

SEAPORT

THERAPEUTICS

Goldman Sachs
Life Sciences Symposium

September 2026



Turning the Tide on Mental Health

Disclaimer

September 15, 2026

This presentation includes forward-looking statements, including, but not limited to, express or implied statements about Seaport's beliefs and expectations regarding: the potential of the Glyph platform to enhance oral bioavailability, bypass first-pass metabolism and reduce hepatotoxicity and other side effects associated with clinically validated neuropsychiatric therapeutics; the continued development and advancement of our Glyph-based product candidates for major depressive disorder, generalized anxiety disorder and other neuropsychiatric disorders, including the timing of the filing of IND and/or CTA applications, the timing of future clinical data, including the timeline data from the GlyphAllo Phase 2b BUOY-1 trial in 1H 2027, timeline data from the GlyphAgo Phase 2a trial in early 2028, timeline data from the GlyphAgo Phase 2b trial by the end of 2028, and the interpretation and clinical regulatory implications of the timeline results from the Phase 1 Driving Simulation Trial of GlyphAllo in healthy volunteers, and our plans to submit the results to the U.S. Food and Drug Administration; complete first-in-human-enabling studies of Glyph2BLSD by YE 2027; the initiation, timing, progress and results of our research and development programs, preclinical studies and future clinical trials, including the release of data related thereto; the timing of, and our ability to achieve, clinical validation and sustained, long-term value creation; projected data announcements; statements related to patient populations and total addressable markets; the implementation of our strategic plans for our business, programs and technology, including our ability to maintain collaborations or strategic relationships and identify and enter into future license agreements and collaborations; regulatory developments in the United States and foreign countries; developments related to our competitors and our industry; our estimates of our expenses, capital requirements, and needs for additional financing; and our expectations regarding the anticipated timeline of our cash runway and future financial performance. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make due to a number of risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including statements regarding our future results of operations and financial position, strategy and plans, industry environment, potential growth opportunities, and our expectations for future operations, are forward-looking statements. The words "believe," "may," "will," "estimate," "continue," "anticipate," "design," "expect," "could," "plan," "potential," "predict," "seek," "should," "would," or the negative of these terms or other similar expressions are intended to identify forward-looking statements. These statements include, among other things, our expectations regarding the potential benefits, activity, effectiveness and safety of our product candidates; our expectations with regard to the results of our clinical trials, preclinical studies and research and development programs, including the timing and availability of data from such studies; our preclinical, clinical and regulatory development plans for our product candidates, including the timing or likelihood of regulatory filings and approvals for our product candidates; our expectations with regard to market growth; and our expectations with regard to our ability to acquire, discover and develop additional product candidates and advance such product candidates into, and successfully complete, clinical trials. These statements involve substantial known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to the Company's research and development activities, including with respect to the Phase 2b BUOY-1 trial; risks that interim results are not predictive of final results in a clinical trial; Seaport's ability to execute on its strategy including obtaining the requisite regulatory approvals on the expected timeline, if at all; uncertainties relating to Seaport's preclinical and clinical development activities; the Company's dependence on third parties to conduct clinical trials, manufacture its product candidates and develop and commercialize its product candidates, if approved; Seaport's ability to attract, integrate and retain key personnel; risks relating to the Company's financial condition, including the need for substantial additional funds to complete development activities and commercialize its product candidates, if approved; risks related to the regulatory developments and approval processes of the FDA and comparable foreign regulatory authorities; risks related to establishing and maintaining Seaport's intellectual property protections; and risks related to the competitive landscape for Seaport's product candidates; as well as other risks and uncertainties described in "Risk Factors" in Seaport's Quarterly Report on Form 10-Q for the three months ended June 30, 2026, filed with the Securities and Exchange Commission ("SEC"), as well as in subsequent filings with the SEC. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation. This presentation concerns product candidates that are under clinical investigation, and which have not yet been approved for marketing by the FDA or any other applicable government agency. Such product candidates are currently limited by Federal law to investigational use, and no representation is made as to the safety or effectiveness for the purposes for which such product candidates are being investigated.

We have based these forward-looking statements on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, strategy, short and long term business operations and objectives, and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions. We operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this presentation may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations. Seaport claims the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

This presentation contains estimates and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, market research or similar methodologies, including prevalence studies which are extrapolated to broader populations, is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from our own internal estimates and research as well as from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. Industry publications and surveys generally state that the information contained therein has been obtained from sources believed to be reasonable and reliable.

Although we believe the industry and market data to be reliable as of the date of this presentation, this information could prove to be inaccurate. Industry and market data could be wrong because of the method by which sources obtained their data and because information cannot always be verified with complete certainty due to the limits on the availability and reliability of raw data, the voluntary nature of the data gathering process and other limitations and uncertainties. While we are responsible for the accuracy of such information and believe our internal company research as to such matters is reliable and the market definitions are appropriate, neither such research nor these definitions have been verified by any independent source. Unless otherwise indicated, information contained in this presentation concerning our industry and the markets in which we operate, including our general expectations, market position and market opportunity, is based on our management's estimates and research, as well as industry and general publications and research, surveys and studies conducted by third parties. Industry publications, studies and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We believe that the information from these third-party publications, research, surveys and studies included in this presentation is reliable. Our management's estimates are derived from publicly available information, their knowledge of our industry and their assumptions based on such information and knowledge, which we believe to be reasonable. This data involves a number of assumptions and limitations which are necessarily subject to a high degree of uncertainty and risk due to a variety of factors. These and other factors could cause our future performance to differ materially from our assumptions and estimates.

