JANUARY 2023

# Small Pharma

Everyone deserves the option of better mental health

TSXV: DMT

OTCQB: DMTTF

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# Leadership team

**George Tziras**
Chief Executive Officer, Director

**Peter Rands**
Chief Innovation & Intellectual Property Officer, Director

**Marie Layzell**
Chief Manufacturing and Development Officer, Director

**Carol Routledge**
Chief Medical & Scientific Officer

**David Steel**
Chief Financial Officer

**Alastair Riddell**
Chief Operating Officer

**Lyne Fortin**
Chair, Independent Director

**Michael Wolfe**
Independent Director

**Paul Maier**
Independent Director

# Introducing Small Pharma [a,b,c]

## Everyone deserves the option of better mental health

1

**Depression represents a huge unmet need**
280m people suffer globally (2019)[1]. Only one-third of patients respond to first line treatments [2], and many struggle with numerous side effects leading to poor treatment adherence[3].

2

**Treatments that target fast-acting, long-lasting symptom relief**
Our primary focus is on the development of novel and protectable psychedelic-based mental health treatments, with the goal of being reimbursed medicines, maximizing patient access.

3

**Short-duration psychedelic effect offers potential for scalable in-clinic treatments**
Our target treatment session is <2.5 hours. This offers enhanced clinical convenience, relative to full-day (up to 12 hours) psychedelic treatments that are in development, such as psilocybin and LSD[4,5].

4

**Data suggests efficacy profile of lead DMT candidate, SPL026, with supportive therapy**
Recent Phase IIa results Q1'23 support its rapid-acting and long-lasting antidepressant effects. SPL026 clinical program awarded MHRA's fast-track ILAP innovation passport, aimed at expediting treatment to UK patients.

5

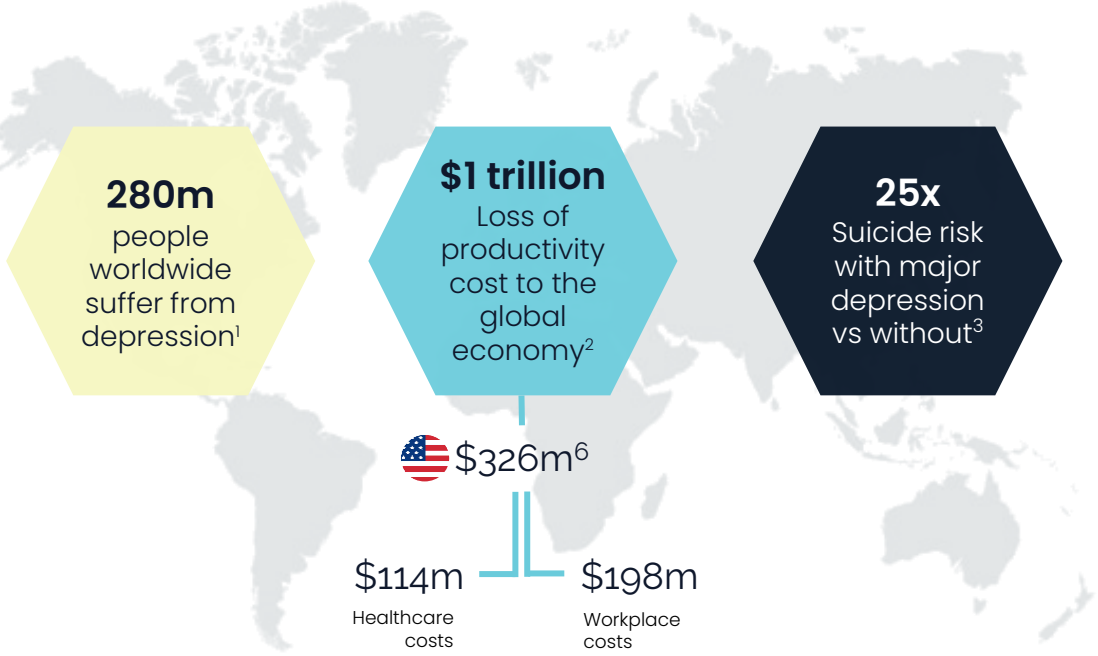
**Advancing a pipeline of short-duration candidates with a robust IP strategy**
Three active development programs; 14 granted patents; 90+ applications pending[6]. Potential for multi-layered exclusivity for SPL026 and SPL028, novel deuterated DMT, afforded by regulatory data exclusivity and patent protection.

(a-c,, 1-5) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims
(6) Based on IP portfolio as disclosed in latest MD&A

# Our focus on depression

## A major contributor to the global burden of disease with critical unmet need

### Global impact of depression




### Human impact of depression

**Major Depressive Disorder ("MDD") -** a mental health disorder characterized by at least two weeks of pervasive low mood, low self-esteem, and loss of interest or pleasure in normally enjoyable activities. [1]

**~60%** Estimated time in the next decade a patient spends in depression[4]

**1 in 8** Who recover from an episode of major depression remain depression-free[5]

(1-6) See Appendix

# Strong opportunity to improve the standard of care for MDD [a,b,c]

## Beyond first line, available treatments offer diminishing benefits for patients, the health system and economy

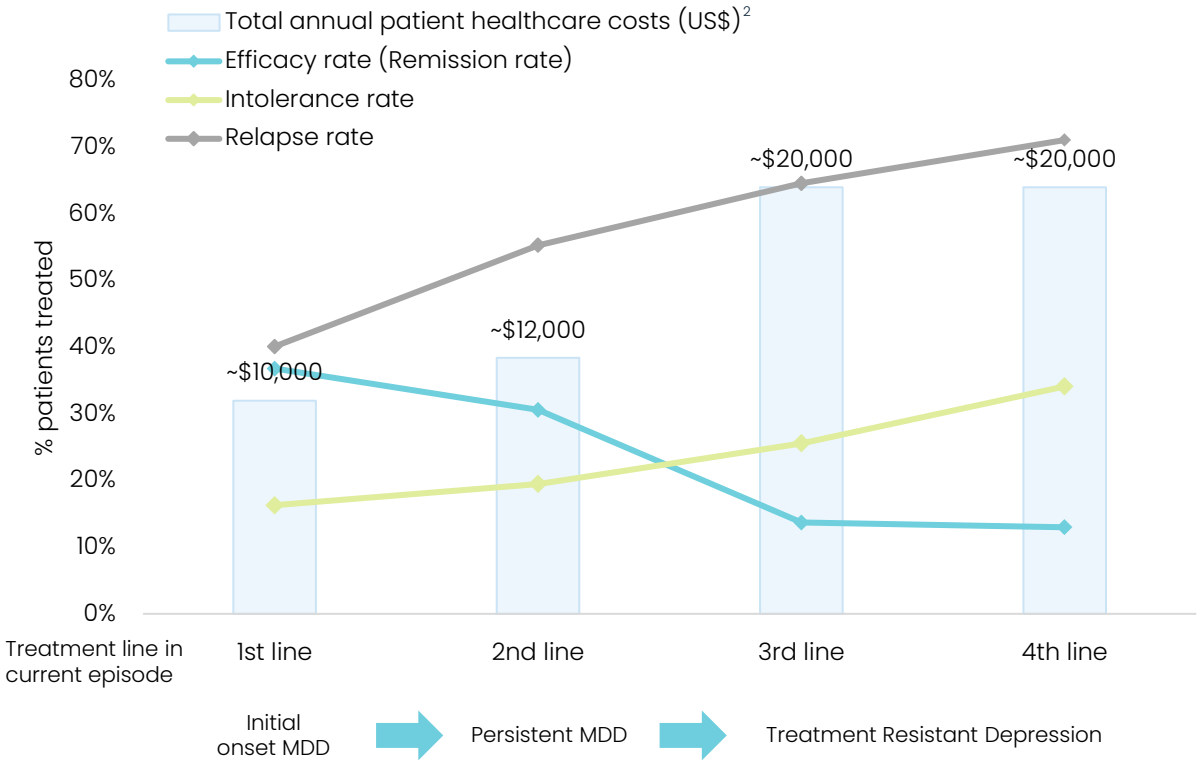



*Diagram represents anticipated patient outcomes as patients cycle through the current depression treatment guidelines (based on STARD trial)[1]*

