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 (Mar 2021): includes claims to oral dosage forms of psilocybin and methods of treating major depressive disorder (MDD) with those forms
- 3rd US patent (Mar 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 (Oct 2021), composition claims to an alternative crystalline psilocybin
- 5th US patent (Nov 2021): covers methods of treating treatment-resistant depression (TRD) with crystalline psilocybin as well as with oral dosage forms of crystalline psilocybin with an excipient

European and 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

COMPASS's broad expertise

George Goldsmith
Chairman, CEO and Co-founder

Ekaterina Malievskaia, MD
Chief Innovation Officer, Co-founder

Mike Falvey
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

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

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

2022 anticipated milestones

- ✓ Hold end-of-phase II meeting with FDA and other regulators
- ✓ Commence phase III clinical program in TRD
- ✓ Launch additional COMP360 clinical development programs
- ✓ Data published from IISs using COMP360
- ✓ Expand current IP portfolio with additional patent grants
- ✓ Further strategic partnerships and collaborations
- ✓ Expand Centres of Excellence
- ✓ Develop pipeline of future compounds through our Discovery Center and other partnerships
- ✓ Continue to evolve data and technology strategy
- ✓ Develop scalable therapist training platform
- ✓ Advance COMP360 payor partnerships in anticipation of commercial launch

Note: TRD = treatment-resistant depression

“I feel like I’m living again.

I feel this is one of the greatest gifts that I have been given.”

Quote from a patient in the COMPASS Pathways phase IIb clinical trial of COMP360 psilocybin therapy for treatment-resistant depression. The patient was one of 29 in the 25mg group (n=79) of the trial who had a response to treatment at week 3. The image is representative and not of a patient

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COMPASS
Navigating Mental Health Pathways