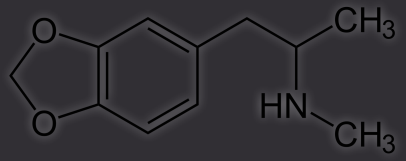
# **emyria** (ASX:EMD)

## MDMA-Inspired Drug Discovery

*Developing novel medicines for neuropsychiatric conditions, inspired by MDMA*




**13 Oct 2022** | Webinar

Dr Michael Winlo (Emyria)

Prof Matt Piggott (UWA)

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**Presentation release authorised by Michael Winlo, CEO and Managing Director**



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# MDMA-INSPIRED DRUG DISCOVERY | EMYRIA & UWA


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**Michael Winlo**

**Matt Piggott**


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THE UNIVERSITY OF WESTERN AUSTRALIA



# emyria

A clinical stage biotech, informed by patient experience, focused on unmet needs in neuroscience and mental health

emyria

**An Australian public biotech company listed on the Australian Stock Exchange**

**(EMD:ASX)** 2019

| | |
|---|---|
| **CLINICAL FOCUS** | **Neuroscience** and **mental health** |
| **LEADING PROGRAMS & TRACTION** | **CLINICAL: ULTRA-PURE CANNABINOID MEDICINES**<br>• Emyria's proprietary "RX" platform improves the bioavailability, release profile, safety & tolerability of cannabinoid-based medicines<br>• Supports multiple global drug registration opportunities; FDA-ready<br>• *First dose form (EMD-RX5) in Phase 3 clinical trials*<br><br>**PRECLINICAL: MDMA-INSPIRED MEDICINE DISCOVERY**<br>• One of world's largest libraries of unique entities inspired by MDMA<br>• Partnership with Prof Matt Piggott, world recognised expert in amphetamine chemistry, from University of Western Australia<br>• *Preclinical program commenced with global leaders* |
| **COMPARATIVE ADVANTAGES** | • **Proprietary Real-World Data & tech** co-created with patients<br>• **A specialist clinical service** *(Emerald Clinics)*<br>• **Unique drug delivery platform**<br>• **Proprietary MDMA-inspired chemical entity library**<br>• **Global leadership** team with drug registration successes |
| **IP & PROTECTION** | **Growing patent library** covering **novel formulations**, **methods of treatment** and **new chemical entities** |

# **EMYRIA** | INVESTMENT HIGHLIGHTS

## 1 **Ultra-Pure cannabinoid** formulation technology, partnership ready

Demonstrated benefits over incumbent technologies. No THC or impurities; low patient variability; slow release and high bioavailability. Can support multiple dose forms and multiple indications.

## 2 **Advanced clinical programs**

**EMD-RX5:** In pivotal *Phase 3* clinical trials to support over-the-counter registrations

**EMD-RX7:** Preparing for *Phase 1* trials, preclinical studies show 4x bioavailability compared to Epidyolex

## 3 Dose response insights from **Real World Data (RWD)**

Emyria's clinical service, **Emerald Clinics**, gathers proprietary clinical data with patients that guides and de-risks indication selection, dose form development and pivotal clinical trial design.

## 4 **Substantial R&D pipeline**

**One of world's largest MDMA analogue libraries** - novel, small, stable, brain-penetrating and neuroactive molecules with potential to become novel neuropsychiatric treatments

## 5 **World-class team** with multiple FDA registrations

**Emyria's in-house expertise** covers drug development, clinical trials, drug registration, data analysis and patient care

**TODAY'S FOCUS**

# emyria | VISION

**Accelerate** the development of promising treatments where *evidence* is lacking **BY COLLABORATING WITH :**

**PATIENTS** to generate **CLINICAL DATA** **&** **GLOBAL EXPERTS** to create **NEW TREATMENTS** *(formulations & analogues)*

Continue **expanding** our well advanced proprietary cannabinoid Drug Development program - Ultra-Pure CBD

**Become a global leader in the development of neurological treatments inspired by MDMA**



1. See ASX announcement 5 August 2021 2. See ASX announcements August 2022

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THE GROWING INTEREST IN

# PSYCHEDELIC ASSISTED THERAPY

# MENTAL HEALTH DISORDERS

*"Affects **1 in 4 People**, Globally"*

## POST-TRAUMATIC STRESS DISORDER (PTSD)



**2 in 3**

**Veterans suffer** from PTSD

**20-30%** of PTSD sufferers show some response to pharmacotherapy

**50%** respond to any treatments.

**Remission rates are as low as 5%.**

Cohen Veterans Network

## MAJOR DEPRESSION

**264 million**



People **suffer depression** globally

**40-60%** show *some* response to pharmacotherapy

**50-80%** relapse after treatment stops

**Common side effects of antidepressants**: Insomnia, psychosis, blurred vision, dry mouth, fatigue,GI distress, weight gain, nausea and sexual dysfunction