### Treatment outcomes

Lower probability of treatment success as patients progress through existing treatment guidelines:

- Relapse rates
- Treatment intolerance
- Efficacy benefits

### Societal impact

Negative outcomes if inadequate early and sustained treatment of major depression

- Healthcare costs
- Unemployment rates
- Loss of productivity

(a-c,1,2) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"

Definitions as defined by STARD trial
Efficacy rate (Remission): (QIDS-SR), was administered at each clinic visit, and remission was measured as a score of ≤5
Intolerance: Patients who failed to complete at least 4 weeks of treatment
Relapse: QIDS-SR 16 score ≥11 (corresponding to an HRSD 17 ≥14)

# SPL026 with supportive therapy

## A scalable in-clinic treatment with differentiated clinical & commercial benefits [a,b,c]

### Anticipated treatment profile

| | |
|---|---|
| Chemical compound | N,N, dimethyltryptamine (DMT) |
| Treatment regimen | Fixed dose injectable psychoactive drug administered with supportive therapy |
| Treatment setting | In-clinic supervised by licensed practitioner |
| Dosing frequency | Few doses a year[2] |

### Target value proposition

| | |
|---|---|
| EFFICACY PROFILE | Rapid and sustained improvements[1,2] |
| TOLERABILITY | Well tolerated[3]<br>Minimal transient side effects[4] |
| SAFETY PROFILE | Favorable safety profile[5] |
| PATIENT ADHERENCE | Low treatment burden[6] |
| CONVENIENCE | Short in-clinic treatment vs. other potential full day psychedelic-based treatments lasting 6 hours+ (psilocybin and LSD)[7,8] |

**Anticipated treatment journey**


(a-c, 7,8) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
(1) Based on rapid onset antidepressant effects demonstrated in the Small Pharma's IV SPL026 Phase IIa study in MDD
(2) Based on durable antidepressant effects demonstrated to 12 weeks in Small Pharma's IV SPL026 Phase IIa study in MDD
(3) Based on Phase I/IIa SPL026 study, SPL026 demonstrated a favorable tolerability profile
(4) Based on reported AEs determined as mild to moderate in severity with majority transient in nature in Small Pharma's IV SPL026 Phase IIa study
(5) No drug related SAEs reported in Small Pharma's Phase I/IIa trial. Only 1 SAE has been reported of asymptomatic bradycardia and hypotension in an academic study administering DMT that resolved on day of dosing (See Appendix for referenced study)
(6) Relative to other long-acting psychedelic therapies, anticipated treatment session of up to 2.5 hrs is anticipated to be low burden on patient

# Positive Phase IIa results [a,c] (announced Jan 2023)

## SPL026, DMT, data suggests potential *robust* efficacy profile of a short-duration psychedelic with supportive therapy in MDD

**PHASE IIA MET PRIMARY ENDPOINT**

- Primary endpoint met with a statistically significant -7.4 point difference between SPL026 (21.5mg) and placebo at two-weeks post-dose, as measured by MADRS change from baseline (p=0.02)

**RAPID & DURABLE ANTIDEPRESSANT EFFECT**

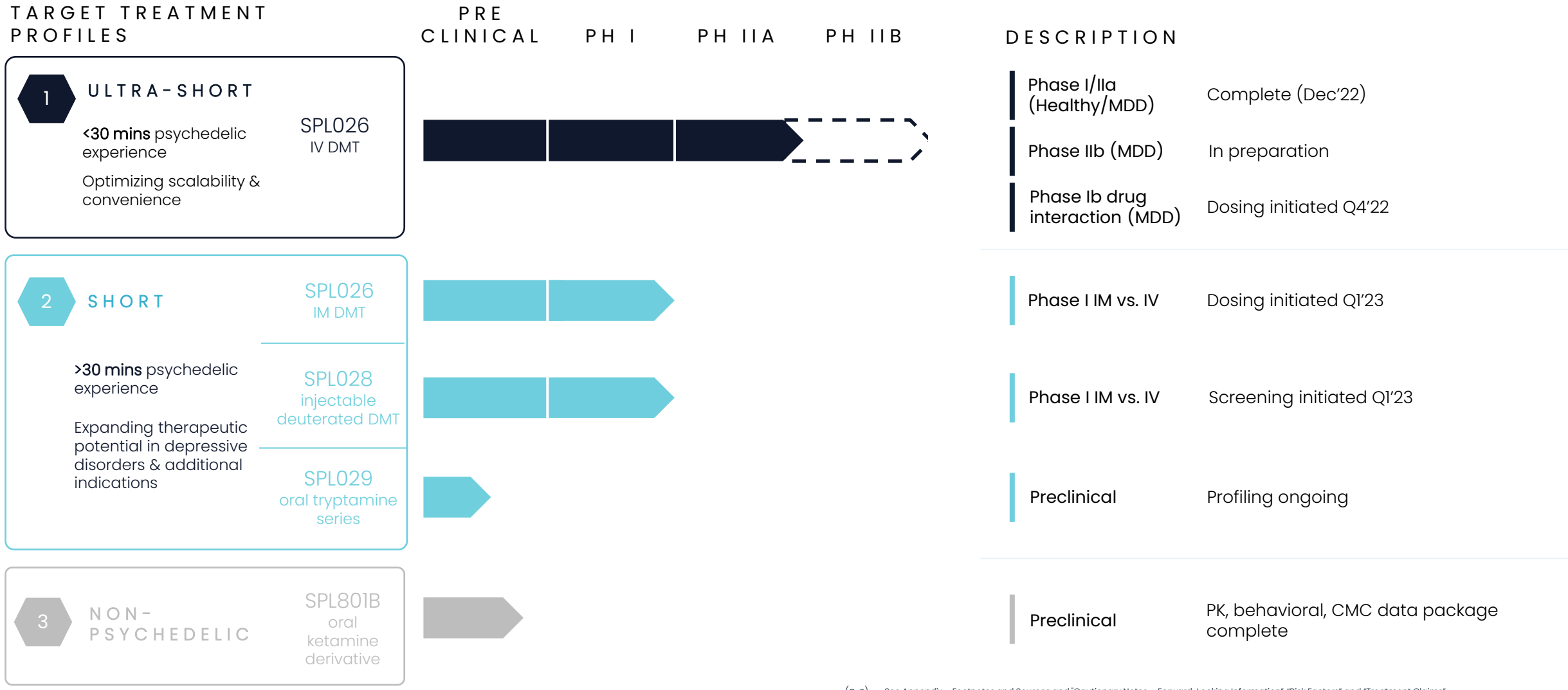
- Rapid onset antidepressant effects demonstrated at one-week post-dose with a statistically significant difference in MADRS of -10.8 versus placebo (p=0.002)
- Durable antidepressant effect with a 57% remission rate at 12-weeks following a single SPL026 dose[1] with supportive therapy
- No apparent differences identified in antidepressant effect between a one and two dose regimen of SPL026

