

Mental health medicines made better

TSXV: DMT
OTCQB: DMTTF

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Drug development involves long lead times, is very expensive and involves many variables of uncertainty. Anticipated timelines regarding drug development are based on reasonable assumptions informed by current knowledge and information available to the Company. Every patient treated on future studies can change those assumptions either positively (to indicate a faster timeline to new drug applications and other approvals) or negatively (to indicate a slower timeline to new drug applications and other approvals). This document contains certain forward-looking statements regarding anticipated or possible drug development timelines. Such statements are informed by, among other things, regulatory guidelines for developing a drug with safety studies, proof of concept studies, and pivotal studies for new drug application submission and approval, and assumes the success of implementation and results of such studies on timelines indicated as possible by such guidelines, other industry examples, and the Company's development efforts to date.

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Unless expressed otherwise, all dollar amounts in this presentation are in United States dollars.



Leadership team



Peter Rands

Chief Executive Officer, Director

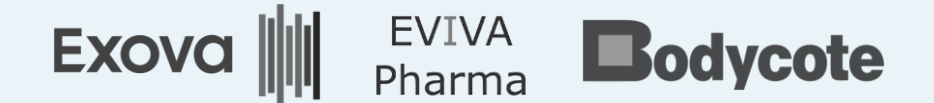
Founded Small Pharma in 2015. Qualified UK & European patent attorney with 10+ years specializing in pharmaceuticals and a background in chemistry



Marie Layzell

Chief Operating Officer,
Head of CMC, Director

20+ years in pharma as an analytical consultant & project manager advising multiple large pharma projects on CMC drug development



Carol Routledge

Chief Medical & Scientific Officer

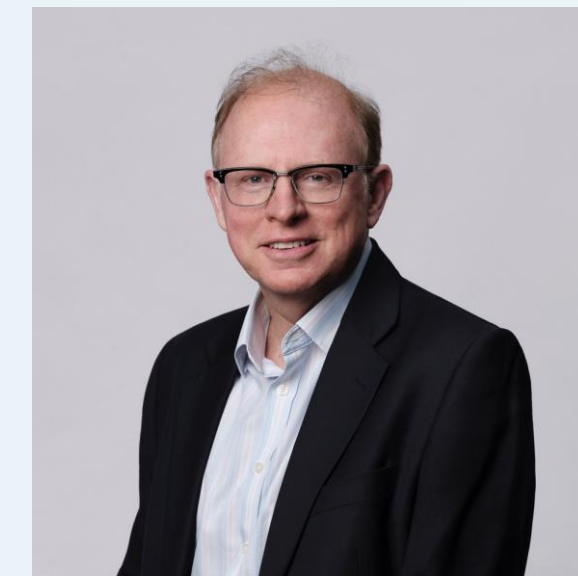
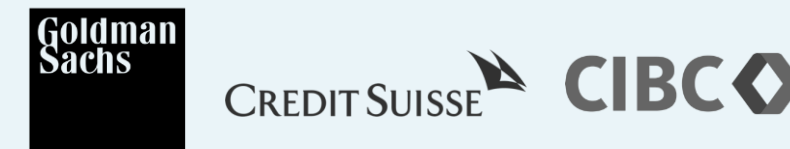
30+ years in pharma in strategic leadership roles across drug discovery & development with a neuropsychiatry focus



George Tziras

Chief Business Officer, Director

15+ years in investment banking and capital markets with expertise in corporate finance



David Steel

Chief Financial Officer

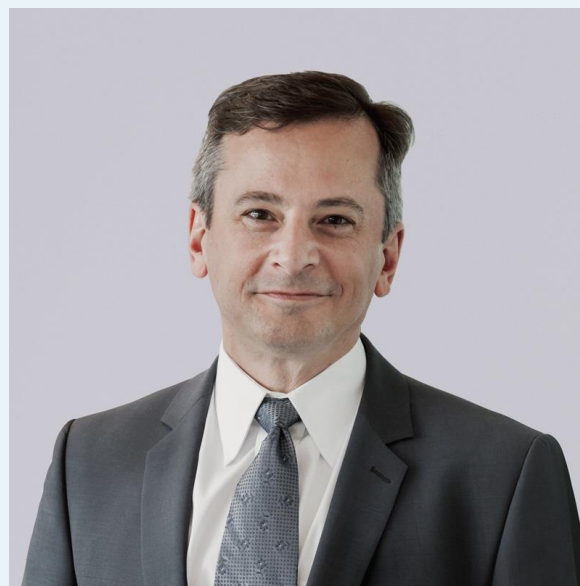
Chartered accountant with extensive international and capital markets experience gained from senior finance roles



Lyne Fortin

Chair, Independent Director

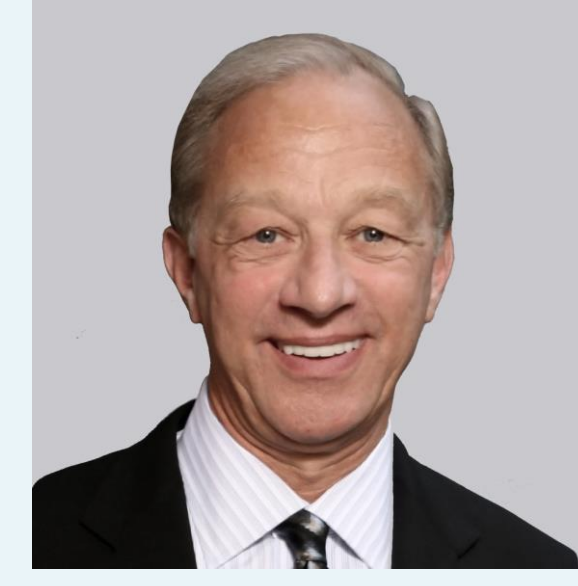
35+ years in pharma including positions at Board and exec levels. Broad expertise and experience in the commercialization of pharmaceutical assets



Michael Wolfe

Independent Director

30+ years experience in finance, accounting, private equity and business valuation. Currently CFO, MindCure Health Inc. Previously CFO, Baylin Technologies Inc.



Paul Maier

Independent Director

35+ years in pharma including senior exec, Board and Audit Committee Chair positions at multiple NASDAQ listed firms. Expertise in transactional and operational strategy



Introducing Small Pharma

A neuroscience company developing life-changing treatments for mental health conditions

FOUNDED IN 2015 TO:

Identify known compounds

Assess meaningful treatment potential

Develop optimized therapies



(a-c,4) See Appendix – Footnotes and Sources and “Cautionary Notes – Forward-Looking Information”, “Risk Factors”, and “Treatment Claims”
(1) Based on Small Pharma’s internal analysis of other tryptamine psychedelics
(2) Composition of matter patent applications pending and 1 UK patent granted covering DMT analogues
(3) Based on review of patents and applications related to SPL801B, SPL026, SPL028 and SPL029 by legal counsel as of Oct 26 2021. See “Cautionary Notes – Forward-Looking Information” and “Risk Factors”