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Charting a Proven Path in Neuropsychiatry

Clinical Validation



Clinically validated mechanisms previously held back by issues Glyph™ can address

Glyph™ Platform



"Glyph™" to overcome limitations and create novel drug candidates with strong IP

Proven Team



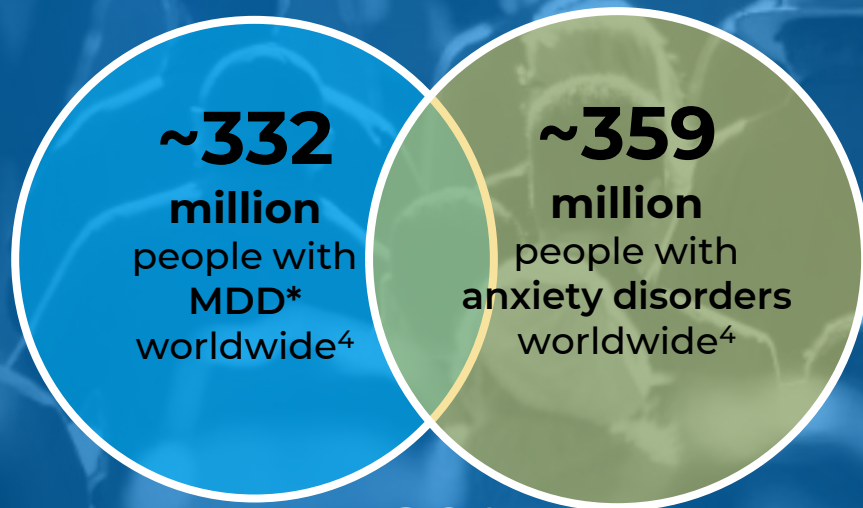
Apply team's expertise to optimize clinical trials and drive successful business outcomes

Cash Runway into 2029 and Through 3 Key Clinical Data Readouts

Over 1 Billion People Are Living with Mental Illness¹



Depression and Anxiety are Highly Comorbid^{2,3}



~60%

of MDD patients also
have **anxious distress**³

Disabling and Deadly

~**20x** increase in suicide risk in
people with MDD⁵

Suicide is a **top 3** cause of death
in ages 10-34⁶

Current Neuropsychiatry Medications

Widely prescribed but have limitations



Peak Sales

ZYPREXA Olanzapine	>\$5B ¹
 Cymbalta chlorhydrate de duloxétine	~\$5B ¹
 Risperdal risperidone	>\$3.5B ¹
Lexapro escitalopram	>\$3.5B ¹
Zoloft (sertraline HCl)	>\$3B ¹
Paxil CR	>\$3B ¹
EFFEXOR XR	~\$3B ¹
PROZAC	>\$2.5B ¹
Celexa citalopram	>\$1.5B ²

Limitations



Modest Efficacy

Ineffective for
~1 in 3 patients ³



Slow Onset

Generally take
weeks to work



Unfavorable Side Effects

Sexual dysfunction,
weight gain, insomnia

A Neuroscience Renaissance

Driven by scientific progress and interest in Big Drugs for Big Diseases



Acquirer	Company	Value
 Bristol Myers Squibb®	 KARUNA THERAPEUTICS	\$14.0B
 Johnson & Johnson	 Intra-Cellular THERAPIES	\$14.6B
 abbvie	 cerevel	\$8.7B

Additional Pharma Companies
Committed to CNS:

 Lilly

 Lundbeck 

 NOVARTIS

 Pfizer

 Roche

 sanofi

 Takeda

 Biogen

 ucb

Seaport Uniquely Positioned to Outperform in Neuropsychiatry Drug Development



Neuropsychiatry Challenges

Fundamental pathophysiology unknown

>90% clinical trial failure rate¹

Poor drug-like properties

Poor oral bioavailability and/or PK*, poor safety & tolerability

Challenging clinical studies

Difficult to demonstrate efficacy

Seaport's Approach



Identify drugs with validated efficacy



Overcome hurdles using Glyph™ platform & generate new IP



Proven team leading better designed & executed trials

Seaport's Proven Team & Approach

Karuna case study: Successful outcome for patients and shareholders



STEVEN PAUL, MD
Former Board Chair
& CEO, Karuna



DAPHNE ZOHAR
Co-founder of Karuna,
originator of KarXT

COBENFY™
FDA-approved
in 2024



Identified drug with
validated efficacy
(xanomeline)



Overcame hurdles
with Cobenfy™



Proven team led better
designed & executed trials

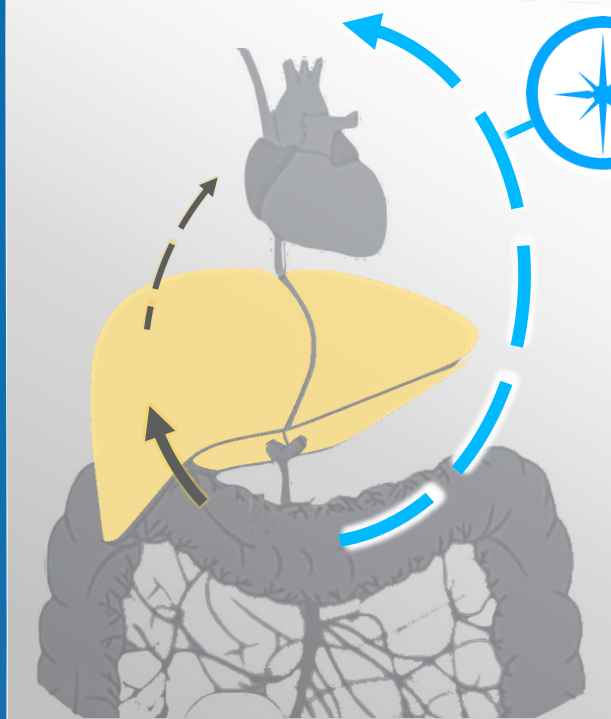
Our Proprietary Glyph™ Platform

Unlocks active drugs previously limited by high first-pass metabolism



Conventional Delivery

Oral drugs with high first-pass metabolism can have **low bioavailability** and **risk of hepatotoxicity**

