# Transforming mental health care

COMPASS Pathways plc
1 December 2020

COMPASSION
Navigating Mental Health Pathways

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# 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

## Sue Stansfield, PhD
Senior Vice President of 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
Director of Preclinical Research

## Steven Levine, MD
Vice President of Patient Access

## Sarah Bateup
Head of Therapy Research and Training

## Dr Stephen Wright
Senior Scientific Advisor

## Emilio Arbe, MD
Interim Clinical Sciences Director


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

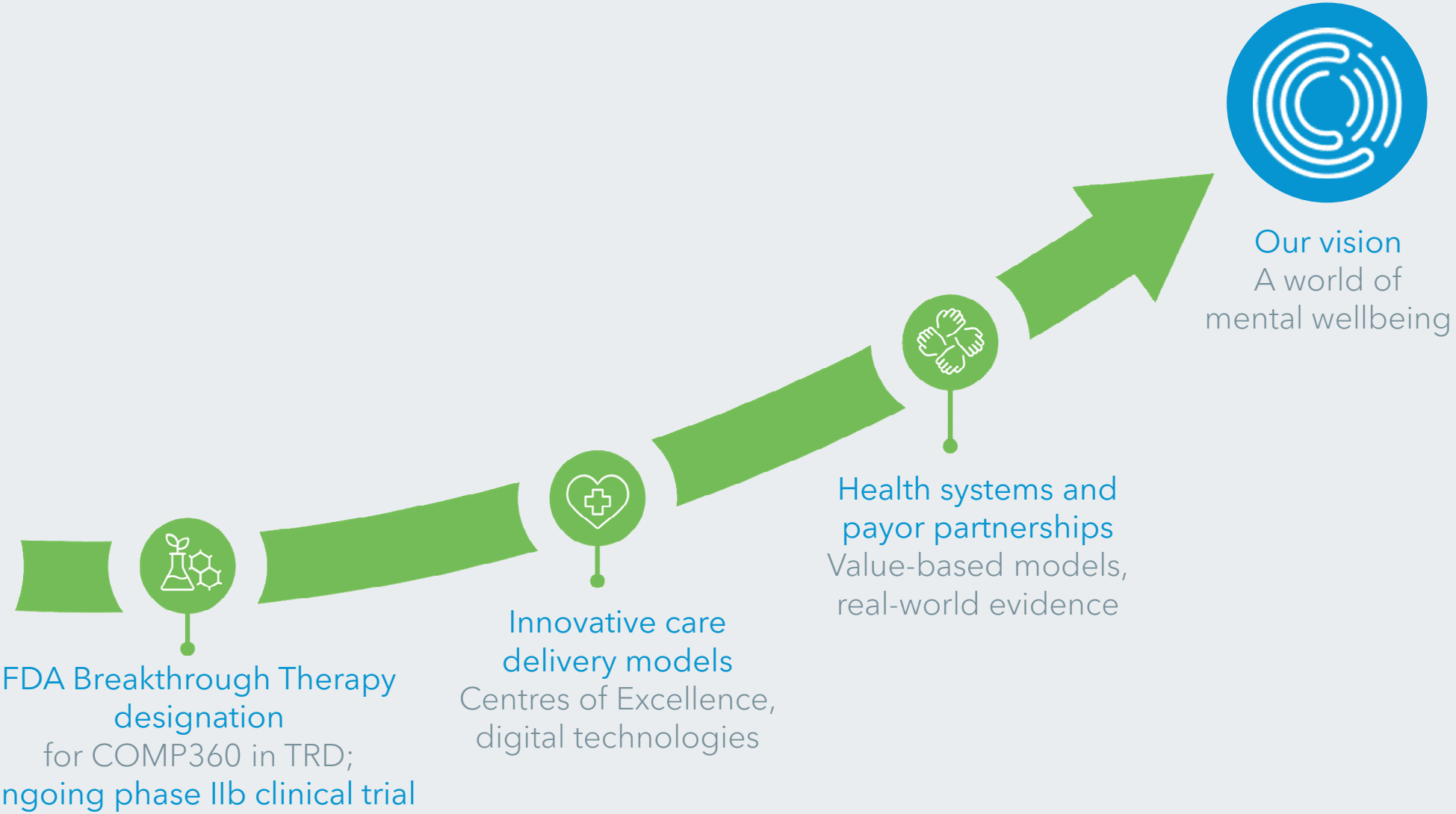
- COMP360 designated a FDA Breakthrough Therapy for TRD
- Completed phase I healthy volunteers trial, largest psilocybin therapy clinical trial to date
- Phase IIb ongoing, with 216 patients expected to have completed the trial by late 2021
- Planned expansion into additional indications