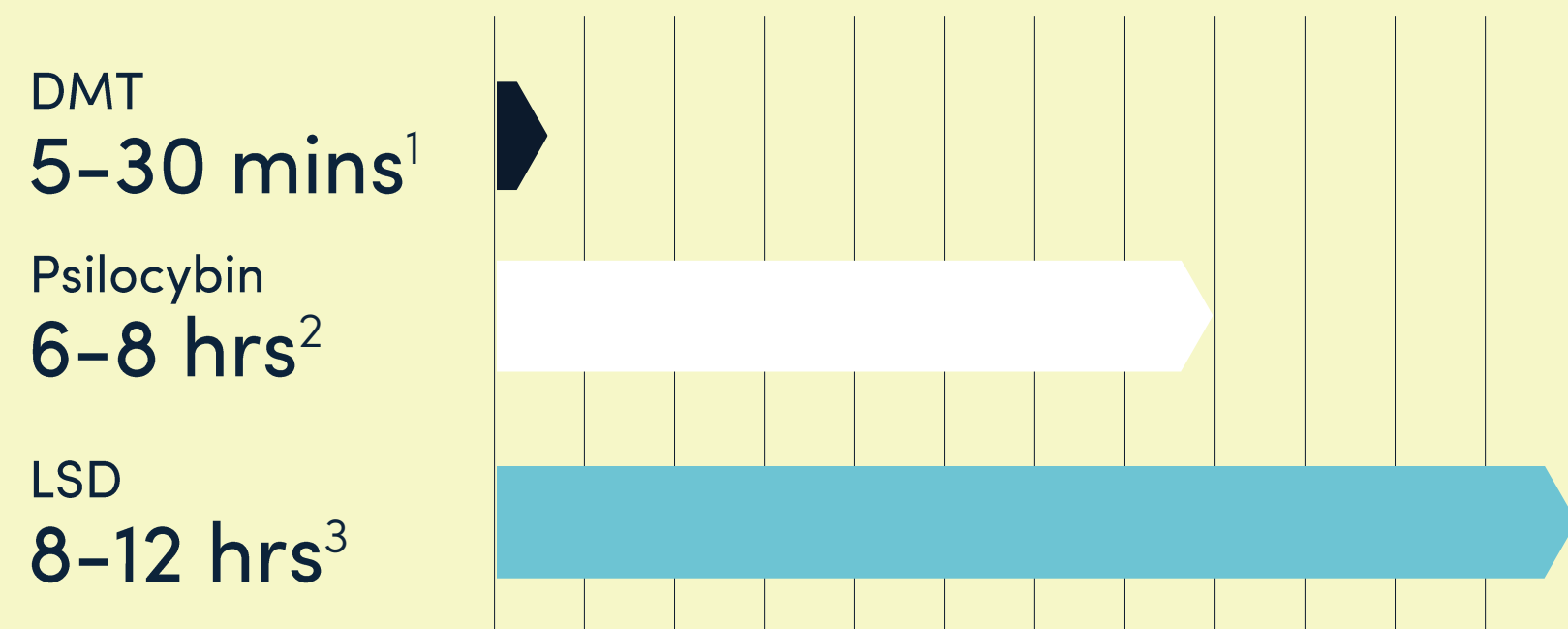
Our Assets

- 01 Potential for a first-in-class DMT treatment
 - Most advanced DMT clinical program in Major Depressive Disorder (MDD)
- 02 Expanding portfolio of DMT analogues
 - Potential for superior drug profiles vs. other psychedelics in development^{b,c,1}
 - Stronger IP protection potential vs. native DMT²
- 03 Robust IP strategy³
 - 50+ patents pending and 4 granted including:
 - Composition of matter grant on psychedelic compound⁴
 - Patent pending on low cost, stable and scalable synthetic GMP route for DMT^{a,b}



Exploring the potential of the psychedelic DMT to treat mental health disorders^{a,b}

Comparison of the duration of the psychedelic experience in various classical psychedelics



What are psychedelics?

“Mind expanding” compounds

Can trigger a temporary altered state of consciousness with psychological, visual and auditory changes (“the psychedelic experience”)

DMT origins⁴

Found in a variety of plants and animals⁴

An active ingredient in Ayahuasca (a brew used ritually and medicinally by Amazonian tribes for centuries)

First chemically synthesized in 1931⁵

DMT chemistry⁴

Tryptamine based structure (others include serotonin, melatonin & other classical psychedelics such as psilocybin)

Effects primarily mediated by 5-HT_{2a} (serotonin) receptors in the brain



(a,b,1-5) See Appendix – Footnotes and Sources and “Cautionary Notes – Forward-Looking Information”, “Risk Factors”, and “Treatment Claims”

In combination with therapy, DMT has unique clinical and commercial potential

CLINICAL POTENTIAL

Fast-acting and long-lasting relief

TODAY's antidepressant treatment	TOMORROW's expected DMT therapy
Daily dose for 9+ months to lifelong ²	Few doses in 12 months¹
4-8 weeks Time to symptom relief ²	<24 hrs Anticipated time to symptom relief¹
Suppress symptoms only	Targets the root cause

Safe treatment

(based on DMT clinical data to-date)

- ▶ **0** serious adverse events³
- ▶ **Low** abuse potential^{a,4}
- ▶ Minimal side effects (vs. typical antidepressants)^{3,5}

COMMERCIAL POTENTIAL

Short-lasting drug effects⁴

- ▶ Potential for clinics to treat multiple patients daily
- ▶ Treatment sessions designed to fit within existing clinical setting

Low cost to manufacture

- ▶ Simple structure allows for manufacture of a range of formulations and doses
- ▶ Small Pharma's proprietary manufacture process is scalable^{b,c,6}, and low-cost^{b,7}



(a-c,1,2,4) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
 (3) Based on published results of academic studies and Small Pharma's Phase I study investigating the effects of DMT in over 130+ healthy volunteers
 (5) Typical side effects of SSRIs (selective serotonin-reuptake inhibitors) anti-depressants include nausea, fatigue, weight gain, low libido
 (6) To the best of our knowledge, the GMP manufacturing route will scale up sufficiently to support intended use
 (7) The starting material in the manufacture of SPL026 is currently inexpensive

We are leading
**the world's first
clinical trial for
DMT-assisted
therapy** to treat
Major Depressive
Disorder (MDD)

CLINICAL PROGRESS

Active Phase I/IIa in lead DMT candidate, SPL026

- ▶ Phase I complete (Q3 2021)
- ▶ Phase IIa MDD patient proof-of-concept study in progress
- ▶ Phase IIa topline data expected H1 2022^{a,b,c}

UK fast track designation awarded for SPL026

- ▶ Granted ILAP innovation passport by MHRA¹
- ▶ Potential for earlier and faster UK market access^{b,c}

Selected SPL028 candidate to take into clinical trials

- ▶ Completed preclinical studies for final candidate selection

CORPORATE PROGRESS

Well funded

- ▶ C\$63m raised in 2021
- ▶ Funded beyond proof of concept Phase IIa results^a

Academic collaboration with Imperial College London

- ▶ Partnership with leading experts from the Centre for Psychedelic Research

**Imperial College
London**



(a-c)
(1)

See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors", and "Treatment Claims"
ILAP – Innovation and Licencing Pathway, a new fast-track designation established by the UK drug regulators, MHRA

An aerial photograph of a river with a white hexagonal overlay in the center. The river's water is dark blue, and the surrounding land is a mix of green and brown, indicating a natural, possibly forested, environment. The hexagon is a solid white color, and the text 'THE OPPORTUNITY' is written in a clean, black, sans-serif font within it.

THE OPPORTUNITY

There is an urgent need to develop alternative therapies to treat depression

25% Increase in prevalence of depression and anxiety due to COVID-19⁴

\$1T Estimated cost to the global economy in lost productivity each year⁶

264 million suffered from depression worldwide in 2020 before COVID¹

20x Suicide risk with major depression vs. without major depression⁵

49.7M DALYS⁷ due to depression globally in 2020⁸ (an increase of 10.7M DALYs from pre-COVID rates)

5.8 MILLION² 2019/2020 (UK)

17.3 MILLION³ 2017 (USA)



(1,3-6,8) See Appendix – Footnotes and Sources
(2) Based on prevalence of 10.1% of adult population in 2019
(7) DALYS – Disability-adjusted life years defines the number of equivalent years of full health lost

Current antidepressants leave a third of patients behind



1 in 8

Americans use antidepressants²

Antidepressant relief can take time

In 12 weeks, only ~2/3 of patients have responded to current treatment¹

Strong placebo effect

Only 40% of patients respond better to SSRIs than if they simply received placebo^{b,3}

Side effects can be unpleasant

Side effects cause ~60% of patients to discontinue or switch SSRI within 12 weeks⁴