World Health Organization

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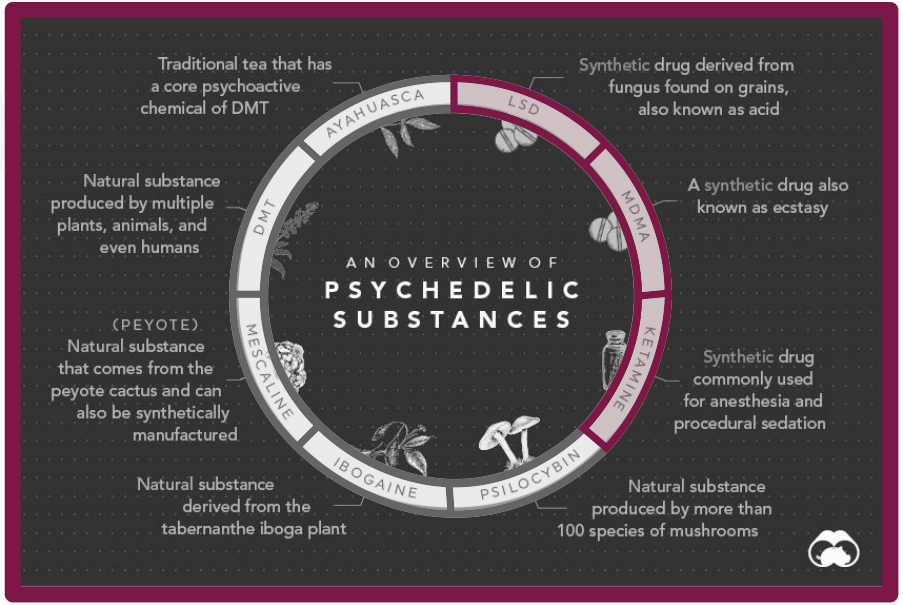
https://jeatdisord.biomedcentral.com/articles/10.1186/s40337-017-0145-3
https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/treatment-recovery

# **PSYCHEDELIC-ASSISTED THERAPY** | WHAT IS IT?

Psychedelics alter communication between brain networks, such as the Default Mode Network (DMN), which are associated with many mental illnesses.

Thought to enable patients to break out of rigid styles of thinking, feeling and behaving.

Promotes a form of “active coping”, restoring patient agency and allowing supportive therapy to become more durable.




https://www.visualcapitalist.com/sp/the-history-of-psychedelics-part-1-of-2/

# NOVEL **PSYCHEDELIC MEDICINE** DEVELOPMENT IS ATTRACTING MAJOR INVESTMENT GLOBALLY

cg Canaccord Genuity

**$100b**

Estimated market for psychedelic medicines

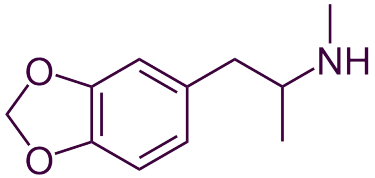
| COMPANY | PROGRAMS + FOCUS | MARKET CAP ($AUD) |
|---|---|---|
| **RELMADA THERAPEUTICS** | **Esmethadone** (NMDAR antagonist), **psilocybin** (5HT2A) and esmethadone derivatives | **$1,600M** |
| **GH RESEARCH** | Exclusively focussed on **5-MeO-DMT** (5HT1A >> 5HT2A agonist) | **$940M** |
| **ATAI LIFE SCIENCES** | Parallel programs: **Psilocybin**, DMT (5HT2A receptor agonists), **MDMA-analogues**, arketamine, Ibogaine, Kratom, Salvinorin A | **$860M** |
| **COMPASS PATHWAYS** | **Psilocybin**, other 5HT2A agonists and unspecified compounds in development | **$780M** |
| **MIND MEDICINE INC** | 3 compounds in clinical development: **LSD**, **MDMA isomer**, and an **ibogaine** derivative. Novel preclinical stage phenethylamine, tryptamine, & ergoline derivatives | **$400M** |
| **emyria** | MDMA-inspired drug discovery AND: Proprietary cannabinoid formulation development **in Phase 3 trials** | **~$60M** |

https://psychedelicalpha.com/psychedelic-stock-watchlist (Accessed 11 Oct 2022)

# WHAT IS **MDMA** ?



# WHAT IS **MDMA?**




**MDMA *(3,4-methylenedioxymethamphetamine or "ecstasy")***
- an amphetamine that causes release of 3 neurotransmitters:

1

**Serotonin**
contributes to mood, prosocial effects

2

**Dopamine**
associated with reward, euphoria

3

**Noradrenaline**
stimulant activity, attention

**MDMA** is the best known member of the **"entactogens"** - drugs that produce feelings of ***emotional communion*****,** oneness, relatedness, emotional openness and fear extinction.