## Driven by science and rigor

- 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



# 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 (~33% of total)** |
| Available treatments | • Antidepressants<br>• Psychological interventions, eg CBT* | • Antidepressants<br>• Antidepressant combinations<br>• Psychological interventions | • Antidepressants<br>• Augmentation therapy (antidepressants, mood stabilizers, anticonvulsants, atypical antipsychotics, esketamine)<br>• Ketamine<br>• Somatic therapy (rTMS*, tDCS*, ECT*, DBS*)<br>• High-intensity psychological interventions |
| % relapse | **60-70%** | **50-75%** | **80-90%** |

**Note:** *CBT = cognitive behavioral 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

# We need a new treatment model in TRD

## Depression: leading cause of disability worldwide

- MDD estimated to account for 7.5% of years of life lost due to disability globally, as defined by DALYs[1]
- Approx sevenfold increase in suicide rate for TRD patients compared with non-TRD MDD patients

## Depression: burden on health systems[2]

- US annual cost of depression: >$200 billion[3]
- A large proportion can be attributed to direct costs (eg outpatient and inpatient medical services and pharmaceutical services)

## TRD: increased economic and societal costs

- US medical costs for TRD patients are ~2-3x costs for non-TRD MDD patients
- TRD patients have ~2x inpatient visits relative to non-TRD MDD patients
- Average US annual healthcare cost between $17-25k per TRD patient per year

### Need for a new treatment paradigm

- ✓ New mechanisms of action
- ✓ Fewer side effects
- ✓ Rapid-acting and durable response

**Note**: 1. DALY = disability-adjusted life years; 2. Indirect costs are associated with the expenses incurred from the cessation or reduction of work productivity due to morbidity and mortality; 3. Accounting for comorbid physical and psychiatric conditions

**Source**: WHO (2017); Depression Therapeutics by David Thomas and Chad Wessel, Bio Industry Analysis (2019); Johnston KM, Powell LC, Anderson IM, Szabo S, Cline S (2018). The burden of treatment-resistant depression: a systematic review of the economic and quality of life literature. Journal of Affective Disorders

# Our COMP360 psilocybin therapy

## COMP360

- Synthetic, high-purity, polymorphic crystalline formulation of psilocybin
- Oral capsule
- Designated Breakthrough Therapy for TRD (in 2018)

## 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

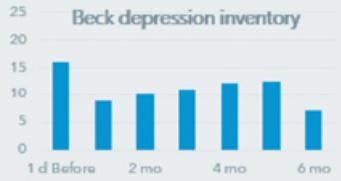
- Preclinical genotoxicity and cardiotoxicity studies completed
- Phase I trial completed: COMP360 generally well-tolerated in healthy participants (n=89)
- Phase IIb trial in TRD: underway in 21 sites in 10 countries (n=216)

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

**2011**

UCLA[1]
Grob et al
*n = 8*[2]

**Existential distress**



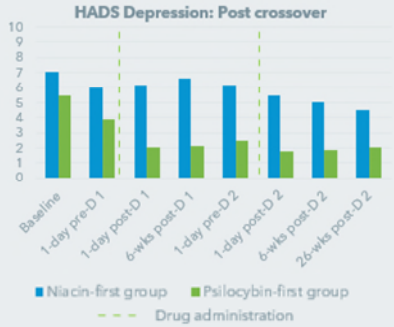

Significant reduction in BDI scores at six months, compared with baseline

Effect size not reported
p-value = 0.03

**2016**

New York University
Ross et al
*n = 23*[2]

**Existential distress**



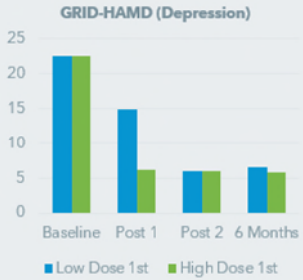

Significant reduction in HADS-D scores at 26 weeks post-dose 2, compared with baseline

Effect size (Cohen's d):
niacin-first group = 0.66
psilocybin-first group =0.81
p-value < 0.05

**2016**

Johns Hopkins
Griffiths et al
*n = 46*[2]

**Existential distress**



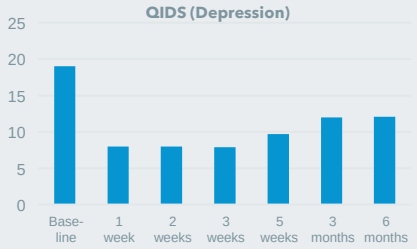

Significant reduction in GRID-HAMD scores at six months across both groups, compared with baseline

Effect size (Cohen's d) = 2.98
p-value < 0.001

**2016, 2018**

Imperial College
Carhart-Harris et al
*n = 19*[3]

**Treatment-resistant depression**



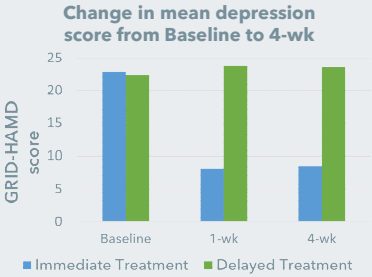

Significant reduction in QIDS score at six months, compared with baseline

Effect size (Cohen's d) = 1.6
p-value = 0.0035

**2020**

Johns Hopkins
Griffiths et al
*n = 24*[4]