Symptoms can reoccur

Sadly, 1/2 of patients relapse within 6 months if current treatments are discontinued⁵

They aren't easy to wean off

Unfortunately, 1/2 of patients experience unpleasant withdrawal symptoms that can last several months⁶



Scientific research is unlocking how psychedelics work in the brain

Default mode network (DMN)

A group of connected brain regions shown to be key to everyday consciousness and active during self reflection and awareness of ourselves

Brain plasticity

The ability of the brain to adapt to changes through structural and functional brain adaptations

In depression

▲ DMN hyperactivity

increased

Believed to be linked to inflexible repetitive negative thoughts and feelings ('ruminations'¹) common in depression²

impaired

▼ Plasticity

In certain brain regions³

Post psychedelic dose

suppressed

▼ DMN activity

▲ Global connectivity

increased

Believed to enable DMN to reset and reconsolidate in a little less rigid way⁴

Brain network changes thought to help overcome depressive thought patterns and improve other depression-related symptoms

▲ Plasticity

promoted

Pre-clinical studies suggest potential neuroplastic potential; mechanisms linked to antidepressant effects⁵



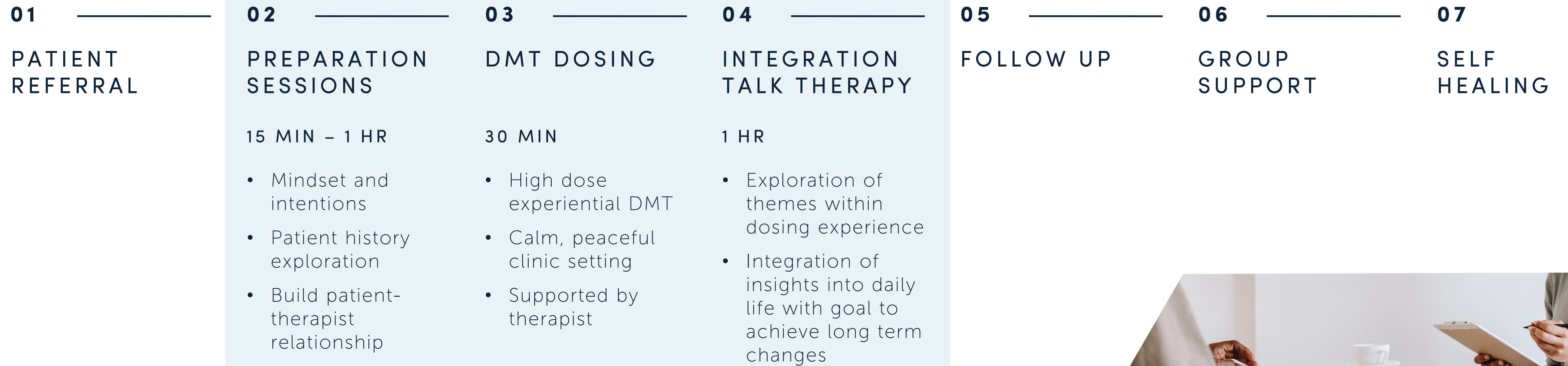
DMT-assisted therapy offers a potential holistic approach^{a,b,c}

Delivered by healthcare professionals trained in our proprietary DMT focused therapy training to maximize the treatment potential and ensure patients feel safe and supported^{a,b,c}

Our therapy training

- ▶ Therapist training program launched (July 2021)
- ▶ Paving the path to a potential scalable therapist training academy^b

Anticipated treatment journey^{a,b,c}



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





OUR PROGRESS

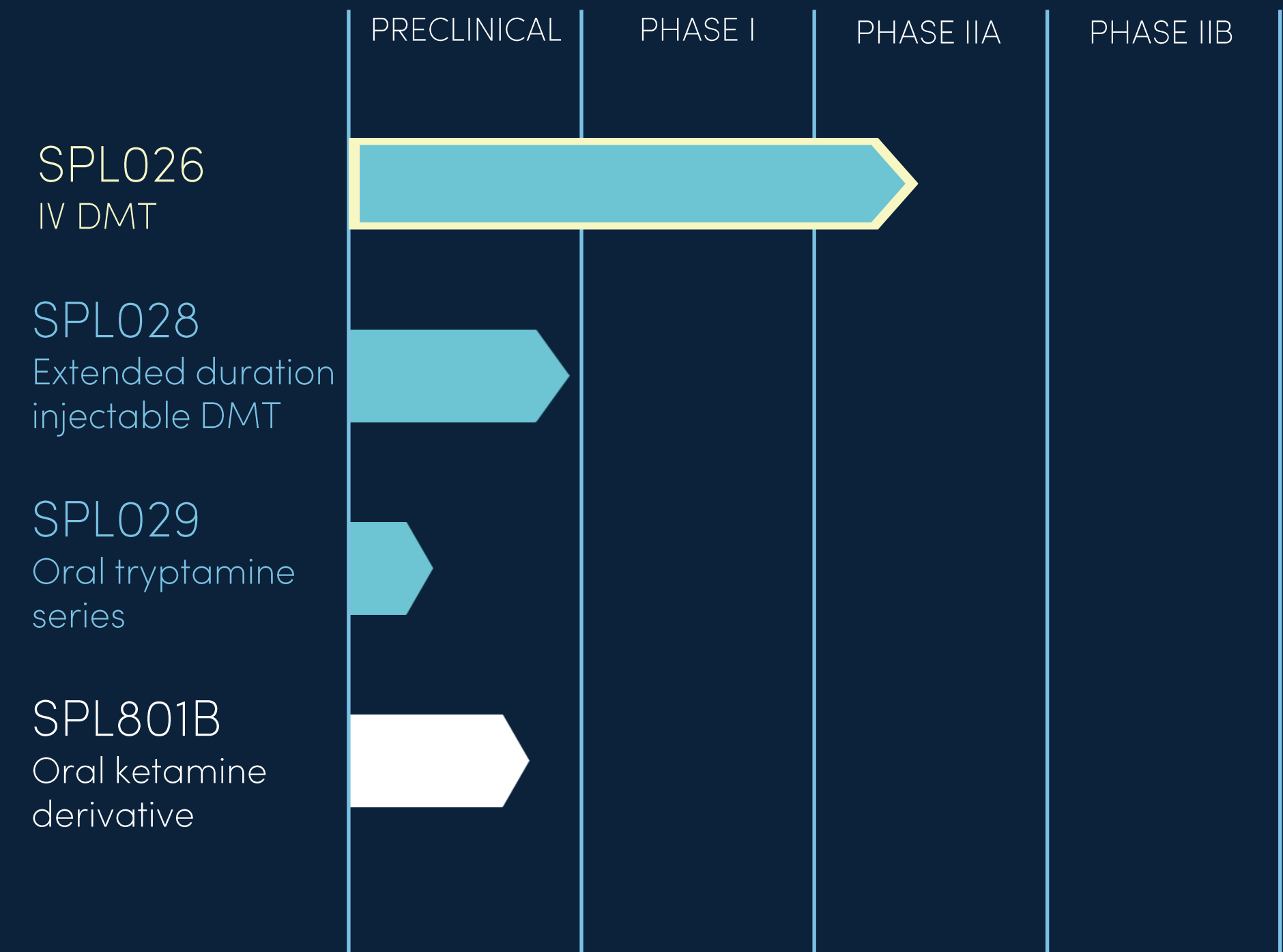
Progressing a pipeline of short-acting psychedelic assisted therapies^{a,b,c}

SPL026 (lead DMT candidate)

- ▶ Offers anticipated ~2-2.5 hr treatment including supportive therapy
- ▶ Expanding clinical program to maximize treatment accessibility

SPL028

- ▶ UK Composition of Matter patent granted
- ▶ Anticipated extended DMT treatment that remains a convenient treatment option