**FAVORABLE SAFETY PROFILE**

- SPL026 demonstrated a favorable safety profile and was well-tolerated
- No drug-related Serious Adverse Events
- 47 Adverse Events deemed possibly related to treatment, all reported to be mild or moderate, and majority resolved during dosing visit

**Note:** p = p-value; MADRS = Montgomery-Asberg Depression Rating Scale
(1) Refers to 12 weeks following the open label dose

# A pipeline of short-duration psychedelics with supportive therapies in development [a,b,c]



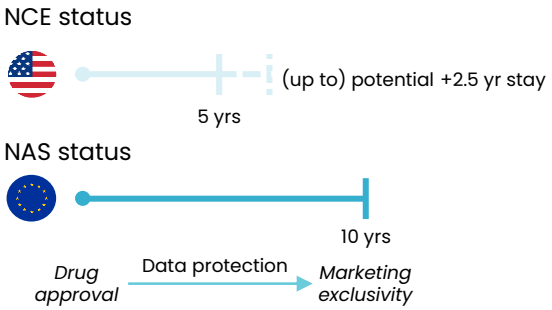

(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
(1) IV: intravenous; PK: pharmacokinetics; IM: intramuscular

# Regulatory and IP protection surrounding our pipeline portfolio [a,b,c]

## Protection

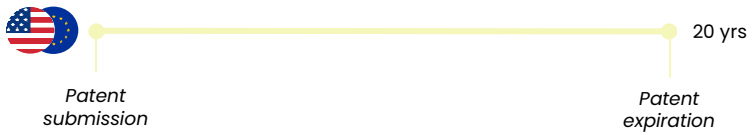
### Regulatory data exclusivity

Exclusive marketing rights granted on regulatory approval of a drug that provides protection from generic drug approval




### Patent protection

Period of time an invention is commercially protected




## IP

**14** granted | **90+** applications | **4** core areas

### Psychedelic portfolio

**1** GRANTED PATENT [1,2]

**Synthetic GMP route**

SPL026 | SPL028

Novel and efficient route producing high purity and low cost drug substance at scale[a,1,2,3,4]

**5** GRANTED PATENTS [6-12]

**Composition of Matter**

SPL028 | SPL029

Novel chemically engineered tryptamine analogues using deuteration technology

**1** GRANTED PATENT [5]

**Drug Product Candidate**

SPL026 | SPL028

Novel optimized injectable formulation across range of psychedelic compounds[2,3]

**2** GRANTED PATENT [13,14]

**First Medical Use**

SPL028

Covers therapeutic compositions of specified deuterated compounds and medical use

Abbreviations: NCE = New Chemical Entity; NAS = New Active Substance

(a,b,l) See Appendix – Footnotes and Sources and "Cautionary Notes – Treatment Claims", "Forward-Looking Information" and "Risk Factors"
(2) Based upon a comparison with the prior art
(3) The starting material in the manufacture of SPL026 is currently inexpensive
(4) To the best of our knowledge, the GMP manufacturing route will scale up sufficiently to support intended use
(5) US patent no. 11 406 619
(6) UK patent no. 2585978
(7) European patent no. 3 826 632
(8) Canadian patent no. 3104072
(9) European patent no. 3 844 147
(10) Australian patent no. 2020381103
(11) Granted patents for SPL029 are subject to advancing forward with SPL029 candidate selection based on current candidates under investigation
(12) European patent no. 3 873 883
(13) US patent no. 11,471,417
(14) European patent no 3902541

# Targeting treatments optimized for scalability

## Accessible & responsibly delivered [a,b,c]

### Clinical setting

1 **Identifying appropriate treatment centers**

- TMS centers[2]
- Spravato approved centers
- ECT centers[2]
- Academic centers

2 **Treatment protocol in development with scalability in mind**

- Potential for physicians to treat multiple patients in a day

### Training and digital tools

1 **Therapist training**

- Condensed structured Small Pharma therapy training program in development
- Potential for digital tools to **scale therapist training and delivery**

2 **Patient tools**

- Opportunity for digital tools to support preparation and integration program
- Potential to **improve patient outcomes and experience**

### Reimbursement[1]

1 **Payer & professional bodies engagement**

- **Refine value proposition** for key stakeholders
- Identify **relevant evidence requirements** to ensure insights incorporated into design of late-stage trials
- Focus to understand the **potential reimbursement framework**

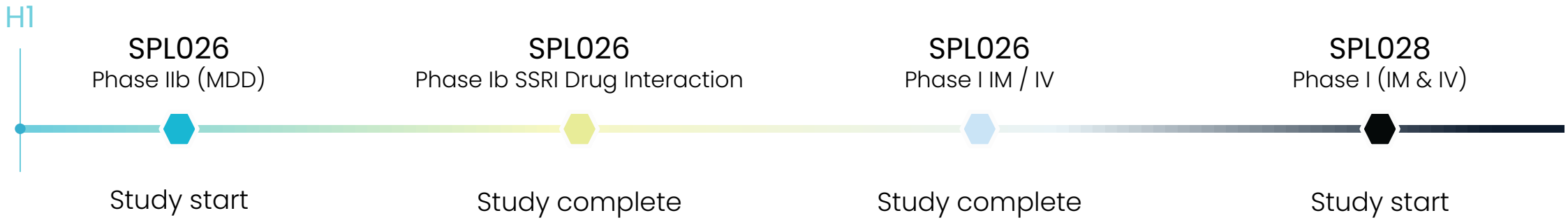
(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
(1) Based on internal conducted US market research. Commercial considerations reflect key priorities highlighted by research conducted with psychiatrists, patients and payers
(2) "TMS" means Transcranial Magnetic Stimulation; "ECT" means Electroconvulsive Therapy

# Multiple meaningful R&D catalysts expected in 2023 [a,b,c]

## Financial overview

| Cash raised | Cash position | Common shares outstanding | Fully diluted shares outstanding |
|---|---|---|---|
| ~C$63m | ~C$22.7m | 321.6m | 348.9m |
| 2021 | Nov 22[1] | Jan 23 | Jan 23 |

## Expected Key milestones in H1 2023[2]




(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
(1) Refers to latest quarterly results
(2) Milestone timelines refer to calendar year

# OUR PROGRESS

# SPL026 Potential first-in-class [a,b,c]

## Profile

- Potential for fast route to market
- Innovation Passport designation awarded in UK

