ASX Announcement

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Emyria highlights promising *in vivo* and *in vitro* results from early UWA MDMA-analogue studies

MDMA-analogue UWA-101 shown to improve duration and quality of L-DOPA treatment in a parkinsonian animal model; results demonstrate potential of MDMA analogues to treat Parkinson's disease and other neurological and psychiatric disorders

Highlights:

- Emyria highlights promising results from a previously published study assessing the effects of MDMA (ecstasy) and a unique MDMA-analogue (**UWA-101**) in a Parkinson's disease (PD) model [1]
- Emyria to broaden its screening program to reveal similar MDMA-analogues as potential treatments for PD and other neurodegenerative disorders
- Results indicate that both MDMA and UWA-101 extend the duration of action of L-DOPA (a common treatment for PD) and reduce the proportion of time associated with L-DOPA induced dyskinesia (LID)
- UWA-101 was also shown to have fewer psychoactive effects compared with standard MDMA in animals
- Results highlight the potential of uniquely designed MDMA-analogues to elicit different neurological effects, which may lead to new treatments for psychiatric and neurological disorders such as Parkinson's disease
- Emyria has an exclusive agreement to licence more than 100 MDMA-analogues from UWA, of which UWA-101 is a member; Emyria now driving a comprehensive screening, expansion and IP strategy to identify, develop and commercialise additional promising MDMA-like compounds with psychedelic and other therapeutic potential

Emyria Limited (ASX: EMD) (Emyria or the Company), a data-backed drug development and care delivery company, is pleased to highlight previously published positive results assessing a unique MDMA-analogue (UWA-101) for antiparkinsonian effects.

UWA-101 was discovered by Dr. Matt Piggott and his team at the University of Western Australia (UWA) and is a member of a library of over 100 MDMA-like compounds recently optioned to Emyria exclusively. (*See ASX Announcement 05 August 2021).*

In a study involving a gold standard model of Parkinson's disease (PD), MDMA demonstrated an ability to enhance the effect of the most common PD treatment, L-DOPA. The MDMA-analogue, UWA-101 maintained these beneficial effects but is predicted to be non-psychoactive.

Emyria's Managing Director, Dr. Michael Winlo, said: *"These studies highlight how MDMA-analogues, like UWA-101, can have quite distinct neurological and behavioural effects in animal models. In this case, UWA-101 has shown promise as a potential treatment for Parkinson's disease - a major unmet need, globally.*

These rich data serve as an example of the kind of robust preclinical evidence we already have and anticipate to generate during our comprehensive screening program currently evaluating UWA's unique MDMA-analogue library of more than 100 compounds that our company has exclusive access too.

Emyria and UWA are working diligently to screen and identify additional, novel and patentable MDMA-analogues from within the large compound library. Further positive screening results will form the basis of new drug development programs targeting major psychiatric and neurological disorders, such as Parkinson's disease.

These drug development programs compliment Emyria's interests in MDMA-assisted psychotherapy and are focussed on registering safe and promising treatments with major global regulators like the FDA in the USA once the required clinical development and trials are complete.

Parkinson's disease

Parkinson's disease (PD) is a common, incurable neurological disorder affecting nearly five million people worldwide, including more than 80,000 Australians. The number of Australians with PD is expected to nearly quadruple by 2033. PD is associated with progressive degeneration of dopaminergic neurons and is generally treated with dopamine-replacing agents such as L-DOPA. However, long term L-DOPA therapy is plagued by side effects, such as deteriorating duration and quality of antiparkinsonian action (wearing-off and on-off), and disabling involuntary movements known as L-DOPA-induced dyskinesia (LID). These complications are a major obstacle to the successful pharmacotherapy of PD, and severely impact on patients' quality of life.

Background to UWA-101

Dopaminergic agents, such as L-3,4-dihydroxyphenylalanine (L-DOPA) are commonly used in the treatment of PD and other movement disorders.

In some patients, L-DOPA may have disabling side effects such as dyskinesia, an involuntary movement disorder also called "L-DOPA induced dyskinesia" (LID).

Studies in animal models, and anecdotal evidence from patients with PD, have suggested that 3,4,-methylenedioxymethamphetamine ('MDMA' or 'ecstasy') can alleviate these side effects, albeit with some unwanted effects (e.g., psychoactivity).

By considering existing structure-psychoactivity relationships, Dr. Matt Piggott and his team at UWA created a series of MDMA analogues, including UWA-101 and evaluated these compounds in a series of *in vitro* and *in vivo* studies.

UWA-101 was shown to enhance the quality and duration of L-DOPA action, elicit a unique profile of interactions with brain targets and show a favourable toxicology profile but with reduced psychoactivity compared with MDMA.

Overview of assessments

The experiments to assess the potential of UWA-101 and MDMA comprised:

(1) **Anti-LID assessment:**

A gold standard *in vivo* PD model was used comparing L-DOPA alone and in combination with two dose levels of MDMA and UWA-101, respectively (1mg/kg and 3mg/kg).