**Major depressive disorder**




Significant reduction in GRID-HAMD scores in Immediate Treatment group at one and four weeks, compared with Delayed Treatment group

Effect size (Cohen's d):
1-wk = 2.2
4-wk = 2.6
p-value = <0.001 (1-wk and 4-wk)

**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

# 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

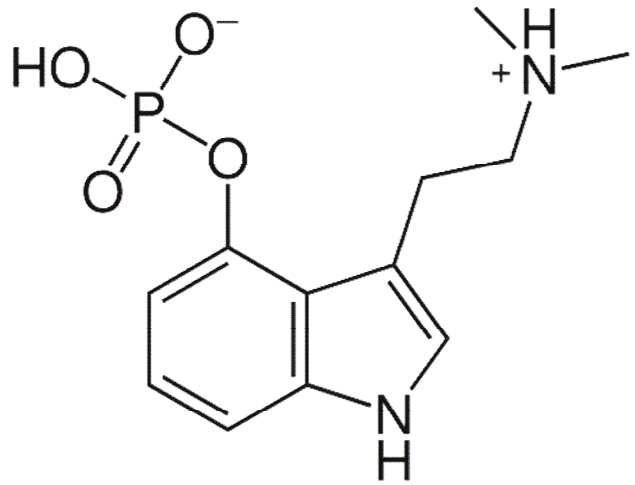
## Potential economic benefits

Reduction in total cost of care

Lower healthcare resource utilisation

Increased productivity, reduced absenteeism

# Psilocybin is a psychoactive substance



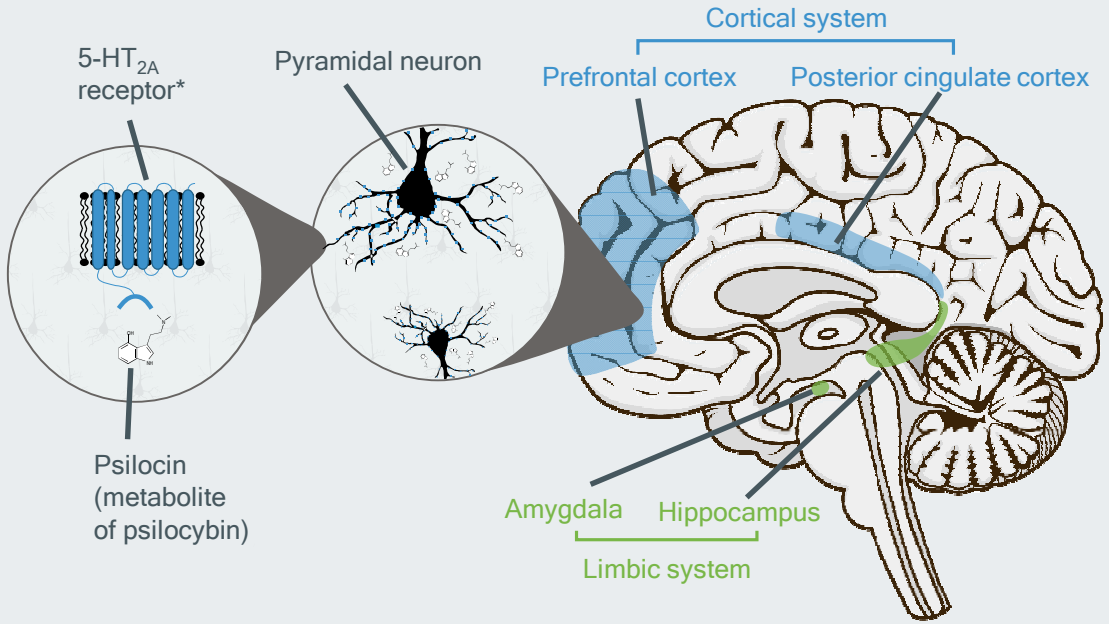

Psilocybin molecule

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-$HT_{2A}$ 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