## Programs

**IV**

**Profile:** Ultra-short duration

**Lead indication:**
Major Depressive Disorder

**Clinical trial(s)**
- Phase I/IIa: complete
- Phase IIb: in preparation
- Phase I SSRI DDI: active

**IM**

**Profile**: Short-duration

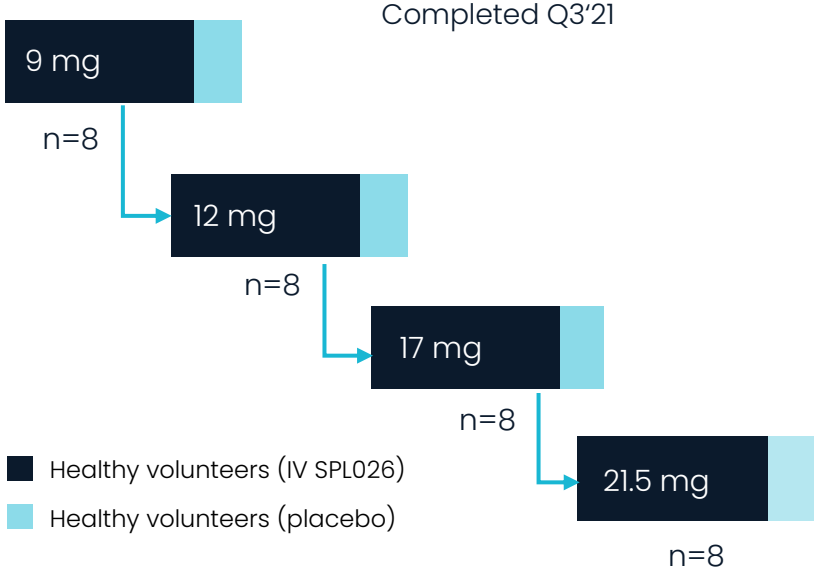
**Clinical trial(s)**: Phase I IM/IV: active

(a,b) See Appendix – Footnotes and Sources and "Cautionary Notes – Treatment Claims", "Forward-Looking Information" and "Risk Factors"

# Phase I /IIa IV SPL026[a,b,c]

## PHASE I Placebo-controlled dose escalating

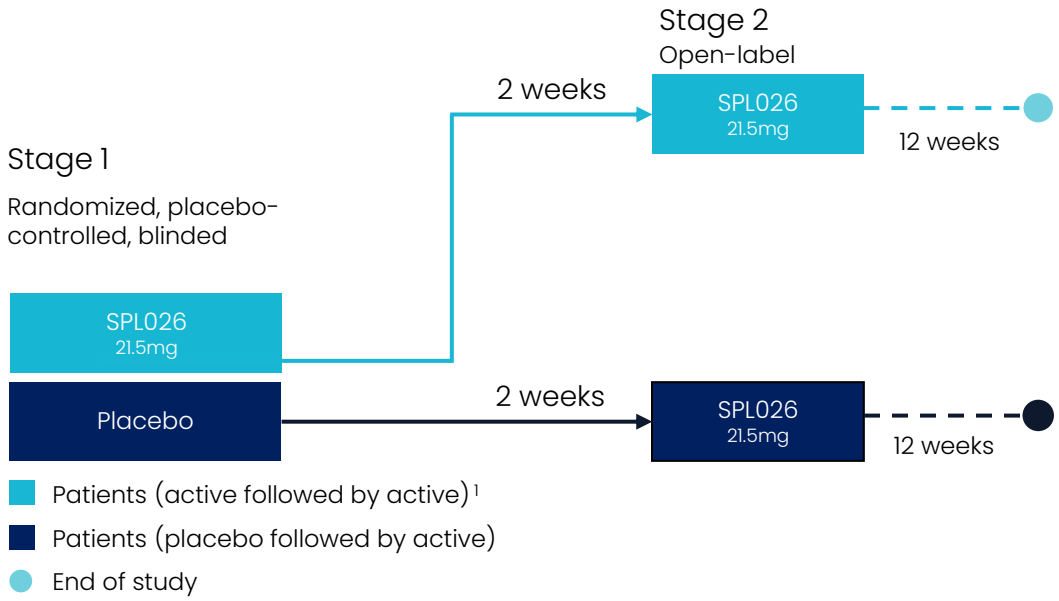
Psychedelic naïve healthy volunteers
N=32
Completed Q3'21




21.5mg selected for Phase IIa

## PHASE IIA

MDD patients (moderate/severe)
Not on antidepressant medication/willing to discontinue
N=34
Completed Q4'22




| | | |
|---|---|---|
| Primary endpoint | Safety and tolerability | MADRS score (change in baseline 2 weeks post first dose) |
| Secondary / exploratory endpoints | ▶ Pharmacokinetics<br>▶ Intensity & quality of subjective psychedelic experience measures<br>▶ EEG | ▶ MADRS change from baseline at W1, M1, M3 and M6[2]<br>▶ Safety and tolerability measures<br>▶ Intensity & quality of subjective psychedelic experience measures<br>▶ Assess 1 vs. 2 doses |

(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
(1) Active refers to 21.5mg dose of IV SPL026
(2) 6 month follow-up out of study

# Phase I IV SPL026

SAFETY & TOLERABILITY

## SPL026 safe at all tested doses [a,b,c,1]

- No drug-related Serious Adverse Events ("SAEs") reported across all doses
- Few drug-related Adverse Events ("AEs") reported in the study
- All AEs were short-lived and resolved on the day of dosing

## SPL026 well-tolerated at all tested doses [a,b,c,1]

- All subjects reported that they did NOT regret the experience
- No statistically significant negative effect on wellbeing and anxiety

| Drug-related AEs | Occurrences |
|---|---|
| Total | n=22 |
| Mild | 100% |
| Pain/burning/sensation at cannula site | 7 |
| Sensation of heart racing | 2 |
| Sleep disturbance | 2 |
| Mild euphoria | 2 |
| Pallor | 2 |
| Headache | 2 |
| Other [2] | 5 |

Figure 1. Summary of drug-related adverse events deemed possibly related to the administration of SPL026

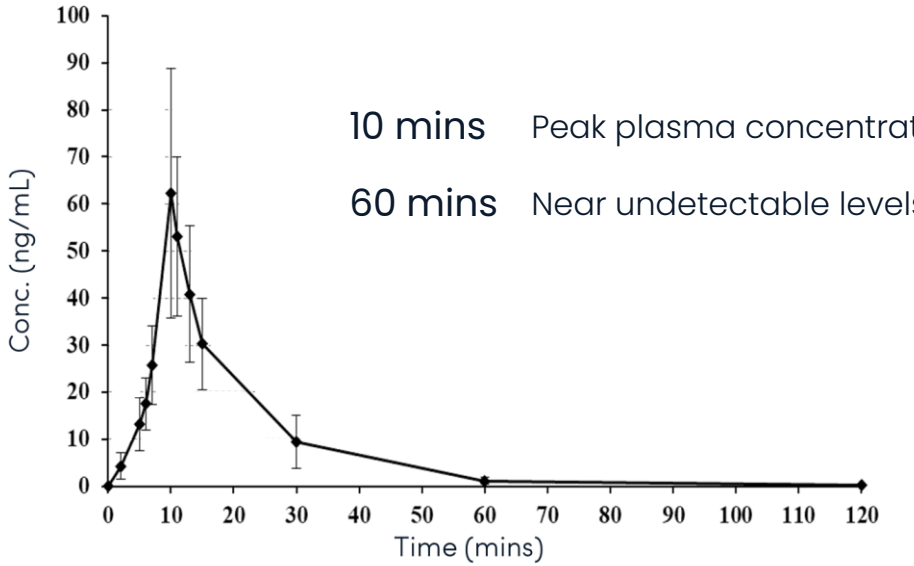
(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
(1) Additional data to be published in a peer reviewed journal
(2) Refers to drug-related AEs incident equal to 1 and includes: Abdominal discomfort, nausea, dizziness , anxiety, cold sweat