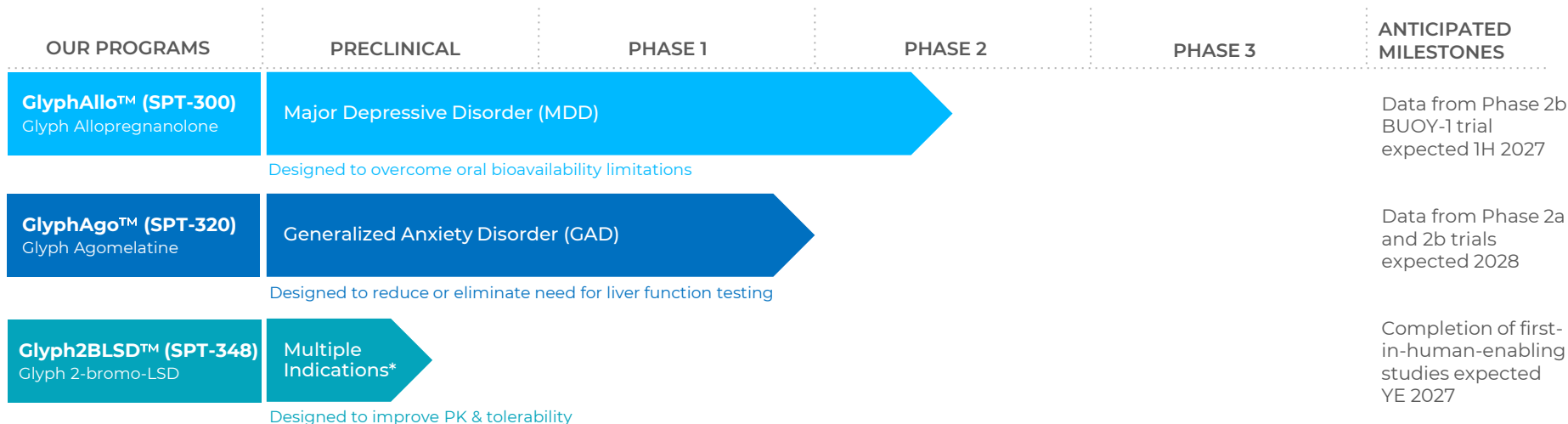


Glyph™ Platform

Employs the lymphatic system's natural lipid absorption and transport process to **bypass the liver**

- Reduces first-pass hepatotoxicity
- Enhances oral bioavailability
- Reduces PK* variability
- Reduces dose
- Generates new IP

Pipeline of Novel Potential Treatments for Neuropsychiatric Disorders



*Neuropsychiatric and headache disorders with significant unmet need

**Glyph™ aims to unlock potential of drugs in CNS and beyond:
Multiple preclinical programs underway**

GlyphAllo™ is Designed to Overcome Low Bioavailability of Allopregnanolone



Allopregnanolone Benefits

- Naturally occurring molecule that reduces stress¹
- Clinically validated in third-party trials as a rapidly acting antidepressant with anxiolytic and sleep-promoting effects^{2,3}
- 5 of 6 trials of a synthetic analog (zuranolone) met primary endpoint in MDD⁴



Key Limitation

Due to poor oral bioavailability, allopregnanolone has only been available via 60-hour infusion



GlyphAllo™ Approach

Overcome poor bioavailability of allopregnanolone and deliver rapid, durable efficacy in MDD

Overcome trial design limitations

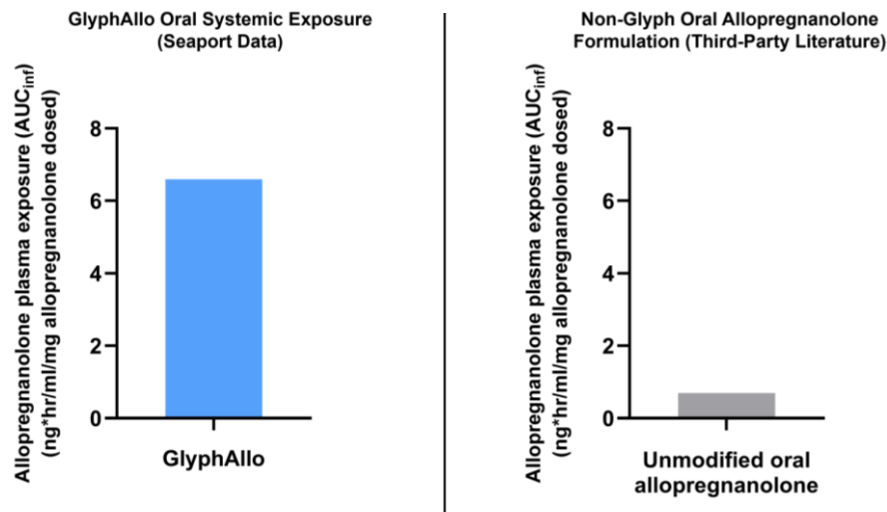
GlyphAllo™ Reaches Therapeutically Relevant Exposures with a Favorable Tolerability Profile



Key PK and Safety Data

- Bioavailability **>9X** vs. oral allopregnanolone¹
- Generally well-tolerated, adverse events generally mild & transient
- Most common AE was somnolence (on-target effect of GABA_A)
- No treatment-related severe or serious AEs

Clinical GlyphAllo™ Oral Systemic Exposure and Literature Data^{2,3}



1. In preclinical studies in non-human primates; 2. Not a head-to-head; comparative values from brexanolone NDA 211371 Multi-disciplinary Review and Evaluation, FDA CDER, 2018. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials; 3. Chen et al. (2024). A First-in-Human Phase I Study of SPT-300, a First-in-Class Orally Bioavailable Prodrug of the Neurosteroid Allopregnanolone That is Absorbed via the Lymphatic System. Society of Biological Psychiatry (SOBP) Annual Meeting, 2024, Austin, TX, United States; AUC(0-inf) of SPT-300 and Study 547-CLP-107 (in ref 1: Brexanolone NDA) were divided by mg allopregnanolone dosed, then both values divided by that dose-normalized AUC of 547-CLP-107 to show relative exposure at an equivalent dose.