Symptoms of parkinsonism (incorporating measures of impairment of range of movements, posture, bradykinesia, and alertness) and dyskinesia (including chorea and dystonia) were assessed by a movement disorder neurologist blinded to the treatments given.

Duration of antiparkinsonian action ("ON-time") was also calculated. This is the amount of time for which disability scores are mild or absent. ON-time is considered "good" quality when there is an absence of disabling dyskinesia or "bad" quality in the presence of disabling dyskinesia.

(2) **Psychoactivity assessments:**

To evaluate whether UWA-101 might have reduced psychoactivity in comparison to MDMA, a series of *in vivo* assessments were made in a variety of models that are traditionally used to define psychopharmacology of MDMA and related drugs.

These tests comprised:

- prepulse inhibition (PPI) - a measure of information processing that may decrease in the presence of a psychoactive drug
- drug discrimination - a measure of an animal's preference for a familiar drug (e.g. amphetamine) which may lead to either a selection of a new (test) drug or less use of it.
- food intake comparisons - a measure of appetite following administration of drug.

(3) **Receptor and transporter affinity binding:**

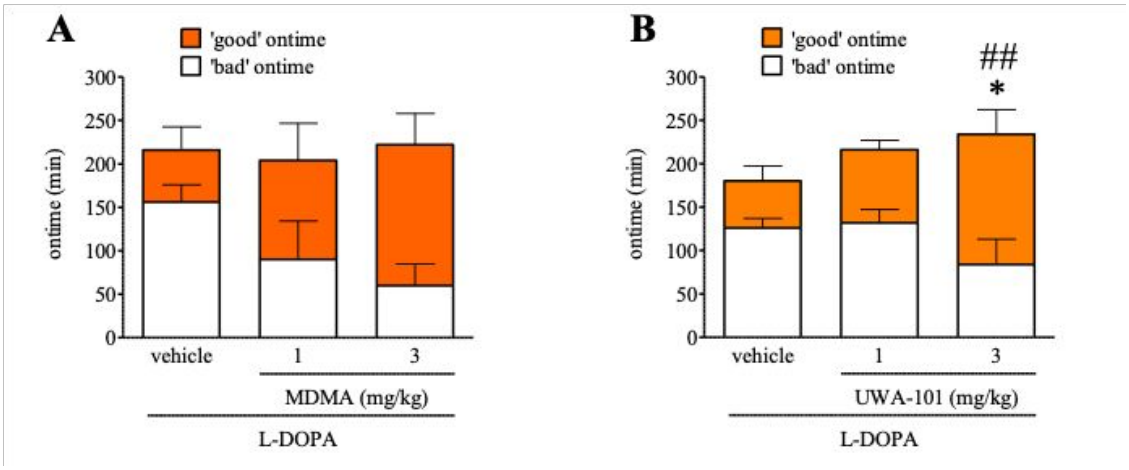
A series of assays were performed to determine the targets that UWA-101 interacts with in the brain. These included neuroreceptor and transporter affinity binding as well as monoamine reuptake assays.

(4) **Toxicology assessments:**

A series of *in vitro* cell viability assays were performed on serotonergic cell lines by exposing those cell lines to different concentrations of UWA-101.

Results

(1) **Effect on quality of "ON-time":**:

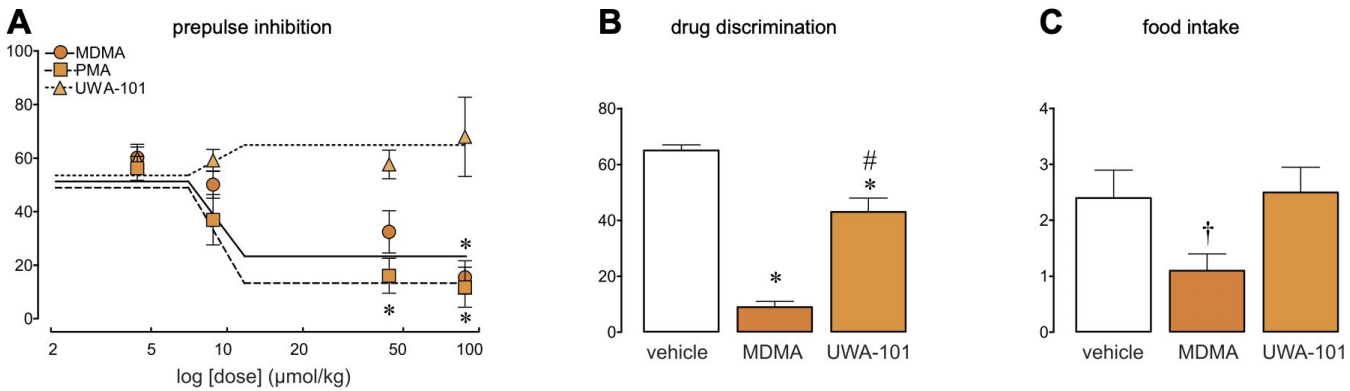


In combination with a vehicle (i.e. in the control experiment), L-DOPA evoked, on average, 204 minutes of ON-time. Less than one-third of this ON-time was of "good" quality (with only mild, moderate or no dyskinesia).