# UNIQUE PSYCHOPHARMACOLOGICAL **EFFECTS OF MDMA**

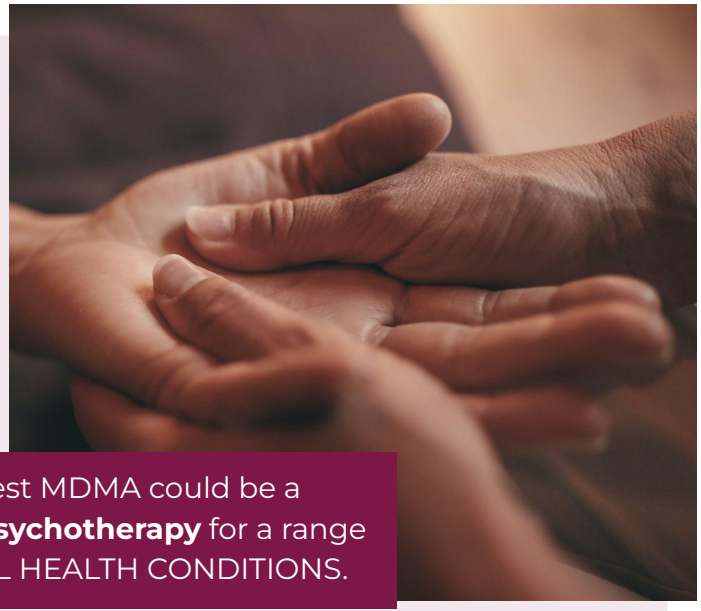
**INCREASED**

- feelings of wellbeing
- sociability and extroversion
- interpersonal trust

**AN ALERT BUT ALTERED STATE OF CONSCIOUSNESS**

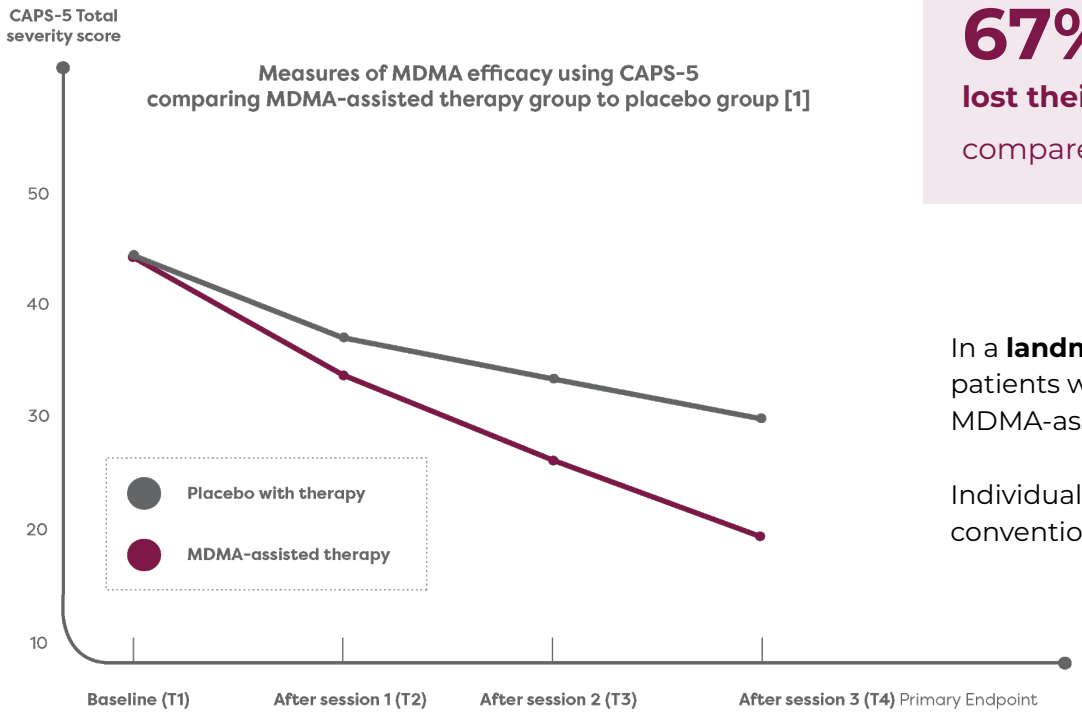
**DECREASED**

- feelings of fear & defensiveness



These effects suggest MDMA could be a promising **adjunct to psychotherapy** for a range of challenging MENTAL HEALTH CONDITIONS.

# **THERAPEUTIC APPLICATIONS** - MDMA-ASSISTED THERAPY **FOR PTSD**




**67%** Of participants in the MDMA group **lost their PTSD diagnosis** following treatment, compared to **32%** in the therapy-only group.

In a **landmark Phase 3 study** (n = 91) [1], patients with PTSD were randomized to receive MDMA-assisted therapy or therapy with placebo.

Individuals had severe illness refractory to all conventional treatment for an **average of 15 years**.

1. Trial of MDMA-assisted therapy for severe PTSD, Multidisciplinary Association for Psychedelic Studies (MAPS), 2021

# MDMA-INSPIRED
## DRUG DISCOVERY

with

THE UNIVERSITY OF WESTERN AUSTRALIA



# MDMA-INSPIRED DRUG DISCOVERY

NEW DRUG DEVELOPMENT

**"Emyria is creating new chemical entities with the potential to become neuropsychiatric treatments"**



## WHY MDMA?

**Privileged chemistry**
- Small, stable, brain-penetrating molecules
- Many points of diversification (create)

**Neurologically active**
- MDMA hits many brain targets
- Opportunities to tune selectivity

**Promising adjunct to psychotherapy**
- Receptiveness & positive mood
- Unique prosocial effects
- Effective adjunct to psychotherapy for PTSD *(but long, 8-12 hour sessions)*

## INNOVATION OPPORTUNITIES WITH MDMA-ANALOGUES

**Adjust metabolism?**
- Shorter treatments
- Avoid potentially toxic metabolites

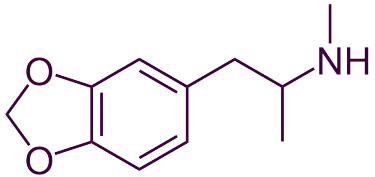
**Adjust neurological effects?**
- Reduce stimulant "amphetamine effects"
- Moderate or remove euphoria

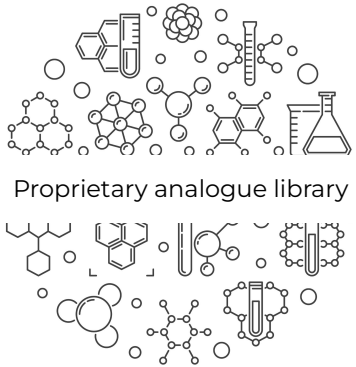
**New treatment opportunities?**
- Improve safety of psychedelic-assisted therapy
- Shorter psychotherapy sessions
- Treatments for other neurological conditions