# Phase I IV SPL026

## PHARMACOKINETIC PROFILE

## A rapid rise to a peak plasma DMT level and rapid clearance at all tested doses [a,b,c]

Rapid clearance supports the potential for SPL026 regimen to require limited monitoring post dosing




**10 mins** Peak plasma concentration ($C_{max}$)[1]

**60 mins** Near undetectable levels in the body

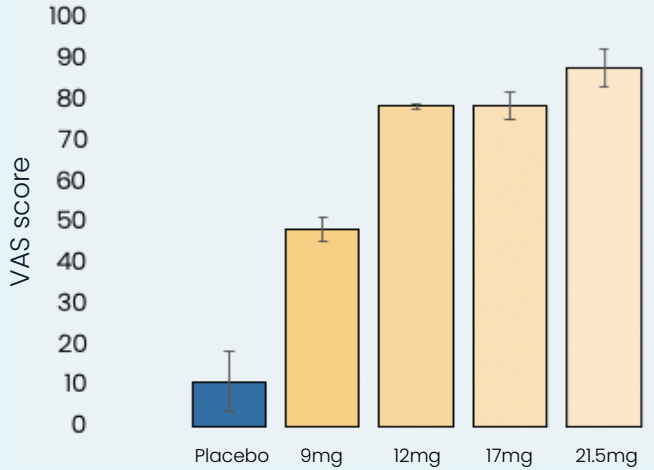
Figure 1. Mean linear PK concentrations of SPL026 (±SD) (n=6)[1] over time

(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
(1) "$C_{max}$" means maximum concentration of drug in serum

## SUBJECTIVE MEASURES OF PSYCHEDELIC EXPERIENCE (INTENSITY & QUALITY)

## Dose correlation vs. range of pharmacodynamic parameters including dimensions on richness, intensity and degree the experience was defined as pleasurable and meaningful

Figure 1. Participant-reported averaged scores (0-100 scale) on the 'richness' of the treatment experience[1]
(Representative of correlation across most patient reported scores)




How 'rich' was your conscious experience?

## Phase IIa IV SPL026[a,b,c]

# Safety and adverse events[1]

## ***Favorable*** safety and tolerability profile

- No drug-related Serious Adverse Events including suicidal ideation or behavior
- 100% of Adverse Events ("AEs") deemed possibly related to treatment were mild to moderate in severity
- The most commonly reported AEs were infusion site pain or reaction, nausea and mild to moderate anxiety
- Majority of AEs (~80%) resolved during dosing visit
- No clinically significant safety concerns, including no concerns with vital signs, ECG or clinical laboratory findings in any treatment group

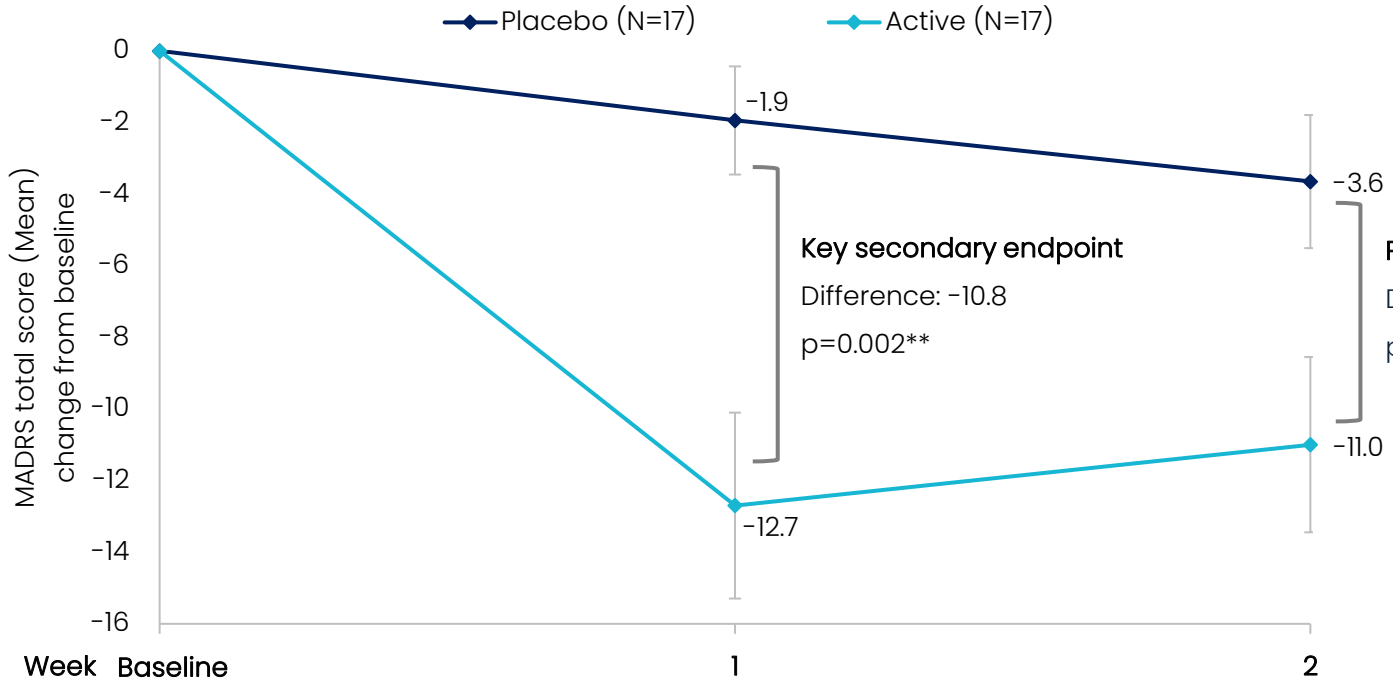
| AEs possibly related to treatment | Blinded phase (to Day 14) | | Total study |
|---|---|---|---|
| | Active | Placebo | All subjects |
| Infusion site pain or reaction | 7 | 3 | 17 |
| Musculoskeletal and connective tissue disorder | 1 | | 2 |
| Nausea | 3 | | 6 |
| Headache | 1 | | 2 |
| Anxiety | 2 | | 5 |
| Insomnia | | 1 | 3 |
| Restlessness | | | 2 |
| Other[2] | 5 | | 10 |
| **Total mild and moderate** | **19** | **4** | **47** |
| **Total severe** | **0** | **0** | **0** |
| **Total** | **19** | **4** | **47** |

**Note:** AEs = Adverse Events; n = number of datapoints; N = population number
(1) Refers to preliminary analysis of data
(2) Refers to AEs incident possibly related to treatment equal to 1 and includes: disturbance in attention, paresthesia, pseudo-hallucination, hypertension, pallor, tinnitus, depression, patient dissatisfaction with treatment, night sweats, visual snow syndrome

Phase IIa IV SPL026[a,b,c]