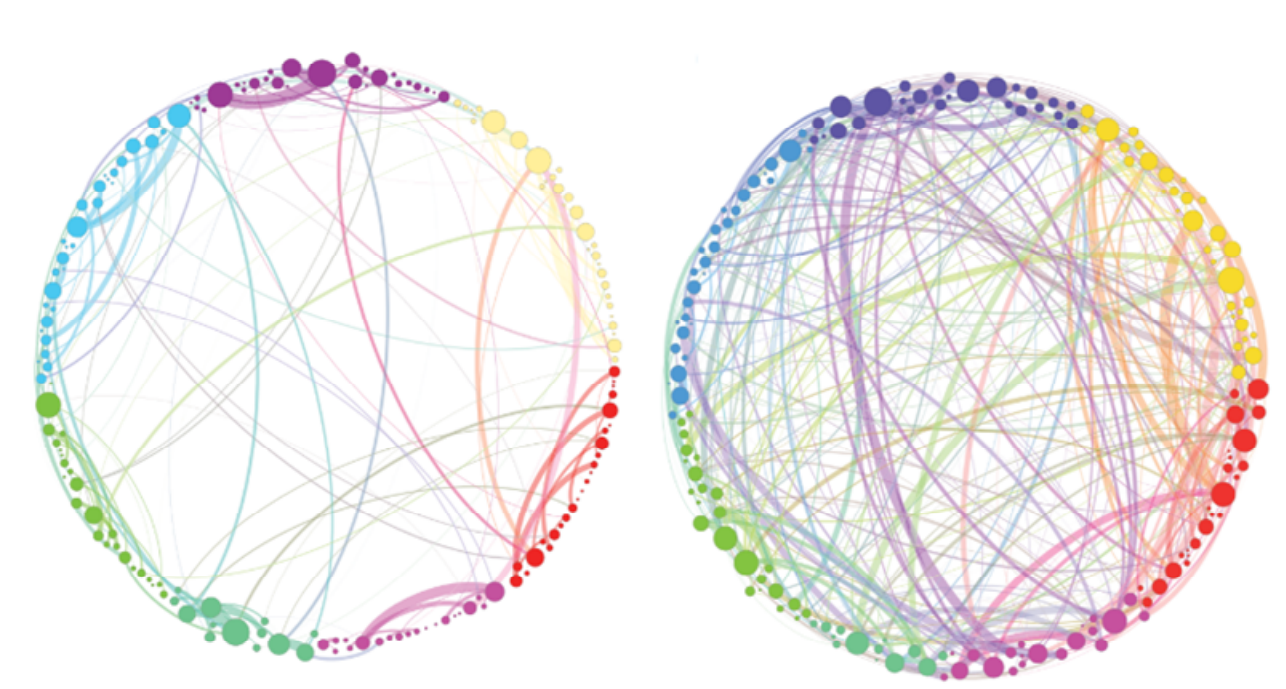
3. Downregulation of the default mode network, or DMN*[5], and de-synchronization of cortical activity as well as the emergence of new patterns of functional connectivity across the brain[6]

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 analyzed 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

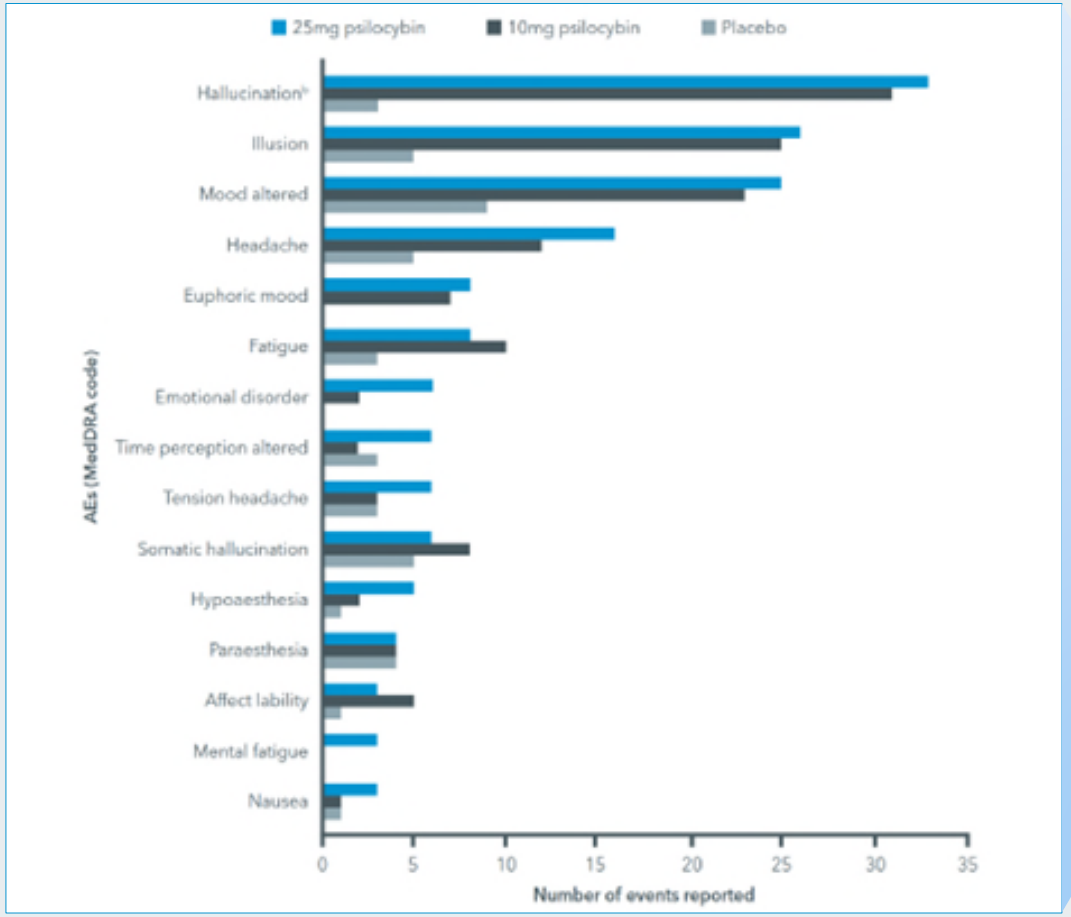
# Phase I safety and feasibility trial – data published in December 2019