- ▶ Lead candidate in psychedelic portfolio
- ▶ Psychedelic focused R&D progress to-date
- ▶ Non-psychedelic focused R&D progress to-date



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

Phase I/IIa trial

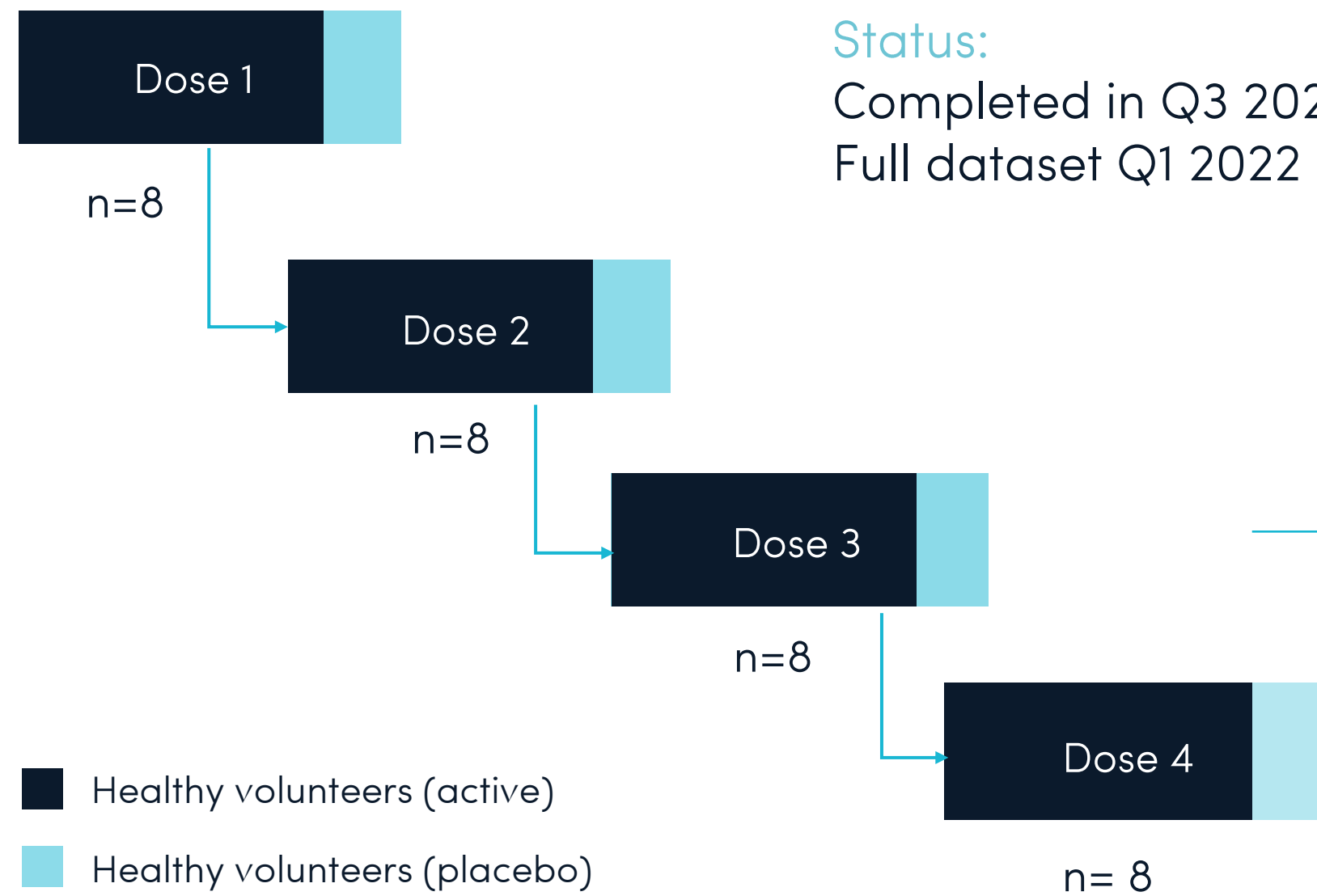
PART A – (PHASE I)

Placebo-controlled dose escalating trial

Dose range: 9-21.5mg

Population:
Psychedelic naïve healthy volunteers
n=32

Status:
Completed in Q3 2021
Full dataset Q1 2022

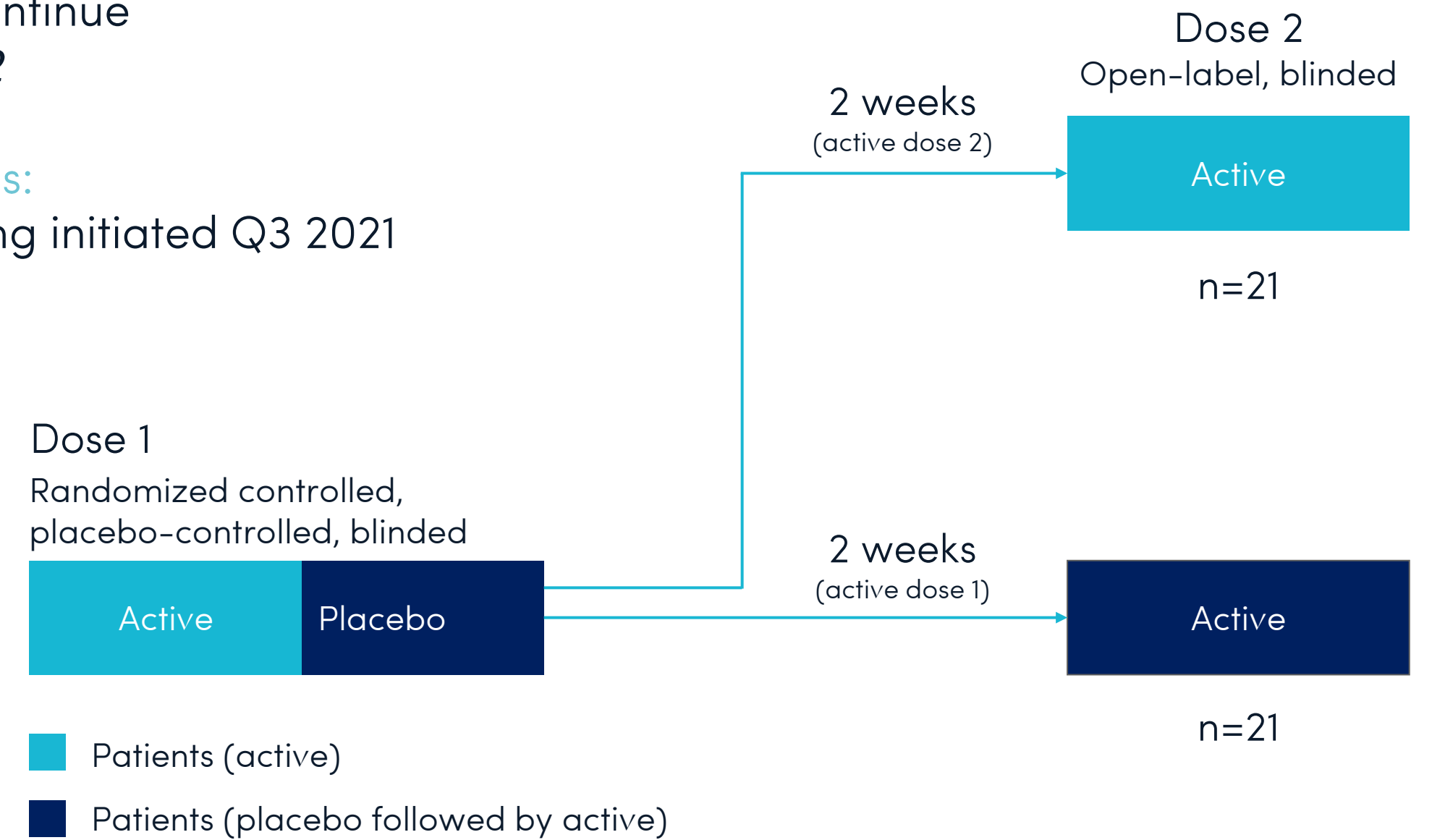


Dose selected for Phase IIa

PART B – (PHASE IIA)