# Primary endpoint

## IV SPL026 with supportive therapy shows ***statistically significant rapid-onset antidepressant effects*** vs. placebo




| *n* | | | |
|---|---|---|---|
| Placebo | 17 | 16 | 17 |
| Active | 17 | 16 | 17 |

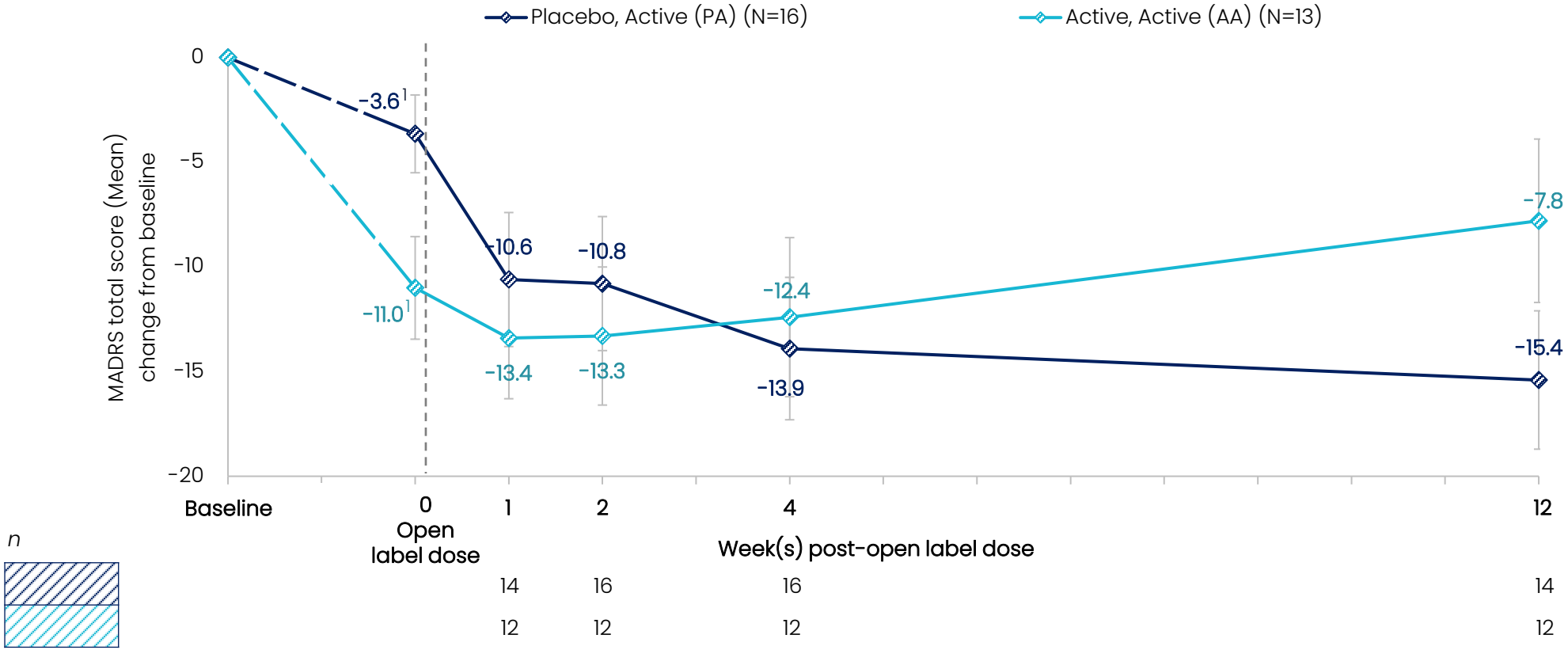
| | Week | |
|---|---|---|
| *Standard deviation* | 1 | 2 |
| Placebo (N=17) | 6.0 | 7.7 |
| Active (N=17) | 10.4 | 10.1 |

**Note:** Error bars represent Standard Error Mean (SEM); MADRS = Montgomery-Asberg Depression Rating Scale; n = number of datapoints; N = population number; p = p-value; * = p<0.05; ** = p<0.01

Phase IIa IV SPL026[a,b,c]

# Change in MADRS over time

## One and two dose regimens of IV SPL026 with supportive therapy show ***durable reduction in depression symptoms***




**Note:** Dashed lines on chart represent blinded phase. Lines are illustrative not representative of data in this phase; Error bars represent Standard Error Mean (SEM); MADRS = Montgomery-Asberg Depression Rating Scale; n = number of data points; N = population number

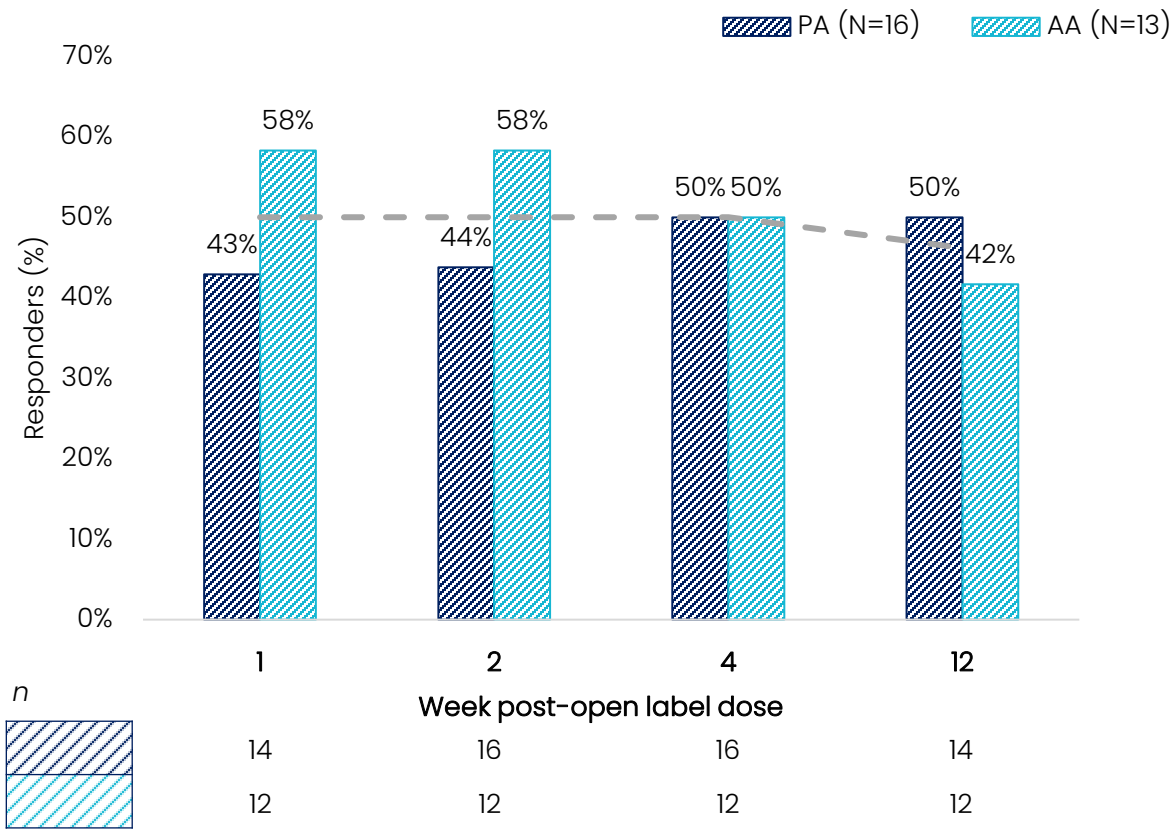
(1) Represents Week 2 endpoint of both treatment groups in the blinded phase taken prior to receiving open label dose