# **MDMA-INSPIRED** DRUG DISCOVERY | WORKFLOW

**NEW DRUG DEVELOPMENT**

**Take MDMA as inspiration** → **Design and synthesise new compounds** → **Screen analogues** (In vitro and In vivo) → **Prioritise indications**



Proprietary analogue library

- Pharmacology (target) screens
- Safety screens
- Behavioural studies
- Metabolism assays
- Peripheral effects



Next-gen MDMA



Neuropsychiatric treatments



Non-neurological treatments

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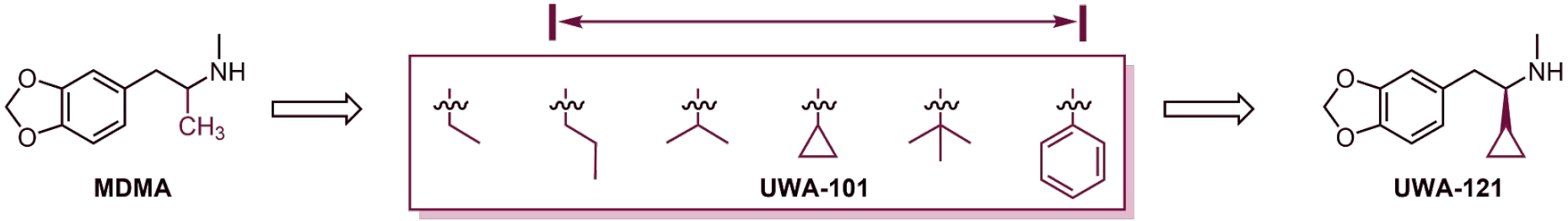
# CASE STUDY: UWA-121, an MDMA-analogue for Parkinson's disease

**NEW DRUG DEVELOPMENT**

Background Video




\+ Profound improvement of PD therapy

— Psychoactivity unsuitable for a chronic condition

Small series of MDMA analogues evaluated in rat and primate models

Single enantiomer (mirror image) most promising

**In the gold-standard PD primate model, UWA-121:**

- **Extends** on-time by **40%**
- Increases **'good quality'** on-time by **215%**

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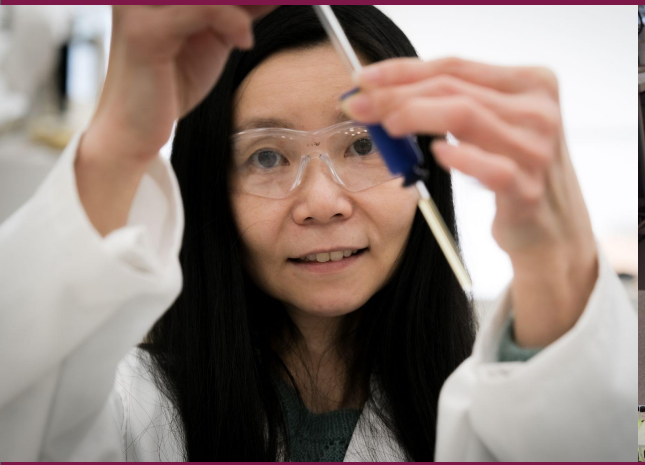
# **THE UWA** TEAM

THE UNIVERSITY OF WESTERN AUSTRALIA



**Dr Joelie Loh**
*Analytical chemistry Data curation*



**Adam Fielding**
*(Honours student)*



**Dr Glenn Pullella**
*Design & Synthesis*

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# PROGRESS

## AND NEXT STEPS *with* THE UNIVERSITY OF WESTERN AUSTRALIA

# **MDMA-INSPIRED DRUG DISCOVERY** | PROGRESS TO DATE

**NEW DRUG DISCOVERY**

**with** THE UNIVERSITY OF WESTERN AUSTRALIA

## THE MDMA ANALOGUE LIBRARY

- **>140** unique MDMA analogues -created and characterised
- Ongoing synthesis and screening [1] *(grew 40% since partnership)*
- Very few with “off-target” effects
- Verified **excellent purity & stability**
- Multiple patent families
- Preclinical program launched



**LIBRARY EXCLUSIVELY OPTIONED TO EMYRIA**



1. See ASX announcement 5 August 2021 2. See ASX announcements August 2022

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# **MDMA-INSPIRED DRUG DISCOVERY** | POTENTIAL OF NEW TREATMENTS

| THERAPEUTIC CLASS | RECEPTOR ACTION | COMMERCIALISED EXAMPLES | MARKET SIZING ($US) |
|---|---|---|---|
| **5HT2B** antagonists | **Antagonism** of 5HT2B | **No approved selective 5HT2B antagonists**<br>One company developing drugs for this target exclusively (**Anamar**) | **Fibrosis**<br>*Sales of Esbriet =* ***$1.0b***<br>*Sales of Ofeb =* ***$2.4b*** |
| Increased **dopamine** neurotransmission | More selective for **DAT** > NET or SERT | **Modafinil** (improves wakefulness in narcolepsy, OSA, shift work) | **Narcolepsy**<br>*Sales of Xyrem+Xywav =* ***$1.8b***<br>*Sales of Sunosi = $58m* |
| Increased **noradrenaline** neurotransmission | More selective for **NET** > DAT or SERT | **Edronax** (Depression)<br>**Strattera** (ADHD)<br>**Qelbree** (ADHD, formerly depression) | **Depression**<br>*8.9m US adults have medication treated depression 2.8m are treatment-resistant [1]* |
| Increased **dopamine and noradrenaline** neurotransmission | More selective for **DAT + NET** > SERT | **Sunosi** (Daytime sleepiness due to Narcolepsy, OSA)<br>**Ritalin** (Narcolepsy, ADHD)<br>**Adderall** (Narcolepsy, ADHD)<br>**Dexedrine** (Narcolepsy, ADHD) | **ADHD**<br>*~12m have ADHD in the US in 2021 [2], [3]* |