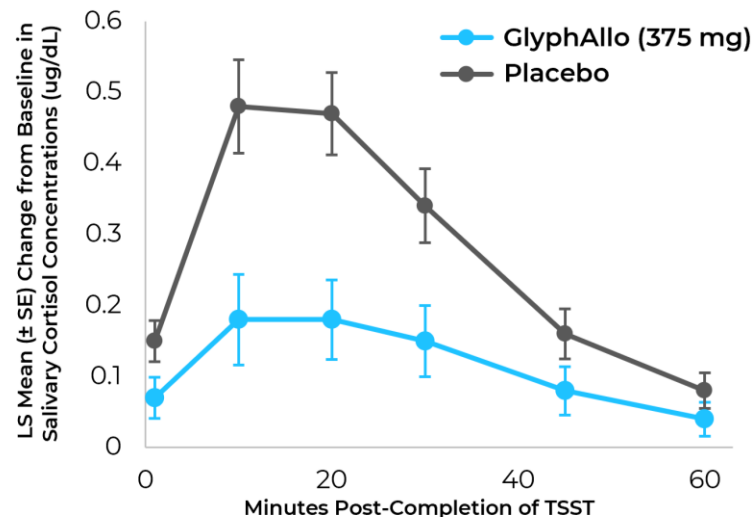
Phase 2a Results: GlyphAllo™ Significantly Reduced Stress Response Compared to Placebo ($p=0.0001$)¹



GlyphAllo™ Demonstrated Initial Proof-of-Concept

- Generally well tolerated: All treatment-related AEs were transient & mild or moderate
- Phase 1 and Phase 2a results support the continued development of GlyphAllo™ as a potential novel medicine for MDD with or without anxious distress

GlyphAllo™ Potently Blunted Salivary Cortisol Response to the TSST*



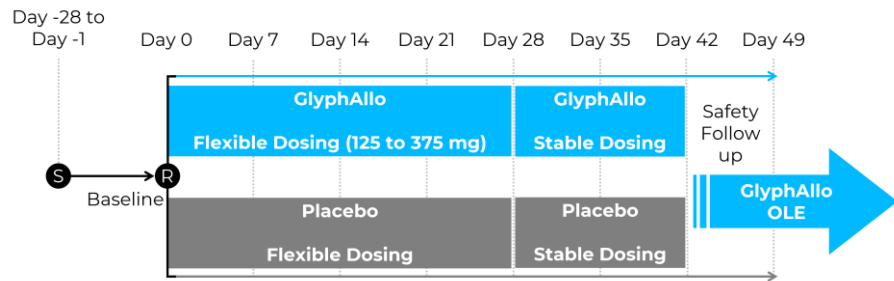
1. Chen, M., Harnett, M., Elenko, E., and Hellhammer J. (2024 May 9) GlyphAllo (SPT-300), an Oral Prodrug of Allopregnanolone, Potently Reduces Salivary Cortisol Response to the Trier Social Stress Test in a Randomized, Placebo-Controlled Phase 2a Study in Healthy Participants. Society of Biological Psychiatry (SOBP) Annual Meeting, 2024, Austin, TX, United States; * = Trier Social Stress Test.

Design of Phase 2b BUOY-1 Trial of GlyphAllo™ in MDD With or Without Anxious Distress



BUOY-1: Global, randomized, double-blind, placebo-controlled Phase 2b trial to evaluate efficacy, safety, and tolerability of GlyphAllo™ in MDD

- ~360 participants randomized 1:1 to GlyphAllo™ or placebo
- Primary endpoint: Hamilton Depression Rating Scale-17 total score (day 42)



Key Trial Objectives & Design Elements

Assess durable efficacy

- Treat for 6 weeks
- Enrich for anxious distress

Reduce placebo response

- Reduce assessment frequency
- Single active arm

Further evaluate safety

- Completed ISM* (U.S. subset)
- Driving limitation (U.S., full; EU, 6h)

Phase 1 Driving Simulation Trial: GlyphAllo did not impair next-morning driving performance in healthy volunteers

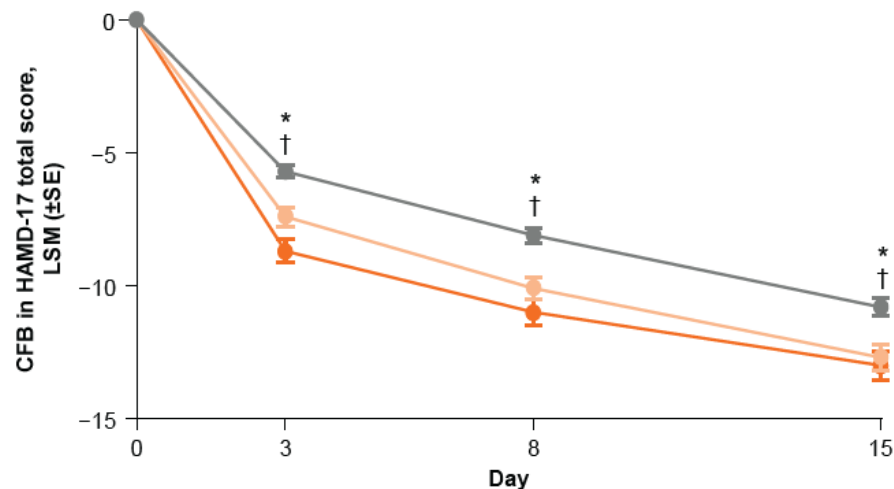
Zuranolone Showed Strong Early Efficacy in MDD, But Treatment Duration Was Only Two Weeks



Zuranolone: Synthetic Analog of Allopregnanolone

- Treatment duration in most MDD trials is 6-8 weeks
- Zuranolone MDD trials had a high placebo response, likely driven by the elevated frequency of clinician-administered assessments
- 5 of 6 zuranolone trials in MDD met primary endpoint¹

Zuranolone Had a Continuing Response in MDD Over Two-Week Treatment Period²



*nominal $p < 0.05$ for ZRN 30 mg vs placebo; † nominal $p < 0.05$ for ZRN 50 mg vs placebo.