- 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

**Note:** Study run in conjunction with Institute of Psychiatry, Psychology & Neuroscience, King's College London
**Source:** 'Eriksson - 2020 - Psilocybin therapy for treatment-resistant depression' and also 'COMPASS Pathways COMP 002 Safety Tables revised 2019-11-05' see table 14.3.1.2

# COMP360 induced psychedelic experiences that correlate with therapeutic effect

**Most frequently reported AEs* (MedDRA Code)[a] in our phase I trial with healthy volunteers**




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

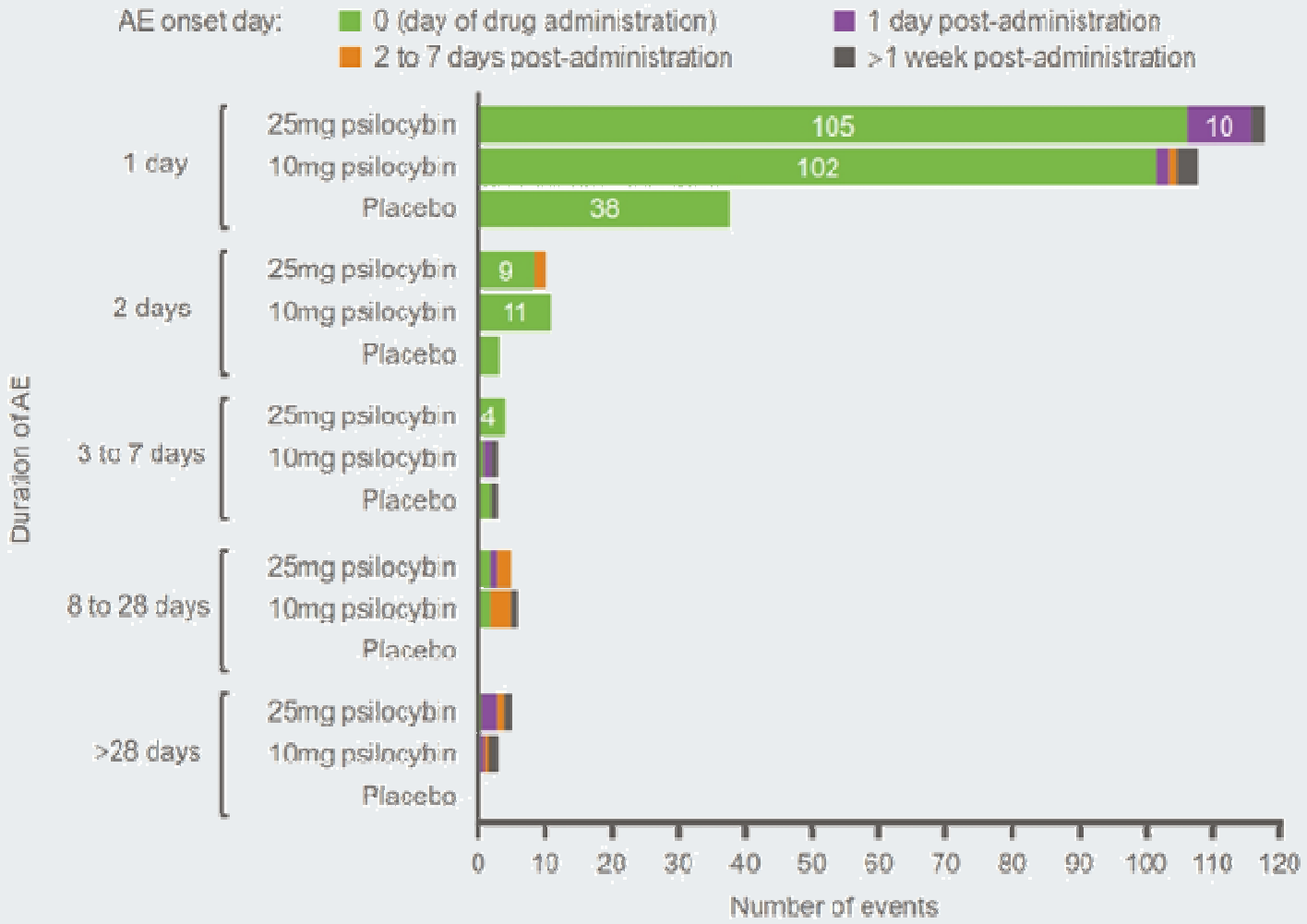
| | 25mg COMP360 (n=30) | 10mg COMP360 (n=30) | Placebo (n=29) |
|---|---|---|---|
| Any "mood altered" AE | 15 (50.0) | 13 (43.3) | 6 (20.7) |
| Introspection | 7 (23.3) | 5 (6.7) | 1 (3.4) |
| Reflections | 3 (10.0) | 2 (6.7) | 2 (6.9) |
| Increased empathy | 2 (6.7) | 3 (10.0) | 0 |
| Sense of oneness | 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) |