Phase IIa IV SPL026[a,b,c]

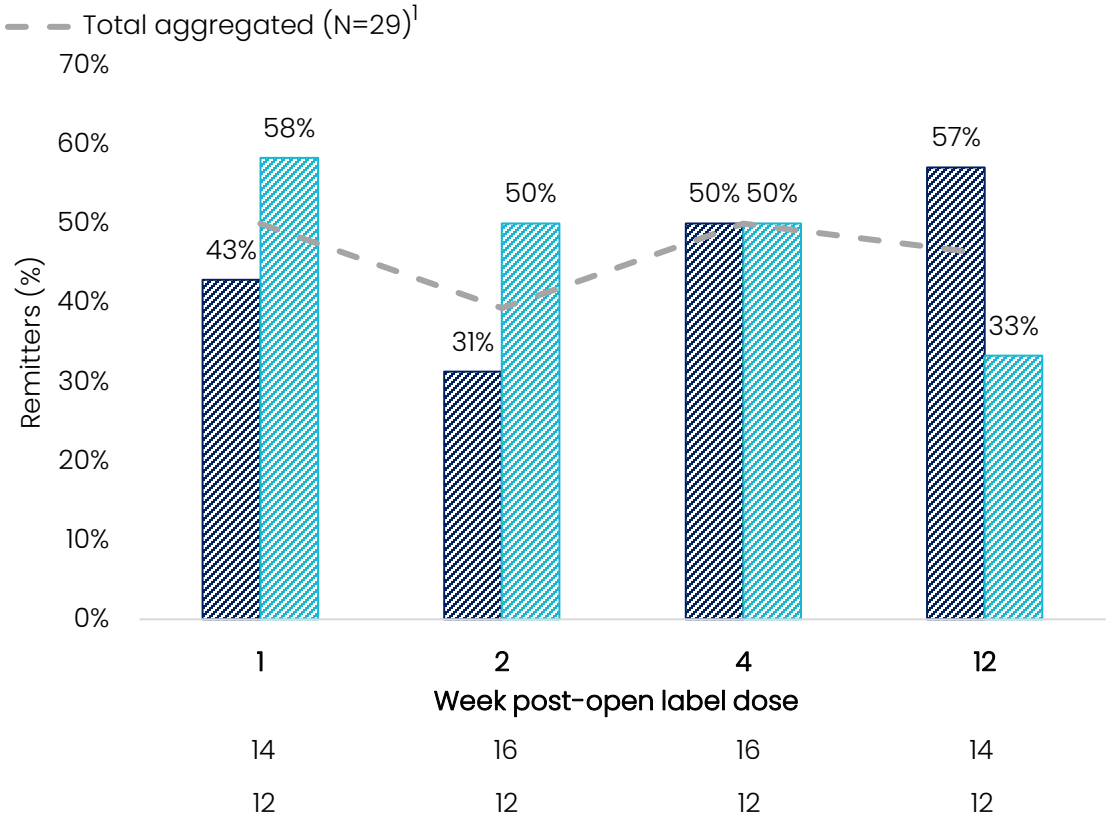
# Response & remission

## ***Durable*** response and remission in one and two dose SPL026 regimens

### Responders (%) (≥50% MADRS reduction from baseline)




### Remitters (%) (MADRS score ≤10)




**Note:** PA = 1st dose: Placebo, 2nd dose: Active; AA – 1st & 2nd dose: Active; MADRS = Montgomery-Asberg Depression Rating Scale; n = number of datapoints; N = population number

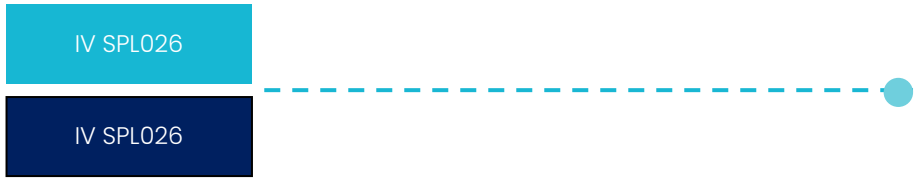
(1) Refers to mean aggregated outcomes of all patients receiving an active dose in the open label phase

# Phase I studies[a,b,c]

## PHASE IB — Assessing the interaction between SSRIs[1] and IV[1] SPL026

MDD patients
Dosing initiated Q4'22

- Patients (on an ineffective SSRI[1])
- Patients (not on antidepressant medication)
- End of study




**Primary endpoint:** Safety and tolerability

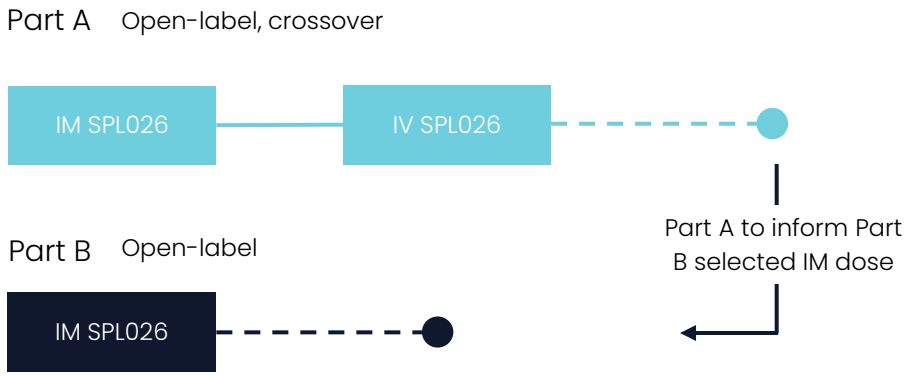
**Secondary / exploratory endpoints:**

- Pharmacokinetics
- PD measures including intensity & quality of subjective psychedelic experience measures
- Exploratory efficacy

## PHASE I — Comparing the profile of IM[1] versus IV SPL026 administration

Healthy volunteers
Dosing initiated Q1'23

- Healthy volunteers (IM followed by IV SPL026)
- Healthy volunteers (IM SPL026)
- End of study




**Safety and tolerability**

- Pharmacokinetics
- PD measures including intensity & quality of subjective psychedelic experience measures

(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
(1) "SSRI" means Selective Serotonin Reuptake Inhibitor; "IV" means Intravenous; "IM" means Intramuscular

Phase IIb IV SPL026

# Advancing towards a Phase IIb [a,b,c,1]

## Overview

| Anticipated start | Target jurisdictions | Potential no. of sites | Estimated population size |
|---|---|---|---|
| H1 2023 | US, EU, UK | 15-25 | 150-250 |

## Potential trial design

**Design**
Double-blind, randomized, placebo-controlled trial to investigate the efficacy and safety of SPL026 with supportive therapy in three parallel groups

A single dose administered in a 3-month blinded phase followed by a 9-month open label extension with the option for an open label second dose if the participant relapses