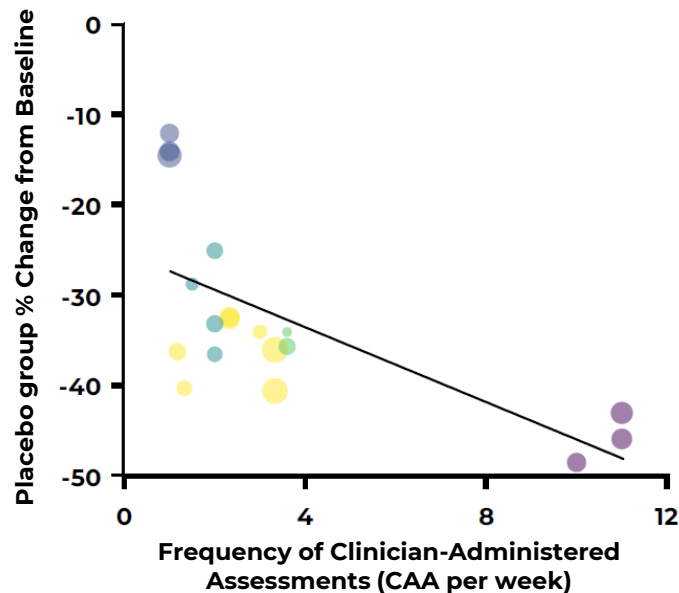
1. Phase 2 MDD-201B, Phase 3 WATERFALL, Phase 3 CORAL, Phase 3 MOUNTAIN, Phase 2 trial in Japan (JapicCTI-205276), Phase 3 trial in Japan (JRCT2031210577); 2. Clayton, A., Parikh, S., Iovin, R., Vera, T., Li, S., Forrestal, F., Motomiya, T., Baba, T., Czersky, A. (2023 Sept 6-10) Improvements in Depressive Symptoms in Patients With Major Depressive Disorder: Analysis of Zuranolone Efficacy From 4 Randomized, Placebo-Controlled Trials. Psych Congress, 2023, Nashville TX, United States.

Number and Frequency of Clinical Assessments are Associated with Placebo Response in MDD Trials



Seaport Meta-Analysis of MDD Trials in Last 10 Years

- Increasing number and frequency of clinician-administered assessments (CAAs) were significantly associated with greater placebo response
- Reducing number and frequency of CAAs in MDD trials may decrease placebo response



Defining a Successful Outcome for GlyphAllo in the Phase 2b BUOY-1 Trial



Demonstrate a Statistically Significant and Clinically Meaningful Difference for GlyphAllo vs. Placebo on the Primary Endpoint

Marketed Antidepressants Have Effect Sizes Ranging From 0.16 to 0.42^{1,2}



Exploratory Opportunities for GlyphAllo to Address Unmet Needs in MDD

Standard of Care Therapies



Slow Onset of Action



Sexual Dysfunction, Weight Gain, and Insomnia



Patients with MDD and Anxious Distress Have Lower Response Rates³

GlyphAllo Potential Benefit



Provide More Rapid Efficacy

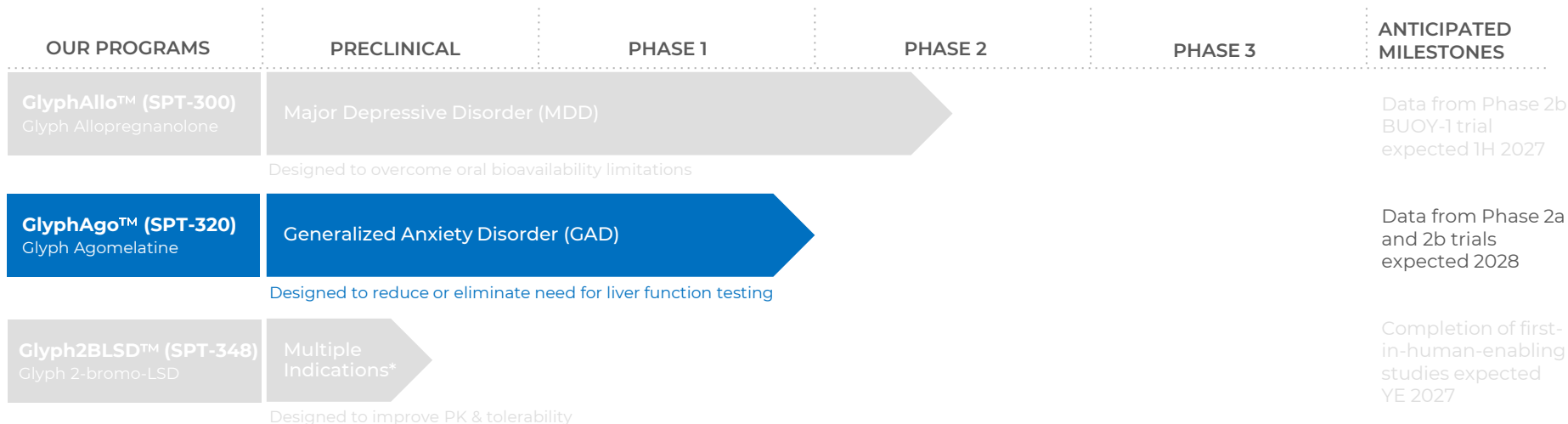


Deliver a Differentiated Tolerability Profile



Show Benefit for Patients with Anxious Distress

Pipeline of Novel Potential Treatments for Neuropsychiatric Disorders



*Neuropsychiatric and headache disorders with significant unmet need

**Glyph™ aims to unlock potential of drugs in CNS and beyond:
Multiple preclinical programs underway**

GlyphAgo™ is Designed to Overcome Liver Monitoring Requirements of Agomelatine



Agomelatine Benefits

- Novel mechanism: Melatonin receptor (MT1/MT2) agonist and 5-HT2C antagonist
- Statistical separation from placebo in all four third-party trials in GAD¹⁻⁴
- Approved for GAD in Australia; approved for MDD in Australia and EU



Key Limitation

Due to high first-pass metabolism, agomelatine can cause liver enzyme elevations and requires frequent liver function testing⁵