a. Ranked by incidence in the 25mg psilocybin group
b. Includes auditory, gustatory, olfactory, tactile and visual hallucinations

**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 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

**Source:** 1.Griffiths et al (2016)

# Technology applications support psilocybin therapy throughout patient journey

Preparation → Administration → Integration → Maintenance

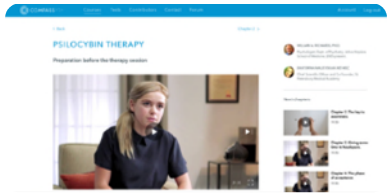
## COMPASS solutions

Patients: preparation platform

Therapists:

- Online learning platform
- Virtual training approved by FDA*

Web application


## Digital partnerships

- Collection of digital phenotyping information; data will be used after the phase IIb trial to develop potential digital applications to help anticipate relapse
- AI* and NLP* (speech recognition) to characterise mechanism of change and assess therapist fidelity to our treatment protocol
- Future plans include expanding our research into additional technologies to augment and complement our therapies

**Note:** *AI = artificial intelligence; FDA = Food & Drug Administration; NLP = natural language processing

# Phase IIb clinical trial: COMP360 psilocybin therapy for TRD

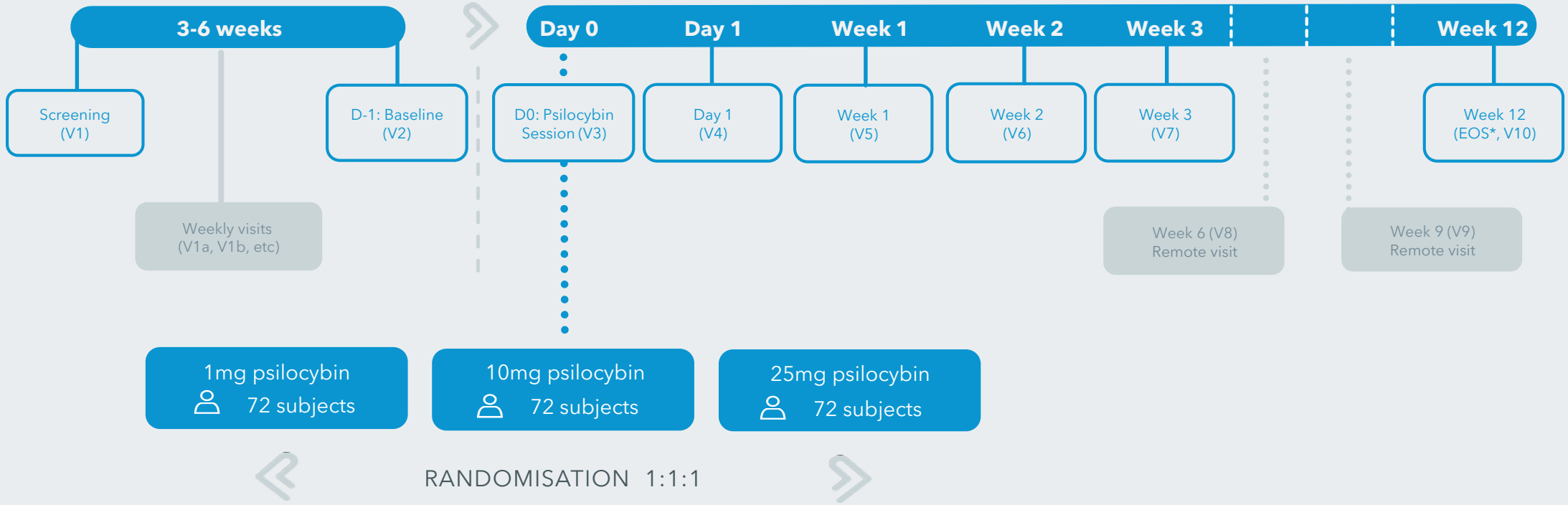
## Target enrolment of 216 patients; data expected late 2021