1. Zhdanava, M., Pilon, D., Ghelerter, I., Chow, W., Joshi, K., Lefebvre, P., & Sheehan, J. J. (2021). The prevalence and national burden of treatment-resistant depression and major depressive disorder in the United States. The Journal of Clinical Psychiatry, 82(2), 29169.
2. Willcutt, E. G. (2012). The prevalence of DSM-IV attention-deficit/hyperactivity disorder: a meta-analytic review. Neurotherapeutics, 9(3), 490-499.
3. Fayyad, J., Sampson, N. A., Hwang, I., Adamowski, T., Aguilar-Gaxiola, S., Al-Hamzawi, A., ... & Kessler, R. C. (2017). The descriptive epidemiology of DSM-IV adult ADHD in the world health organization world mental health surveys. ADHD Attention Deficit and Hyperactivity Disorders, 9(1), 47-65.

# **MDMA-INSPIRED DRUG DISCOVERY** | PROMISING EARLY RESULTS

| THERAPEUTIC CLASS | RECEPTOR ACTION | # EMYRIA COMPOUNDS THAT DEMONSTRATE RECEPTOR ACTION |
|---|---|---|
| **5HT2B** antagonists | **Antagonism** of 5HT2B | **Several** |
| **Dopamine** reuptake inhibition (DRI) | More selective for **DAT** > NET or SERT | **Several** |
| **Norepinephrine** reuptake inhibition (NRI) | More selective for **NET** > DAT or SERT | **Several** |
| **Norepinephrine-dopamine** reuptake inhibition (NDRI) | More selective for **DAT + NET** > SERT | **Several** |
| **Serotonin-norepinephrine-dopamine** reuptake inhibition (SNDRI) | **Nonselective** DAT/SERT/NET binding inhibition | **One** |