Population:
MDD patients (moderate/severe)
Not on antidepressant medication/willing to discontinue
n=42

Status:
Dosing initiated Q3 2021



Primary endpoint

Safety and tolerability

Secondary / exploratory endpoints

- ▶ Pharmacokinetics
- ▶ Outcome PD measures
- ▶ Subjective experience measures
- ▶ EEG

MADRS score (change in baseline 2 weeks post first dose)

- ▶ MADRS change from baseline at W1, M1, M3 and M6⁽¹⁾ (post dose 1)
- ▶ Safety and tolerability measures
- ▶ Outcome PD measures
- ▶ Subjective experience measures
- ▶ Assess 1 vs. 2 doses



(1) 6 month follow-up out of study

At all doses, SPL026 was safe and well tolerated^{a,b,c}

SAFETY¹

- ▶ 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

TOLERABILITY¹

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

Adverse Event (possibly related)	Occurrences
Total	N=20
Mild	85%
Moderate	15%
Severe	0%

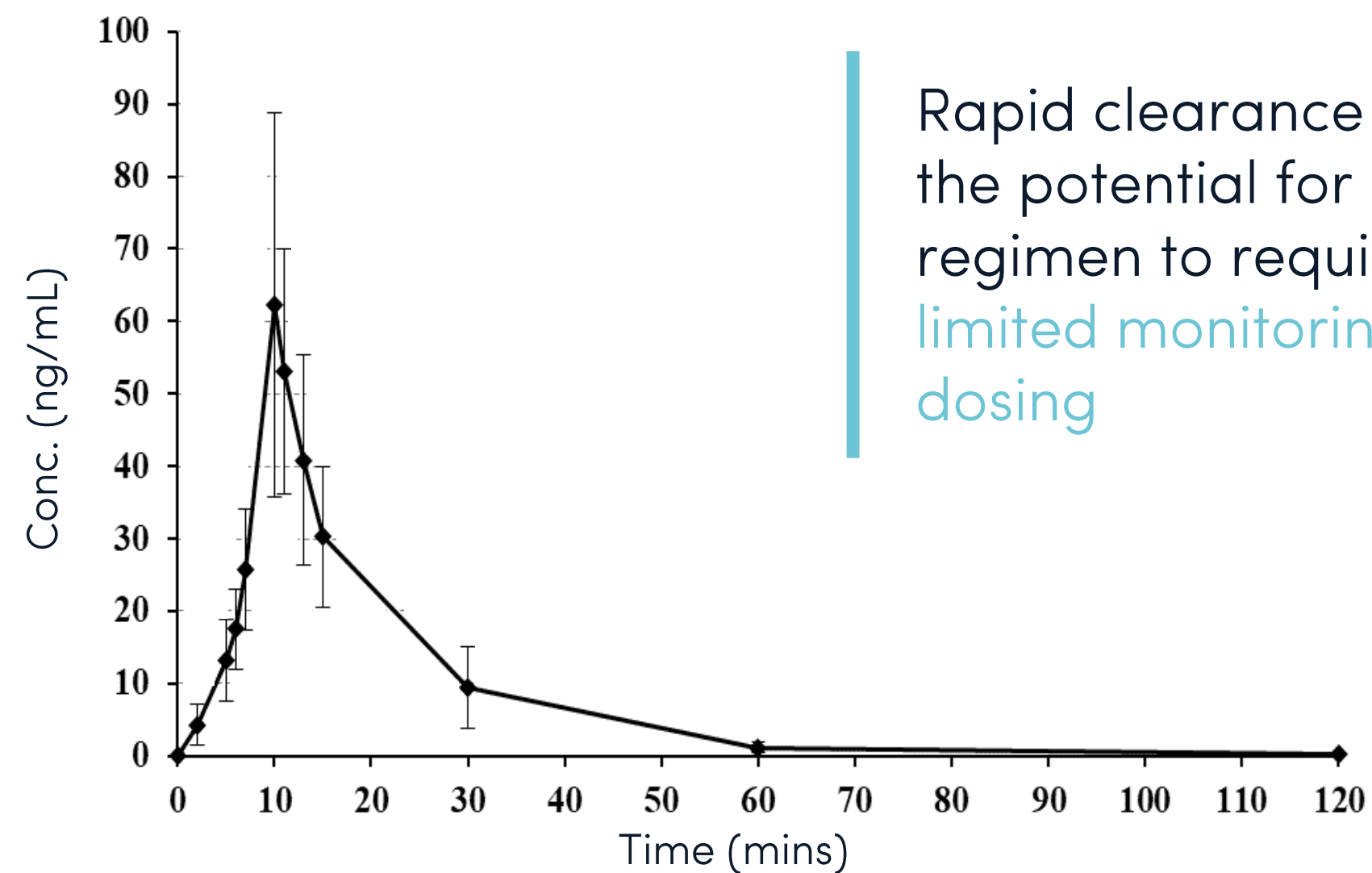
Figure 1. Summary of treatment emergent adverse events deemed possibly related to the administration of SPL026



(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

SPL026: PHASE I RESULTS

The pharmacokinetic profile of IV SPL026 shows a rapid rise to a peak plasma DMT level and rapid clearance at all doses^{a,b,c}



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

Figure 1. Mean linear PK concentrations of SPL026 (\pm SD) dose selected for Phase IIa (n=6)¹ over time

Key parameters¹

at ALL dose concentrations administered via IV infusion

10 mins Peak plasma concentration (C_{max})²

60 mins Near undetectable levels in the body

0 min

Dosing

~20 min

Typical duration of psychedelic experience

~30 min

Duration of dosing clinic session



(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) C_{max} = maximum concentration of drug in serum

SPL026: PHASE I RESULTS

Correlation between assessments on quality of the psychedelic experience and dosing levels^{a,b,c}

Dose correlation vs. averaged participant scores across a range of pharmacodynamic parameters including dimensions on richness, intensity and degree the experience was defined as pleasurable and meaningful



Given the subjectivity of the psychedelic experience it was exciting to see a close correlation between levels of drug in the body and pharmacodynamic endpoints.

As for the subject experience, most reported it to be pleasurable, not too challenging and importantly nobody regretted it.