**Primary endpoint**

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

**Secondary endpoint**

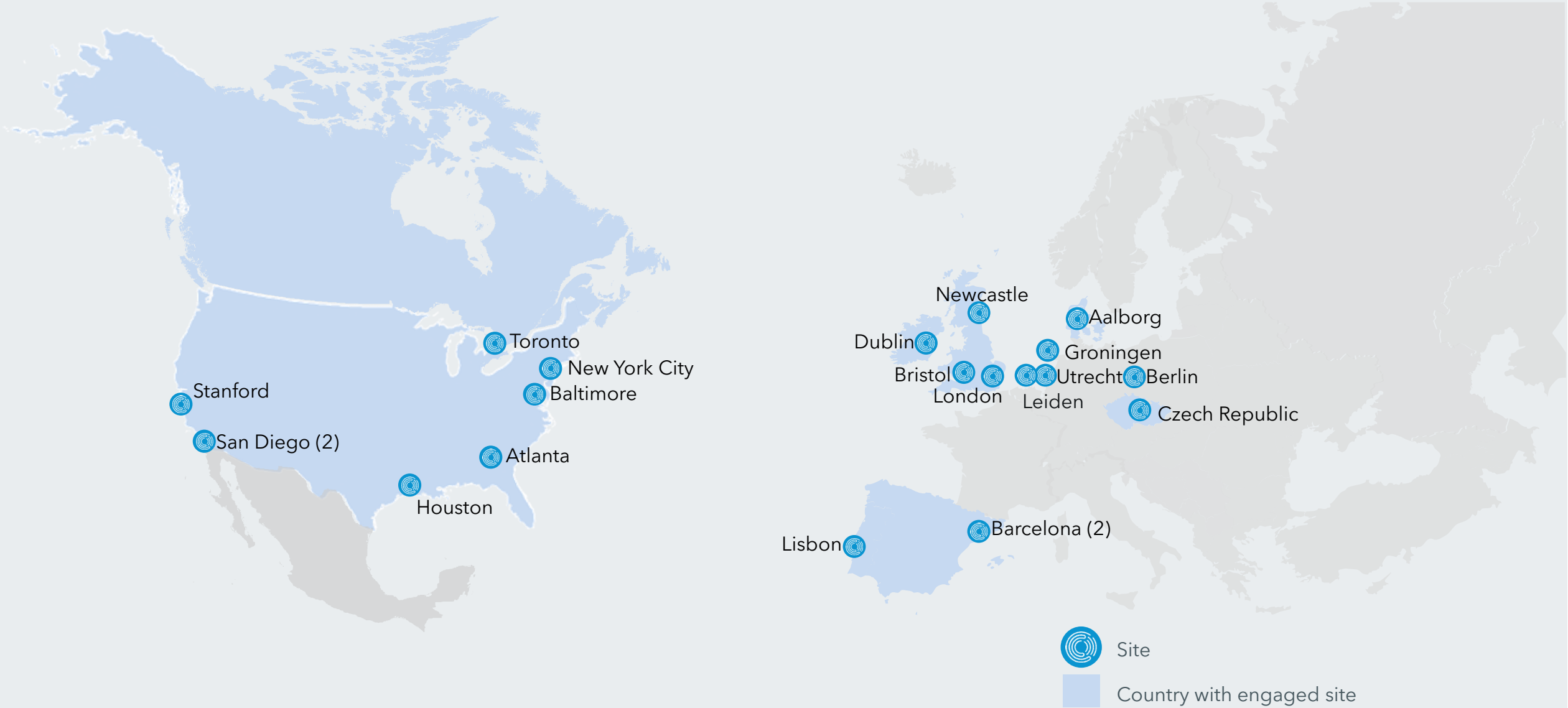
- Proportion of responders who maintained ≥ 50% improvement in MADRS up to week 12




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

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

# Sites engaged for phase IIb TRD study have the reputation and capability to recruit patients



# Our clinical development programme for COMP360 psilocybin therapy in TRD

## Completed clinical trial

**Phase I: safety and feasibility**
*Completed in 2019*
89 participants, King's College London

## Ongoing clinical trials

**Phase IIb: dose-finding study**
*Goal to announce results late 2021*
216 patients, 21 sites in EU, US and Canada
Primary endpoint: change in MADRS

**Phase II: adjunct to SSRI**
*Goal to complete prior to initiating phase III*
Confirm COMP360 is best administered as monotherapy

**Long-term follow-up study**
Of participants from phase II trials

# Further opportunities with COMP360

## Mechanistic, preclinical and investigator-initiated studies

### Mechanistic studies

- Changes in gene expression and epigenetic regulation
- Effects on affective biases
- Psychological and brain effects in healthy volunteers

Imperial College London · University of Bristol · université de Bordeaux

### Preclinical studies in other indications

- Anxiety
- Eating disorders
- Neurocognitive disorders
- Autism
- Epilepsy
- Pain
- Sleep-wake disorders