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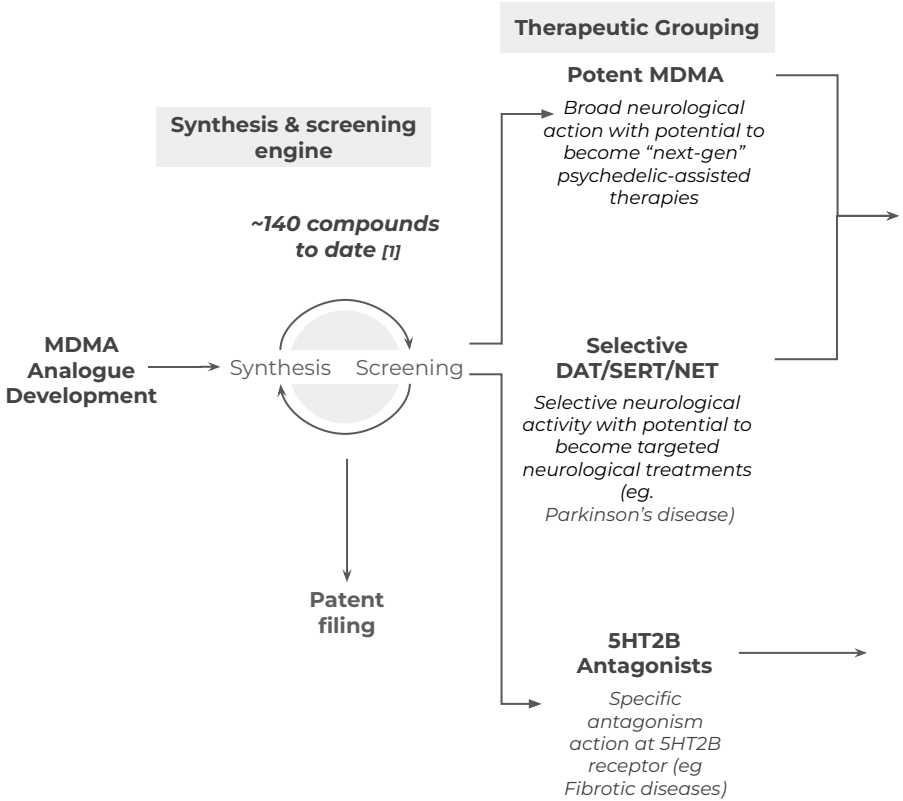
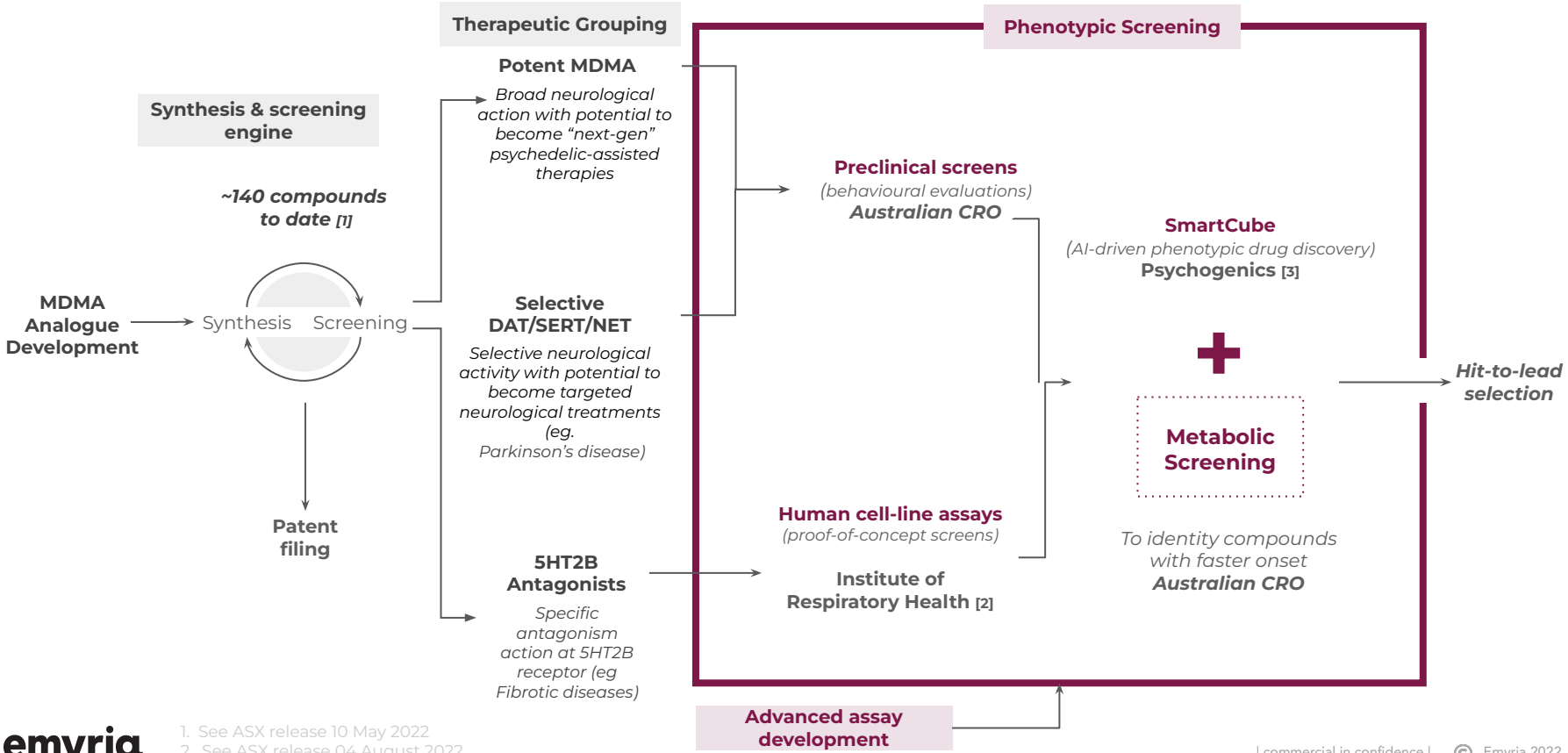
# **MDMA-INSPIRED DRUG DISCOVERY** | SCREENING WORKFLOW