Dr Carol Routledge
Chief Medical & Scientific Officer

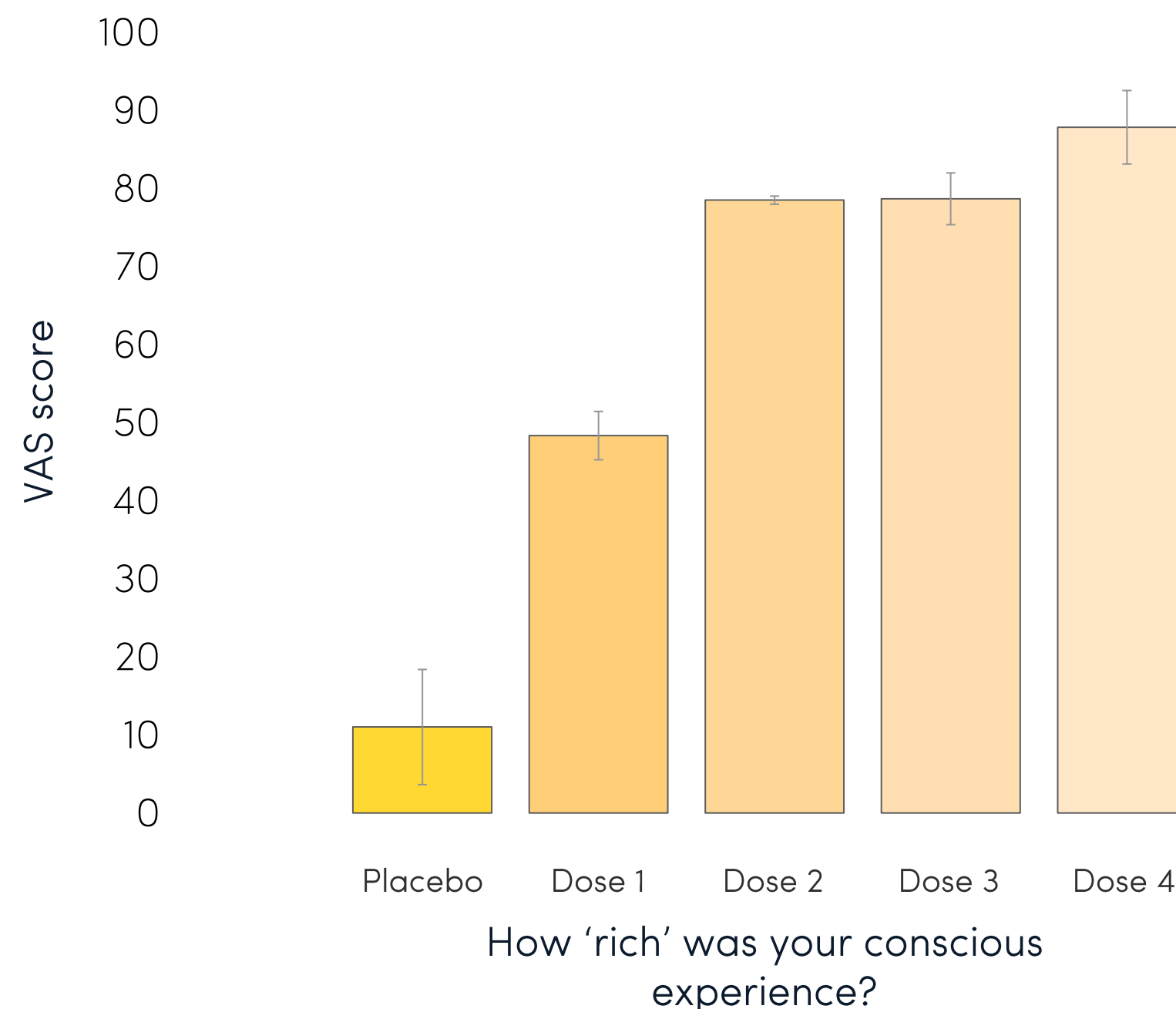


Figure 1. Participant-reported averaged scores (0-100 scale) on the 'richness' of the treatment experience¹
Representative of correlation across most patient reported scores



(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 on additional pharmacodynamic data

A multi-step assessment supports dose selected for Phase IIa in delivering the target treatment profile^{a,b,c}

ON THE DOSE SELECTED FOR PHASE IIA:

// This dose is likely to provide a significant psychedelic experience for people with depression; one that may be more likely to reach the depth required to have meaningful therapeutic impact.



Dr Graham Campbell
Study Psychiatrist

Report on perceived therapeutic potential of dose selected for Phase IIa vs. alternate doses investigated in the Phase I study

01 SAFETY & TOLERABILITY

02 SUBJECTIVE MEASURES OF PSYCHEDELIC EXPERIENCE (INTENSITY & QUALITY)

03 SUBJECT ASSESSMENTS BY STUDY PSYCHIATRIST/THERAPIST



DOSE SELECTED FOR PHASE IIA



Additional studies in 2022 to optimize potential treatment convenience and accessibility^{a,b,c}

PHASE I DRUG INTERACTION STUDY

INVESTIGATION

Exploring the potential interactions between SSRI antidepressants and SPL026 therapy

POPULATION

MDD patients
 i) on SSRI treatment
 ii) not on SSRI treatment

OUTCOMES

Safety, tolerability, pharmacokinetics and pharmacodynamics

PHASE I IM/IV¹ STUDY

Exploring alternative convenient treatment delivery routes

Healthy volunteers

Safety, tolerability, pharmacokinetics and pharmacodynamics



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

PIPELINE

Our pipeline expands the therapeutic and commercial potential of short-acting psychedelic medicines^{a,b,c}

OUR PIPELINE DRUG PROCESS

01

DEVELOP

Deuterated series of psychedelic tryptamines

- ▶ Deuteration approach replaces certain hydrogen atoms with heavier hydrogen atoms
- ▶ Can affect rate of drug metabolism due to kinetic isotope effect

02

TEST

Screening process through *in vitro* and *in vivo* studies

- ▶ Assess pharmacokinetics using different administration routes
- ▶ Explore pharmacology, behaviour and toxicology profiles

03

REFINE

Final candidate selection and GMP manufacture

- ▶ SPL028 (extended duration DMT) ***selected***
- ▶ SPL029 (oral tryptamine) ***pending***



INITIATE
CLINICAL TRIALS



Preclinical SPL028 data suggests potential for a differentiated treatment to SPL026^{a,b,c}

01 Differentiated PK profile (vs. SPL026)

- ▶ IM administration *in vivo* showed marked reduction in clearance rate resulting in increase in C_{max}^1 and exposure (AUC²) levels

02 Similar pharmacological and behavioural 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 prolonged behavioural profiles noted across *in vivo* studies – potential for extended psychedelic experience vs. SPL026

03 Safe toxicological profile

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

Potential for expedited route to clinic^{a,b}



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

Potential treatment opportunity

- ▶ An extended therapeutic window
- ▶ Enables optimization for routes of administration beyond IV