GlyphAgo™ Approach

Designed to avoid first-pass metabolism, reduce PK* variability, and reduce/eliminate liver testing

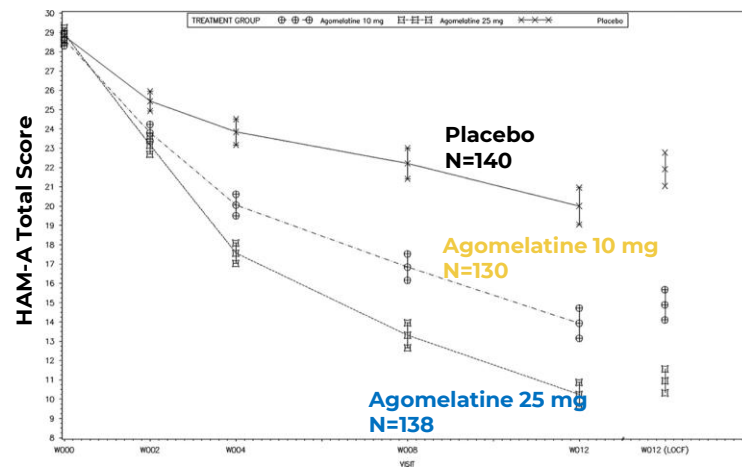
Agomelatine is an Effective Treatment for Generalized Anxiety Disorder (GAD)



Agomelatine Profile in GAD

- Statistical separation from placebo in all four third-party trials in GAD¹⁻⁴
- Better efficacy and tolerability compared to SSRIs and benzodiazepines in GAD⁵

Agomelatine Significantly Reduces Anxiety in Patients with GAD⁴



1. Stein, D.J., et al. (2008). Efficacy of agomelatine in generalized anxiety disorder: a randomized, double-blind, placebo-controlled study. *J Clin Psychopharmacol*, 28(5), 561-566; 2. Stein, D.J., et al. (2012). Agomelatine prevents relapse in generalized anxiety disorder: a 6-month randomized, double-blind, placebo-controlled discontinuation study. *J Clin Psychiatry*, 73(7), 1002-1008; 3. Stein, D.J., et al. (2014). Agomelatine in generalized anxiety disorder: an active comparator and placebo-controlled study. *J Clin Psychiatry*, 75(4), 362-368; 4. Stein, D.J., et al. (2017). Efficacy and safety of agomelatine (10 or 25 mg/day) in non-depressed out-patients with generalized anxiety disorder: A 12-week, double-blind, placebo-controlled study. *Eur Neuropsychopharmacol*, 27(5), 526-537; 5. Slee, A., et al. (2019). Pharmacological treatments for generalised anxiety disorder: a systematic review and network meta-analysis. *The Lancet*, 393(10173), 768-777.

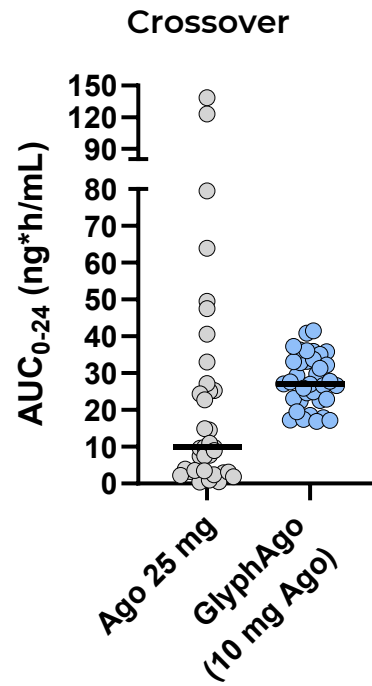
Phase 1 Topline: GlyphAgo™ Provided Therapeutic Exposures at Doses Projected to Avoid Liver Issues



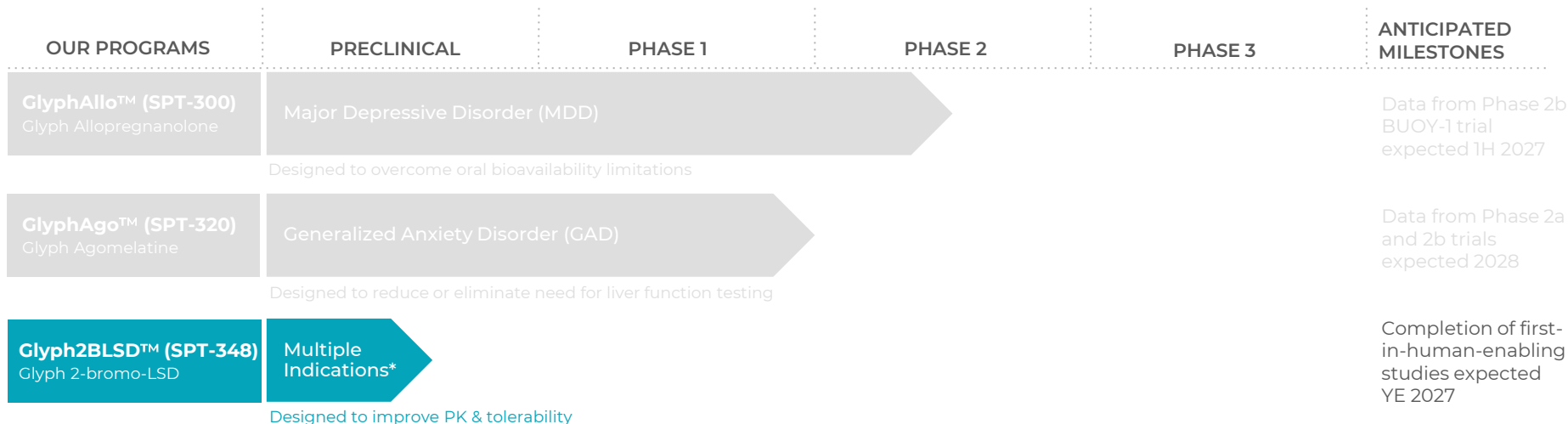
Data from Head-to-Head Crossover Portion of Trial