Imperial College London · University of Bristol · UMC Utrecht · Various CROs*

### Investigator-initiated studies in other indications

- Anorexia
- Bipolar type II disorder
- Body dysmorphic disorder
- Chronic cluster headache
- Depression in cancer
- MDD*
- Severe TRD*

Sheppard Pratt · Columbia University Medical Center · UCLA · University of Zurich[UZH] · King's College London · UCSD · Maryland Oncology Hematology · Imperial College London · University of Copenhagen

**Note:** *CRO = contract research organization; MDD = major depressive disorder; TRD = treatment-resistant depression

We do not sponsor investigator-initiated studies; we encourage the open publication of all associated findings

# COMPASS Drug Discovery Center

## Focus on developing novel psychedelic compounds with optimized properties

- Compounds targeting 5-$HT_{2A}$ receptor

## Sponsored research agreement between COMPASS and University of the Sciences (USciences) in Philadelphia, Pennsylvania

- COMPASS joint owner (with USciences) and exclusive licensee for all new compounds generated

# IP and regulatory strategy

## Combine patent with 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

## Implement patent strategy

### First US patent granted in December 2019

- Claims directed to methods of treating drug-resistant depression with high-purity polymorphic crystalline psilocybin
- Petition for Post Grant Review was dismissed on merits in August 2020

### European patents granted/registered

- German utility model (March 2020): covering forms of crystalline psilocybin, its use in medicine and methods of synthesis
- First UK patent (May 2020): includes two independent method of manufacture claims, and product-by-process and formulation claims
- Second UK patent (July 2020): includes claims covering crystalline psilocybin, pharmaceutical formulations, medical uses, and a method of manufacturing

### Multiple related applications pending

- To expand claim scope
- To extend coverage in over 20 additional countries/regions

### Three PCT applications and Taiwanese application pending

- Additional formulations, administration, therapeutic and digital supports, combination treatments, methods of treating variety additional indications
- Additional indications include: anxiety disorders, headache disorders, eating disorders, neurocognitive disorders, autism, epilepsy, inflammation, ADHD*, substance use disorders, inflammatory bowel disease, stroke, ALS*, multiple sclerosis, anti-social personality disorder, pain, sleep-wake disorders, and bipolar type II depression

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

# Achieving broad patient access

## Comprehensive and payer-relevant evidence generation plan

- Early dialogues on clinical development plan, pricing and reimbursement
- Real world evidence
- Payer-focused trials

## Differentiated and modular commercial offering

- Therapist training
- Treatment center support services
- Digital solutions

## Strategic partnerships with payers, health systems and clinic networks

- Centres of Excellence
- Potential franchise model

Prototype design Centre of Excellence treatment room

Prototype design Centre of Excellence post-treatment space

**Note:** Centre of Excellence prototype designs by Gensler (architecture, design, planning and consulting firm)

# Financial overview

Cash and cash equivalents at 30 September 2020:

- $196.5 million

IPO raise:

- $146.6 million[1]

Issued shares:

- 35,930,331

Covering analysts:

- Ritu Baral, Cowen
- Josh Schimmer, Evercore
- Esther Hong, Berenberg
- Sumant Kulkarni, Canaccord Genuity
- Patrick Trucchio, HC Wainwright & Co

**Note:**
1. IPO effective 18 September 2020; Greenshoe fully exercised

# A strong and growing team

# Backed by high calibre boards

## Board of directors

- George Goldsmith
- Ekaterina Malievskaia, MD
- Florian Brand
- Jason Camm
- Annalisa Jenkins, MBBS
- Thomas Lönngren
- Linda McGoldrick
- Robert McQuade, PhD
- David Norton

## Scientific advisory board

- Prof David Nutt, MD, PhD
- Gül Dölen, MD, PhD
- Thomas Insel, MD
- Prof Diego Pizzagalli, PhD
- Prof Augustus John Rush, MD
- Prof Alan Schatzberg, MD
- Paul Summergrad, MD
- Kirk Rutter (Patient Advisor)

**Note:** Companies listed reflect prior and present relevant experience

# Pioneering the development of a new model of psilocybin therapy

## Achievements

- ✓ Breakthrough Therapy designation for COMP360 in TRD
- ✓ Phase I healthy volunteers trial completed; largest randomised, controlled psilocybin therapy trial
- ✓ Phase IIb clinical trial making steady progress
- ✓ Patent awards in US, UK, Germany; further patent applications filed; petition for Post Grant Review dismissed on merits
- ✓ Experienced leadership team, board of directors, scientific advisory board; leadership team and board strengthened with recent hires
- ✓ $80m raised in Series B round
- ✓ Preclinical studies in new indications; Discovery Center launched
- ✓ Additional trials underway in TRD programme
- ✓ 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
- ✓ $146.6m raised in IPO

## Anticipated milestones

- → First Centre of Excellence
- → Further senior appointments
- → Further partnerships and collaborations
- → Further patent grants
- → Data published from IISs using COMP360
- → Phase IIb trial: data expected late 2021

*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