1. See ASX release 10 May 2022
2. See ASX release 04 August 2022
3. See ASX release 19 September 2022

# **MDMA-INSPIRED DRUG DISCOVERY** | PRECLINICAL WORKFLOW

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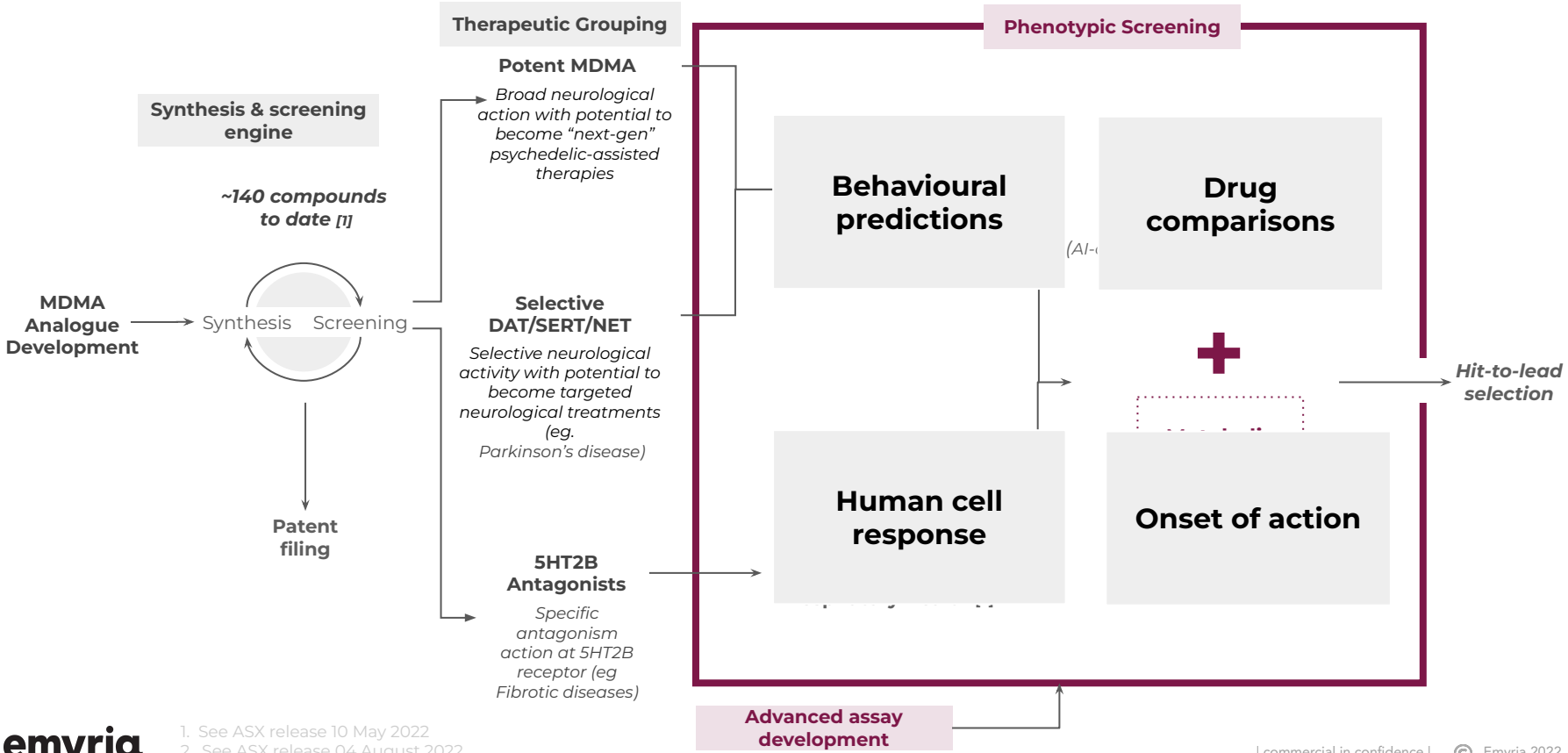
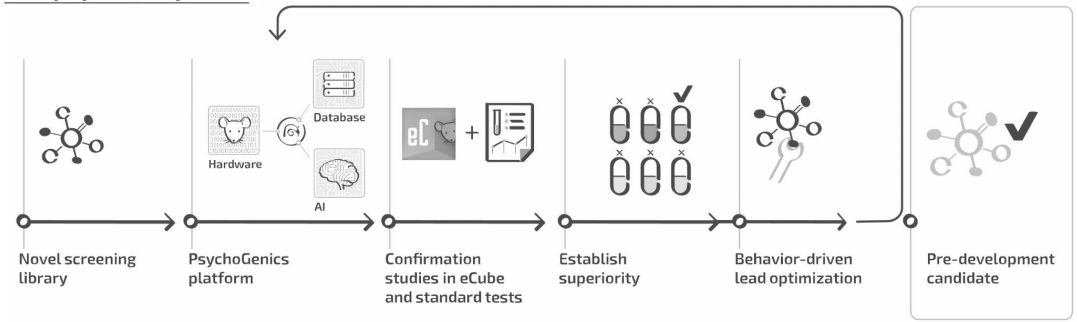
# **MDMA-INSPIRED DRUG DISCOVERY** | PRECLINICAL WORKFLOW




1. See ASX release 10 May 2022
2. See ASX release 04 August 2022
3. See ASX release 19 September 2022

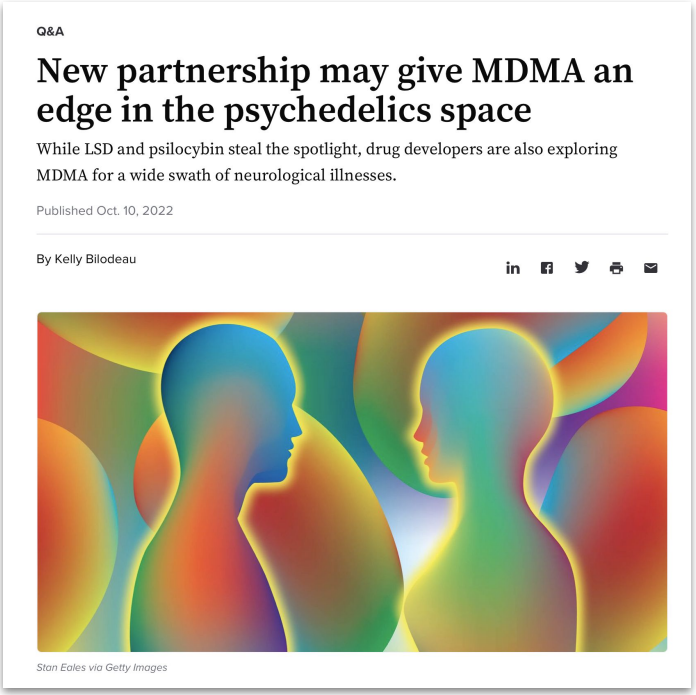
# **ADVANCED PRECLINICAL SCREENING** | SMARTCUBE(R) - computer vision and AI

PsychoGenics
Redefining Drug Discovery Through Innovation




SmartCube® is an automated testing platform that presents a sequence of challenges to a mouse and incorporates computer vision and AI to process and analyze more than half a million data points per mouse per session.

The SmartCube® platform uses proprietary bioinformatics to detect and assess the potential of compounds to treat psychiatric disorders in an unbiased way by comparing their complex behavioral profiles with those from a reference database at the drug class (primary therapeutic indication) and subclass (primary mechanism of action) level.