- GlyphAgo achieved 6.8-fold increase in bioavailability compared to agomelatine
- GlyphAgo showed 10-fold reduction in PK variability compared to agomelatine
- GlyphAgo showed 1.9-fold increase in dose-normalized C_{max} compared to agomelatine
- Well-tolerated; no serious or severe AEs, no liver-related AEs

GlyphAgo™ Exceeded Target of Two-Fold Increase in Bioavailability Compared to Unmodified Agomelatine



Pipeline of Novel Potential Treatments for Neuropsychiatric Disorders



*Neuropsychiatric and headache disorders with significant unmet need

**Glyph™ aims to unlock potential of drugs in CNS and beyond:
Multiple preclinical programs underway**

Glyph2BLSD™ is Designed to Harness Efficacy of Psychedelics While Eliminating Hallucinations



Neuroplastogen Benefits

- Offer potential to enhance neuroplasticity in brain circuits implicated in neuropsychiatric disorders¹
- Demonstrated clinical efficacy for depression and other disorders²



Key Limitations

Functional unblinding of clinical trials, need for supervised administration, concerns over long-term safety²



Glyph2BLSD™ Approach

Designed to harness neuroplastic effects associated with psychedelics while avoiding hallucinations to enable outpatient dosing

Anticipated Key Milestones Across our Portfolio



Program	2025-2026	2027-2028
GlyphAllo™ (SPT-300) Glyph Allopregnanolone	✓ Q3 2025: Initiated Phase 2b BUOY-1 trial ✓ 2H 2026: Phase 1 driving trial topline data	★ 1H 2027: Phase 2b BUOY-1 trial topline data • 2028: Initiate Phase 3 program in MDD
GlyphAgo™ (SPT-320) Glyph Agomelatine	✓ Q3 2025: Initiated Phase 1 POC trial ✓ Q2 2026: Phase 1 POC trial topline data	★ Early 2028: Phase 2a trial topline data ★ YE 2028: Phase 2b trial topline data
Glyph2BLSD™ (SPT-348) Glyph 2-bromo-LSD	• 2026: Progress FIH-enabling studies	• YE 2027: Complete FIH-enabling studies

Cash, cash equivalents, and investments expected to fund operations into 2029 and through topline readouts of the Phase 2b BUOY-1 trial of GlyphAllo, the Phase 2a trial of GlyphAgo, and the Phase 2b trial of GlyphAgo, as well as through initiation of the Phase 3 program of GlyphAllo

Our Proven Leadership Team

A track record of success

DAPHNE ZOHAR

Co-founder, CEO, Board Member

Former PureTech CEO & Founder;
Co-founder Karuna (acquired by BMS for \$14B)

STEVEN PAUL, MD

Co-founder, Board Chair

Former Chair & CEO of Karuna;
Former President of Lilly Research Labs. Developed ZYPREXA & CYMBALTA

ANTONY LOEBEL, MD

Chief Medical Officer, President Of Clinical Development

Former CEO & CMO Sunovion, led dev & commercialization of LATUDA

MICHAEL CHEN, PHD

Co-founder, Chief Scientific Officer

Former Head of Innovation at PureTech, led development of Seaport pipeline

LAUREN WHITE

Chief Financial Officer

Former CFO at ImmunoGen prior to acquisition by AbbVie for \$10.1B

LANA GLADSTEIN, JD

General Counsel

Previously at APRINOIA, Arranta Bio (acquired by Recipharma), Brammer Bio (acquired by Thermo Fisher for \$1.7B)



SEAPORT

THERAPEUTICS

Goldman Sachs
Life Sciences Symposium

September 2026



Unlocking Better Days™

Appendix



Driving Simulation Trial Met Primary Endpoint: GlyphAllo Did Not Impair Next-Morning Driving



Study Design:

- Randomized, double-blind, placebo- and active-controlled, three-way crossover Phase 1 trial in healthy volunteers
- GlyphAllo was dosed at bedtime; simulated driving performance was evaluated ~9 hours later
- Driving performance assessed using Standard Deviation of Lateral Position (SDLP) – gold standard measure of “weaving”

Trial Met Primary and Key Secondary Endpoints

Primary endpoint: Evening dosing of GlyphAllo (375 mg) did not impair next-morning driving performance compared to placebo on Day 5, following multiple-day dosing

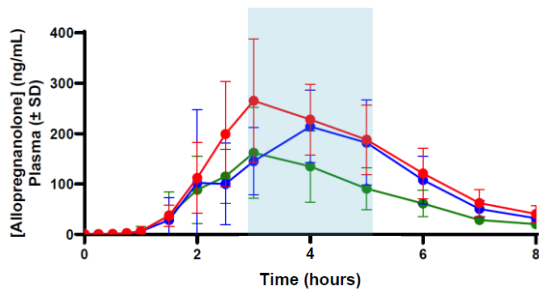
Key secondary endpoint: Evening dosing of GlyphAllo (250 mg) did not impair next-morning driving performance compared to placebo on Day 2

GlyphAllo was well tolerated: most AEs were mild and transient, no serious AEs were reported

GlyphAllo™ Showed Dose-Dependent Allopregnanolone Levels and PD Effects in Phase 1

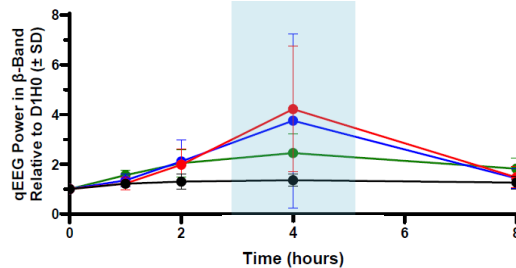


PK

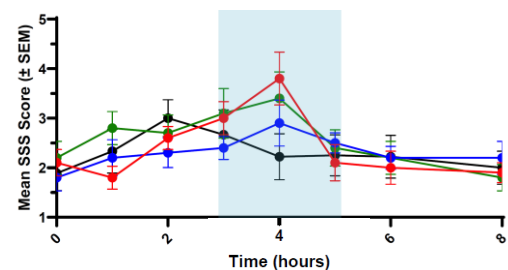


PD

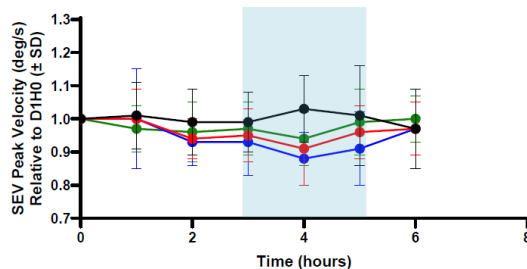
Beta EEG Power



Stanford Sleepiness Score (SSS)