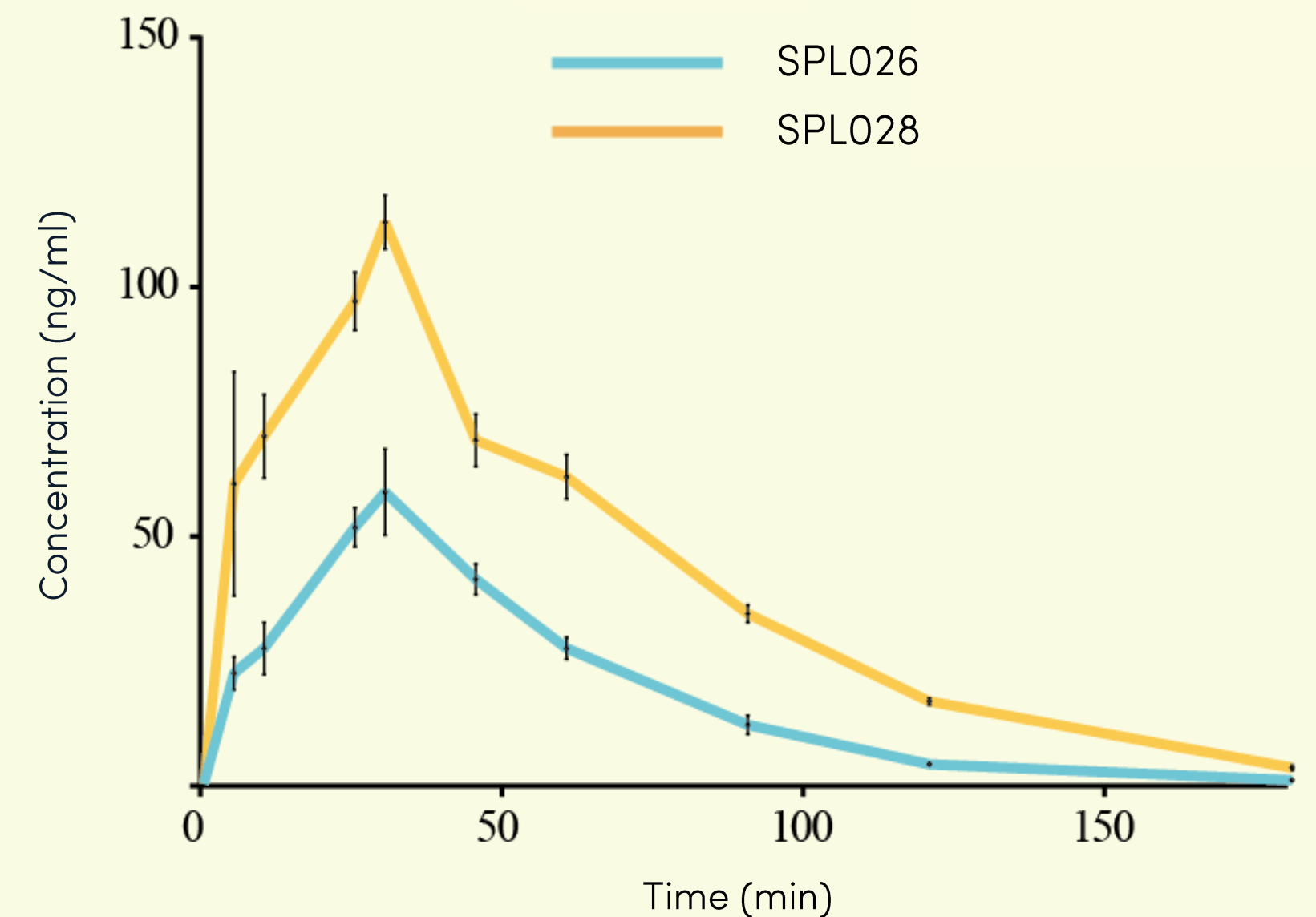


Figure 1. *In vivo* IM pharmacokinetic profile of equal doses SPL026 & SPL028 in rats. Results expressed as means ± SEM

SPL028: POTENTIAL

Our proprietary SPL028 could offer a DMT treatment experience with an extended patient journey^{a,b,c}

01

EXPANDING TREATMENTS FOR MENTAL HEALTH

Anticipated extended DMT experience could offer additional therapeutic potential in:

- ▶ Alternative indications
- ▶ Patient sub-populations

02

OPTIMIZE DELIVERY METHODS

Opportunity to assess administration route delivery on:

- ▶ Treatment convenience
- ▶ Treatment duration

03

PHASE I STUDY PLANNED FOR H2 2022

Exploring safety and tolerability of SPL028 with psychotherapy administered IM and IV vs. placebo

Population: Healthy volunteers

RELATIVE DURATION OF SPL028 PSYCHEDELIC EXPERIENCE¹



(a-c) See Appendix – Footnotes and Sources and "Cautionary Notes – Forward-Looking Information", "Risk Factors" and "Treatment Claims"
 (1) Diagram is illustrative; not representative of scale

Advancing meaningful IP to support our novel and differentiated medicines of DMT and related tryptamines^{a,b}

Synthetic GMP route of DMT & other tryptamines

3 patent applications pending

99.9% High purity vs. literature^{a,1}

65% High yielding^{b,2}

\$ Low cost^{b,3} and scalable^{b,4} proprietary manufacture route

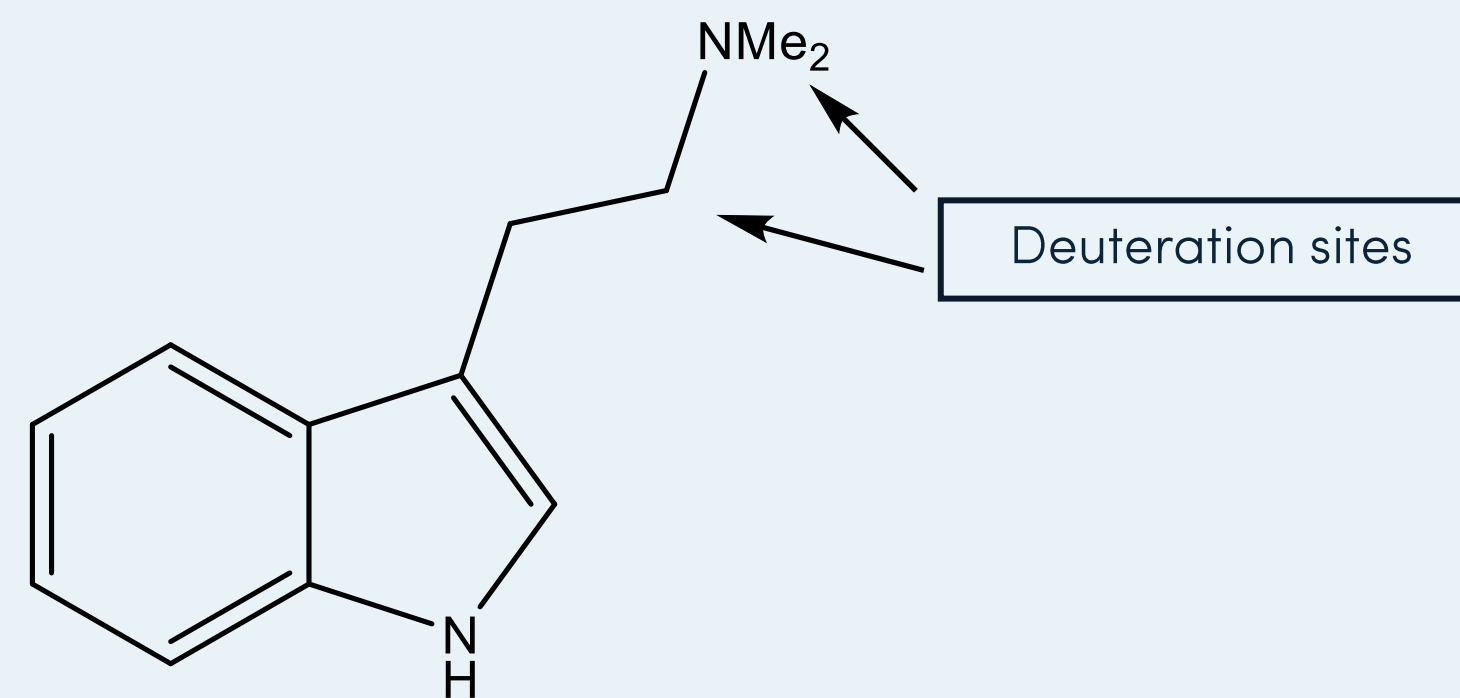


- (a,b,1,5) See Appendix – Footnotes and Sources and "Cautionary Notes – Treatment Claims", "Forward-Looking Information" and "Risk Factors".
(2) Based upon a comparison with the prior art
(3) The starting material in the manufacture of SPL026 is currently inexpensive
(4) To the best of our knowledge, the GMP manufacturing route will scale up sufficiently to support intended use

Deuterium compositions

32 patent applications pending
UK patent granted⁵

Generating novel chemically engineered DMT and related analogues to expand pipeline of psychedelic based medicines



Deuterium modification of DMT

Drug Product

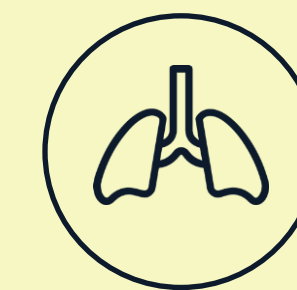
12 patent applications pending



Optimized injectable formulation²









Enhanced oral bioavailability²




Inhaled formulation with extended therapeutic effect²

We have one of the most advanced clinical psychedelic programs in the market

Table compares companies with most advanced psychedelic clinical programs and market capitalization¹

	PHASE I / PHASE IIA	PHASE IIb	PHASE III
DMT	 Small Pharma C\$93M		
5-MEO-DMT	 GH Research C\$1.09Bn		
R-KETAMINE	 ATAI C\$1.17Bn		
PSILOCYBIN		 Compass C\$765M	
LSD	  MindMed C\$652M		

 Short acting psychedelics

C\$ - Market capitalization in Canadian dollars^{2,3}

 Jurisdiction of public listing



(1) To the best of Small Pharma's knowledge, based on available public disclosure as of Mar 1, 2022
 (2) Represents market capitalization as of Mar 1, 2022 as of latest available public disclosures (total shares outstanding * share price at market close)
 (3) Exchange rate as of Mar 1, 2022 USD\$1: C\$1.2698

2022

key upcoming milestones^{a,b,c}

SPL026 R&D

SPL026 Phase IIa study complete

Topline data readout on DMT therapy to treat MDD in H1 2022

SPL026 Phase I drug interaction study start

SPL026 Phase I IM/IV study start

SPL026 Phase IIb study start

- an international, multi-site clinical trial in H2 2022

Pipeline R&D

SPL028 study start

First clinical study of extended duration DMT therapy in humans initiates in H2 2022

SPL029 nonclinical studies to complete

Selection of SPL029 candidate

IP

Maturation and expansion of patent portfolio

across all assets



(a-c)

See Appendix – Footnotes and Sources and “Cautionary Notes – Treatment Claims”, “Forward-Looking Information” and “Risk Factors”

Thank you

Footnotes and sources

General

- a) Certain statements regarding tryptamine-based treatments have not been evaluated by the UK 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.