Q&A

## New partnership may give MDMA an edge in the psychedelics space

While LSD and psilocybin steal the spotlight, drug developers are also exploring MDMA for a wide swath of neurological illnesses.

Published Oct. 10, 2022

By Kelly Bilodeau

*Stan Eales via Getty Images*

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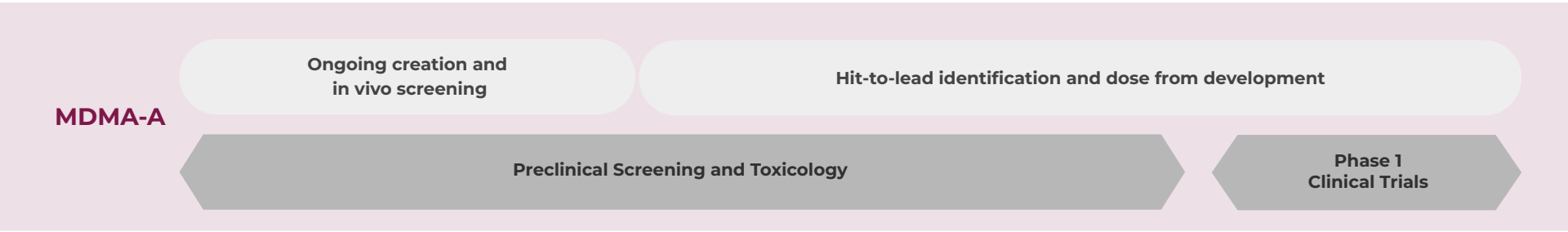
1. See ASX announcement 19 September 2022
2. https://www.pharmavoice.com/news/MDMA-neurological-drug-development-PsychoGenics/633549/

# MDMA-INSPIRED DRUG DISCOVERY | WHAT'S NEXT?

**NEW DRUG DISCOVERY** BACKED BY UWA RESEARCH

**IN THE NEXT 12 MONTHS**, EMYRIA INTENDS TO:

- **Deliver results** from multiple preclinical programs on select MDMA analogues
- **Select leads** by proof-of-concept efficacy studies in animal models
- **Expand** the MDMA-analogue library
- **File** additional patent families and pursue commercialisation discussions



# MDMA-INSPIRED DRUG DISCOVERY | SUMMARY

**NEW DRUG DISCOVERY** BACKED BY UWA RESEARCH

**Emyria-UWA MDMA analogue library captures a unique chemical space with differentiated pharmacology**

- ***Largest reported database*** of MDMA derivatives currently in development with >140 compounds in the library (*and growing*)
- ***Compounds demonstrate diverse receptor binding profiles*** on gold standard screening suggesting broad indication potential
- ***Current list of potential indications spans major unmet needs in:***

**neuropsychiatry** — **&** — **anti-fibrosis**

*(Parkinson's, ADHD, narcolepsy, antidepressants, anxiolytics, antipsychotics, appetite suppression)*

*(currently undergoing preclinical assays)*

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1. See ASX announcement 5 August 2021 2. See ASX announcements August 2022


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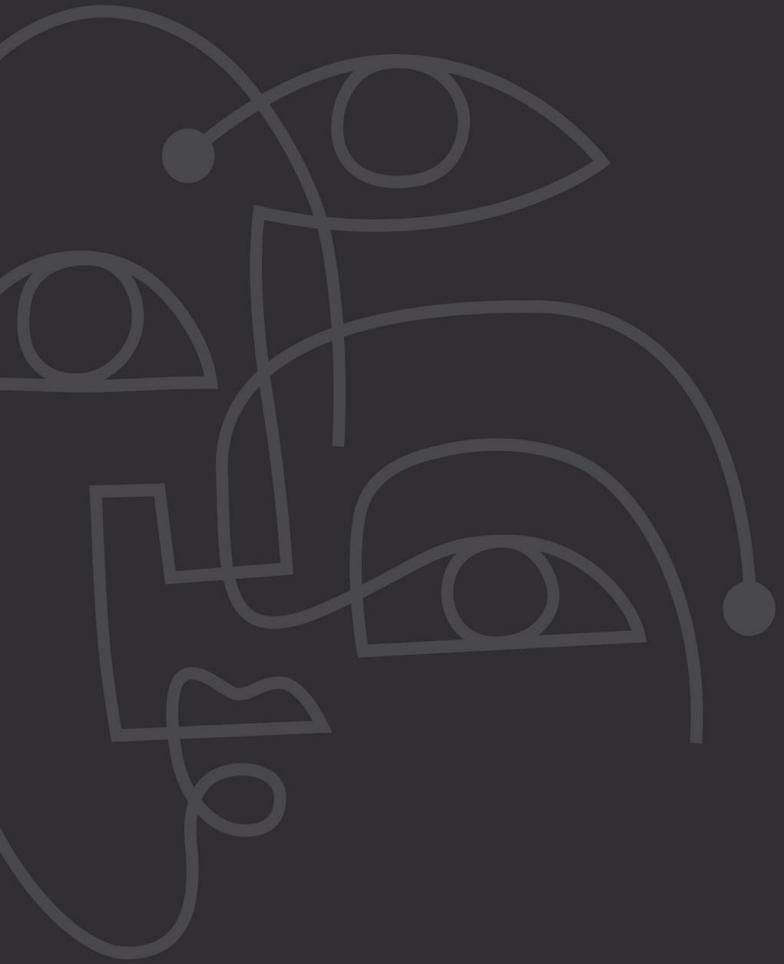
**Questions** & Answers



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