Co-administration of MDMA and L-DOPA evoked no significant change in the total duration of ON-time. However, treatment with MDMA significantly increased (by up to 180%, vehicle vs. 3 mg/kg) the proportion of L-DOPA-induced ON-time that was of "good" quality.

In contrast, UWA-101, had a significant effect on duration of total and good ON-time. UWA-101 increased the total duration of L-DOPA-induced antiparkinsonian benefit (total ON-time) by up to 30%. In addition, UWA-101 (3 mg/kg) significantly increased the duration of "good" quality ON-time by 178%.

(2) **Psychoactivity assessments:**



In agreement with previous reports using agents capable of inducing 5-HT (serotonin) release in rodents, results showed that MDMA and PMA (a structurally related illicit drug with hallucinogenic properties) significantly reduced prepulse inhibition (PPI), whereas treatment with UWA-101 did not elicit any effects consistent with psychoactivity. Further, UWA-101 did not depress appetite, nor did it substitute for MDMA in a drug discrimination assay, indicating that it is highly unlikely that UWA-101 is psychoactive.

(3) **Receptor and transporter affinity binding**

UWA-101 displayed a unique receptor/ transporter binding profile relative to MDMA, with a >5-fold *decrease* in affinity for norepinephrine transporter (NET) and serotonin receptor 5-HT2A, and a 10-fold *increase* in affinity for the dopamine transporter (DAT). Furthermore, in a functional reuptake assay, UWA-101 inhibited both 5-HT (serotonin) and dopamine reuptake, while having no effect on the reuptake of noradrenaline.

(4) **Toxicology**:

UWA-101, did not reduce the cell viability of two neuronal cell lines at any concentration examined.

UWA-101 and potential of other MDMA-analogues

UWA-101 acts to improve both quality and duration of L-DOPA action in a gold standard model of Parkinson's disease.

These positive results suggest UWA-101 could represent a new class of therapeutic in Parkinson's disease but, more broadly, highlights the value of studying MDMA analogues and their potential to become novel therapeutics to address other psychiatric and neurological disorders.

UWA-101 is just one of over 100 MDMA-like compounds that have been synthesised by Dr. Matt Piggott and his research team at UWA and exclusively optioned to Emyria.

Emyria, along with UWA, is now screening and expanding the existing library in order to develop new potential therapies and inform additional drug development programs for Emyria targeting a range of psychiatric and neurological conditions, including Parkinson's disease. This work complements Emyria's interests in MDMA-assisted therapy to treat Post Traumatic Stress Disorder (PTSD) *(See ASX release 05 May 2021)*.

Emyria is also pursuing a global patent strategy to support its commercial objectives and intends to pursue patent protection in key global markets, including the US, Europe and Japan. This aligns with Emyria's global regulatory strategy including plans to pursue registration with the FDA for Emyria's drug development programs.

This announcement has been approved and authorised for release by the Board of Emyria Limited.

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REFERENCES

[1] https://pubmed.ncbi.nlm.nih.gov/22345403/

About Emyria (www.emyria.com)

Emyria Limited is a clinical drug development and care delivery company. **Emyria's Treatments** target large unmet needs and are focused on obtaining approval ("registration") with major global regulators. Emyria's treatment development programs are informed by insights generated from extensive analysis of **Emyria Data** - deep, ethically-sourced clinical evidence that is gathered with patients across Emyria's independent clinical services (**Emerald Clinics** - www.emeraldclinics.com.au)

Emyria Data provides deep treatment insights and is therefore a source of unique IP, strategically designed drug development and personalised care programs.

About University of Western Australia

The University of Western Australia (UWA) is a public research university in the Australian state of Western Australia.

UWA has been ranked as having some of the highest quality undergraduates of any university in Australia and is ranked second in Australia for the quality of its undergraduate programs.

The Academic Ranking of World Universities (ARWU) produced by Shanghai Jiao Tong University has consistently placed UWA as the joint best university in Australia (along with the University of Queensland) in the fields of clinical medicine and pharmacy. UWA is also a leader in the fields of medicinal and biomolecular chemistry according to ERA (Excellence in Research) Research Rankings.

Cautionary Note on Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for the Company, the company's strategy, future operations, and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the Company's ability to successfully develop its product candidates and timely complete its planned clinical programs and the Company's ability to obtain marketing approvals for its product candidates. In addition, the forward-looking statements included in this press release represents the Company's views as of the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date hereof.