**Patient population**
Moderate to severe major depressive disorder

**Treatment arms**
High dose SPL026; Low dose SPL026 and placebo

(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims
(1) The finalized trial design may change from current expectations and remains subject to regulatory approval

# SPL028 deuterated DMT [a,b,c]

## Profile

- Novel chemically engineered DMT with deuterium
- Affects rate of drug metabolism in the body
- Anticipated to extend psychedelic experience vs. SPL026
- Potential to explore additional administration methods for patient and physician convenience
- Differentiated therapeutic profile to target broader depressive populations or alternative indications

## Programs

IM IV

**Profile**: Short-duration

**Clinical trial(s)**: Phase I IM/IV: H1 2023

RELATIVE DURATION OF SPL028 PSYCHEDELIC EXPERIENCE[1]


(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
(1) Refers to relative duration of SPL028 vs other psychedelics in development

## Preclinical SPL026

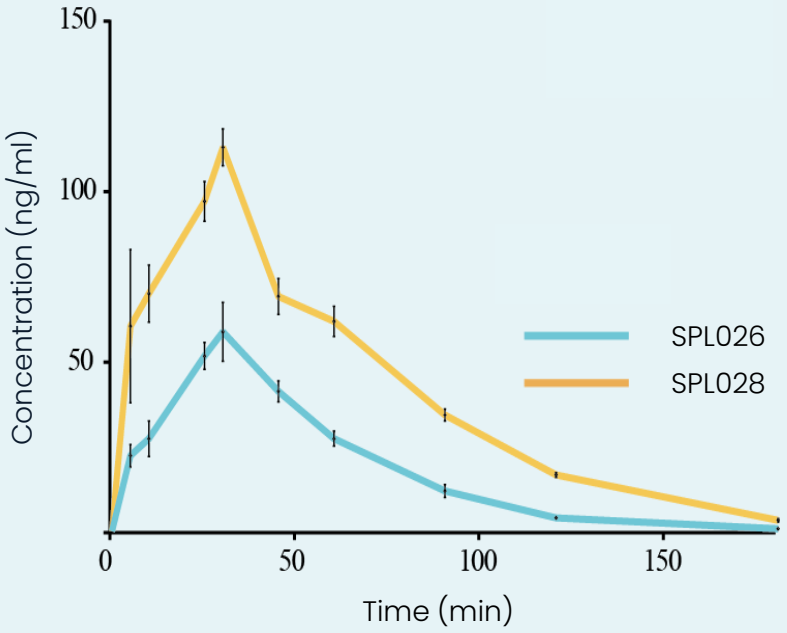



Figure 1. *in vivo* IM pharmacokinetic profile of equal doses SPL026 & SPL028 in rats. Results expressed as means ± SEM

# Data suggests SPL028 offers a differentiated treatment to SPL026 [a,b,c]

1

### Differentiated pharmacokinetic profile (vs. SPL026)

- IM administration *in vivo* showed marked reduction in clearance rate resulting in an increase in $C_{max}$[1] and exposure (AUC[2]) levels

2

### Similar pharmacological and behavioral profile to SPL026

- Same binding profiles against 5-HT receptor subtypes and no significant differences *in vitro* receptor binding profiles across additional receptors
- Similar but with potentially prolonged behavioral profiles noted across *in vivo* studies – potential for extended subjective experience vs. SPL026

3

### Safe toxicological profile

- Safe & well tolerated *in vivo* at all doses tested
- Significant margins for first in-human trials

(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
(1) "$C_{max}$" means maximum concentration of drug in serum
(2) "AUC" means area under the curve

# Company highlights [a,b,c]

1. Advancing portfolio of short-duration psychedelics for mental health disorders that have the potential for rapid acting and long-lasting relief addressing areas of critical unmet need
2. Demonstrated efficacy and favorable safety profile of lead asset, SPL026 with supportive therapy in Major Depressive Disorder in randomized, placebo-controlled Phase IIa trial
3. Maturing and expanding IP portfolio with 14 patents granted and 90+ applications pending[1]
4. Highly experienced executive team with strong record in leadership roles across the pharmaceutical and life sciences sector
5. Cash position of C$22.7m (Nov 22[2]) allows for completion of active trials

(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
(1) Based on IP portfolio as disclosed in latest MD&A
(2) Refers to latest quarterly results

Thank you

# References

## GENERAL

a) Certain statements regarding tryptamine-based treatments have not been evaluated by the U.K. Medicines and Healthcare products Regulatory Agency, the U.S. Food and Drug Administration, Health Canada, or other similar regulatory authorities, nor has the efficacy of tryptamine-based treatments been confirmed by approved research. There is no assurance that tryptamine can be used to diagnose, treat, cure or prevent any disease or condition and robust scientific research and clinical trials are needed.
b) Forward-looking statements are subject to various risks and assumptions. See "Cautionary Notes" on page 2 of this presentation.
c) Subject to receipt of all necessary regulatory approvals from all applicable governmental authorities. There are multiple risk factors regarding the ability to successfully commercially scale and develop tryptamine-based treatments and a portfolio of DMT analogues

## SLIDE 4


1) WHO (2021), Depression factsheet
2) Cipriani A, et al. (2018) Lancet
3) Sansone RA, Sansone LA. Antidepressant adherence: are patients taking their medications?
4) Davis, A. et al. (2021) Effects of Psilocybin-Assisted Psychotherapy on Major Depressive Disorder
5) Small Pharma Phase I SPL026 in Healthy Volunteers study


## SLIDE 5


1) WHO (2021), Depression factsheet
2) Mental health matters (2020), The Lancet Global Health
3) American Association of Suicidology, 2014
4) Judd et al (1998) A Prospective 12-Year Study of Subsyndromal and Syndromal Depressive Symptoms in Unipolar Major Depressive Disorders
5) Mitchell (2006) Depressed patients and treatment adherence
6) Greenberg PE, Fournier AA, Sisitsky T, Simes M, Berman R, Koenigsberg SH, Kessler RC. The Economic Burden of Adults with Major Depressive Disorder in the United States (2010 and 2018). Pharmacoeconomics. 2021 Jun


## SLIDE 6


1) Rush AJ et al. "Acute and longer-term outcomes in depressed outpatient requiring one or several treatment steps: A STAR*D report". The American Journal of Psychiatry. 2006. 163(11):1905-1917
2) Arnaud et al (2021) The Increasing Economic Burden with Additional Steps of Pharmacotherapy in Major Depressive Disorder


## SLIDE 7


5) D'Souza, D.C., Syed, S.A., Flynn, L.T. et al. Exploratory study of the dose-related safety, tolerability, and efficacy of dimethyltryptamine (DMT) in healthy volunteers and major depressive disorder. Neuropsychopharmacol. (2022) https://doi.org/10.1038/s41386-022-01344-y
7) Rafael G. dos Santos, José Carlos Bouso, Miguel Ángel Alcázar-Córcoles & Jaime E. C. Hallak (2018) Efficacy, tolerability, and safety of serotonergic psychedelics for the management of mood, anxiety, and substance-use disorders: a systematic review of systematic reviews, Expert Review of Clinical Pharmacology, 11:9, 889-902.
8) Holze, F., Caluori, T.V., Vizeli, P. et al. Safety pharmacology of acute LSD administration in healthy subjects. Psychopharmacology (2021).