PAGE 4

- 1) <https://www.ipo.gov.uk/p-ipsu/Case/ApplicationNumber/GB2008303.6>

PAGE 5

- 1) Carbonaro, T. M., & Gatch, M. B. (2016). Neuropharmacology of N,N-dimethyltryptamine. *Brain Research Bulletin*, 126, 74–88. <https://doi.org/10.1016/j.brainresbull.2016.04.016>
- 2) Carhart-Harris, R.L., Roseman, L., Bolstridge, M. et al. Psilocybin for treatment-resistant depression: fMRI-measured brain mechanisms. *Sci Rep* 7, 13187 (2017). <https://doi.org/10.1038/s41598-017-13282-7>
- 3) <https://www.healthline.com/health/substance-use/lsd-vs.-shrooms#the-trip>
- 4) Carbonaro, T. M., & Gatch, M. B. (2016). Neuropharmacology of N,N-dimethyltryptamine. *Brain Research Bulletin*, 126, 74–88. <https://doi.org/10.1016/j.brainresbull.2016.04.01> See "Cautionary Notes – Treatment Claims", "Forward-Looking Information" and "Risk Factors"
- 5) Manske R.H.F. (1931). "A synthesis of the methyltryptamines and some derivatives". *Canadian Journal of Research*. 5 (5): 592–600 Bibcode:1931CJRes...5..592M. doi:10.1139/cjr31-097

PAGE 6

- 1) Based on current academic data on speed of onset and durability of potential treatment efficacy (near immediate and lasting months) of psilocybin to treat TRD (see ref 2 on Page 5). Brain imaging data suggests DMT has similar effects in the brain to psilocybin and may suggest possibility of similar efficacy outcomes.
- 2) <https://healthtalk.org/experiences-antidepressants/starting-to-take-an-antidepressant-for-the-first-time>
- 4) Winstock AR, Kaar S, Borschmann R. Dimethyltryptamine (DMT): Prevalence, user characteristics and abuse liability in a large global sample. *Journal of Psychopharmacology*. 2014;28(1):49–54. doi:10.1177/0269881113513852
- 7) The starting material in the manufacture of SPL026 is currently inexpensive

PAGE 9

- 1) <https://www.who.int/teams/mental-health-and-substance-use/mental-health-in-the-workplace>
- 3) National Institute of Mental Health, 2017
- 4) <https://www.who.int/news/item/02-03-2022-covid-19-pandemic-triggers-25-increase-in-prevalence-of-anxiety-and-depression-worldwide>
- 5) American Association of Suicidology, 2009
- 6) <https://www.who.int/news/item/13-04-2016-investing-in-treatment-for-depression-and-anxiety-leads-to-fourfold-return>
- 8) COVID-19 Mental Disorders Collaborators, Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic, *The Lancet* 2021, [https://doi.org/10.1016/S0140-6736\(21\)02143-7](https://doi.org/10.1016/S0140-6736(21)02143-7)

PAGE 10

- 1) Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. *Lancet*. 2018;391(10128):1357–1366. doi:10.1016/S0140-6736(17)32802-7
- 2) <https://www.cdc.gov/nchs/products/databriefs/db377.html>
- 3) Hengartner MP, Plöderl M. Statistically Significant Antidepressant-Placebo Differences on Subjective Symptom-

- Rating Scales Do Not Prove That the Drugs Work: Effect Size and Method Bias Matter!. *Front Psychiatry*. 2018;9:517. Published 2018 Oct 17. doi:10.3389/fpsy.2018.00517
- 4) Bull SA, Hunkeler EM, Lee JY, Rowland CR, Williamson TE, Schwab JR, Hurt SW. Discontinuing or switching selective serotonin-reuptake inhibitors. *Ann Pharmacother*. 2002 Apr;36(4):578–84. doi: 10.1345/aph.1A254. PMID: 11918502.
- 5) Sim K, Lau WK, Sim J, Sum MY, Baldessarini RJ. Prevention of Relapse and Recurrence in Adults with Major Depressive Disorder: Systematic Review and Meta-Analyses of Controlled Trials. *Int J Neuropsychopharmacol*. 2015 Jul 7;19(2):pyv076. doi: 10.1093/ijnp/pyv076. Erratum in: *Int J Neuropsychopharmacol*. 2016 Apr 27;: PMID: 26152228; PMCID: PMC4772815.
- 6) Davies J, Read J. A systematic review into the incidence, severity and duration of antidepressant withdrawal effects: Are guidelines evidence-based? *Addict Behav*. 2019 Oct;97:111–121. doi:10.1016/j.addbeh.2018.08.027. Epub 2018 Sep 4. PMID: 30292574

PAGE 11

- 1) Kaiser RH, Andrews-Hanna JR, Wager TD, Pizzagalli DA . Large-scale network dysfunction in major depressive disorder: a meta-analysis of resting-state functional connectivity. *JAMA Psychiatry* 2015; 72: 603–611.
- 2) Hamilton JP, Farmer M, Fogelman P, Gotlib IH. Depressive Rumination, the Default-Mode Network, and the Dark Matter of Clinical Neuroscience. *Biol Psychiatry*. 2015;78(4):224–230. doi:10.1016/j.biopsych.2015.02.020
- 3) Wei Liu, Tongtong Ge, Yashu Leng, Zhenxiang Pan, Jie Fan, Wei Yang, Ranji Cui, "The Role of Neural Plasticity in Depression: From Hippocampus to Prefrontal Cortex", *Neural Plasticity*, vol. 2017, Article ID 6871089, 11 pages, 2017. <https://doi.org/10.1155/2017/6871089>
- 4) Carhart-Harris Robin, Leech Robert, Hellyer Peter, Shanahan Murray, Feilding Amanda, Tagliazucchi Enzo, Chialvo Dante, Nutt David, "The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs", *Frontiers in Human Neuroscience* , 2014. <https://doi.org/10.3389/fnhum.2014.00020>
- 5) Ly, C., Greb, A. C., Cameron, L. P., Wong, J. M., Barragan, E. V., Wilson, P. C., Burbach, K. F., Soltanzadeh Zarandi, S., Sood, A.,

- Paddy, M. R., Duim, W. C., Dennis, M. Y., McAllister, A. K., Ori-McKenney, K. M., Gray, J. A., & Olson, D. E. (2018). Psychedelics Promote Structural and Functional Neural Plasticity. *Cell Reports*, 23(11), 3170–3182. <https://doi.org/10.1016/j.celrep.2018.05.022>

PAGE 24

- 1) Shulgin, A. T., & Shulgin, A. (1997). *Tihkal: The continuation*. Berkeley, CA: Transform Press.
- 5) <https://www.ipo.gov.uk/p-ipsu/Case/ApplicationNumber/GB2008303.6>