Saccadic Eye Velocity (SEV)

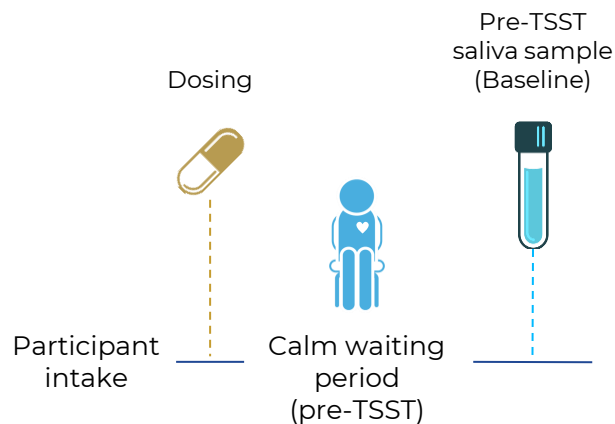


- Pooled Placebo (N=15)
- GlyphAllo 250 mg (N=9)
- GlyphAllo 375 mg (N=9)
- GlyphAllo 500 mg (N=9)

Allopregnanolone Plasma Levels and PD Signals Peaked 3-5 Hours Post-Dose and Declined by 6-8 Hours

Design of Phase 2a Trial of GlyphAllo™

Randomized, placebo-controlled trial using the Trier Social Stress Test (TSST)



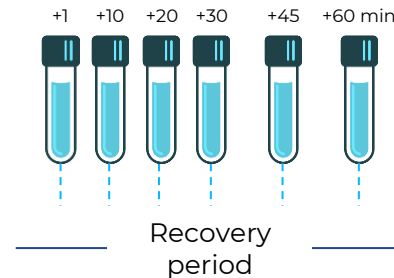
1. Anticipation: prepare a speech
2. Public speaking to a panel
3. Live math test to a panel



Trier Social Stress Test:

Validated model of acute anxiety

Post-TSST salivary cortisol reflects stress during TSST



Primary Aim:

To characterize pharmacology of GlyphAllo for potential anxiety indications

Primary Endpoint:

Reduction in salivary cortisol, a stress hormone

Trial Design:

N=80 healthy volunteers randomized to GlyphAllo (375 mg) or placebo

Neuroplastogens are Poised to Transform Psychiatric Treatment



Science

Psychedelics promote neuroplasticity through the activation of intracellular 5-HT_{2A} receptors

Maximilian
Robert
Joseph
David

nature communications

Identification of 5-HT_{2A} receptor signaling pathways associated with psychedelic potential

Neuron

Psilocybin induces rapid and persistent growth of dendritic spines in frontal cortex *in vivo*

JAMA Psychiatry | Original Investigation

Single-Dose Synthetic Psilocybin With Psychotherapy for Treatment-Resistant Bipolar Type II Major Depressive Episodes: A Nonrandomized Controlled Trial

Scott T. Antonson, MD, Andrewson de la Haza, MD, PhD, Thomas Miller, PhD, Jeffrey J. Gold, PhD

Neuron

Psychedelics Promote Structural and Functional Neural Plasticity

Calvin Ly • Alexandra C. Greb • Lindsay P. Cameron • ... Kassandra M. Ori-McKenney • John A. Gray • David E. Olson • ¹⁰ • Show all authors • Show footnotes

THE NEW ENGLAND
JOURNAL OF MEDICINE

Single-Dose Psilocybin for a Treatment-Resistant Episode of Major Depression

Guy M. Goodwin

nature neuroscience

Psychedelics promote plasticity by directly binding to BDNF receptor TrkB

Rafael Moliner, Mykhailo Grych, Cecilia A. Brunello, Vera Kovaleva, Caroline Bisjone, Giray Enkavi, Lina Antenucci, Erik F. Kot, Sergey A. Goncharov, Katja Kaurinkoski, Mirjami Kuittinen, Senem M. Fred, Leoni V. Elskä, Sven Sakson, Cecilia Cannarozzo, Cassiano R. A. F. Diniz, Nina Seiffert, Anna Rubiolo, Hele Haapaniemi, Elia Meshi, Elina Nagaeva, Tiina Ohman, Tomasz Bóg, Esko Kankuri, ... Eero Castrén

PsychiatricTimes

FDA Grants Breakthrough Designation to MM-120 for Generalized Anxiety Disorder

March 7, 2024
Leah Kuntz

businesswire

MindMed Receives FDA Breakthrough Therapy Designation and Announces Positive 12-Week Durability Data From Phase 2B Study of MM120 for Generalized Anxiety Disorder

March 07, 2024 06:00 AM Eastern Standard Time

NEW YORK, NY, BUSINESSWIRE - Mind Medicine (MindMed) Inc. (NASDAQ: MMDT) (the "Company" or "MindMed")

SCRIP
CITELINE COMMERCIAL

MindMed Ready To Take LSD Therapy Into Phase III For Anxiety

07 Mar 2024 | NEWS

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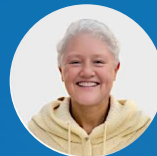
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Founding CEO of PureTech



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former Group Worldwide Chair at J&J



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& Baxalta



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Psychiatry at UNC Chapel Hill

DILIsym Simulations Demonstrate that GlyphAgo™ is Not Projected to Cause Liver Enzyme Elevations

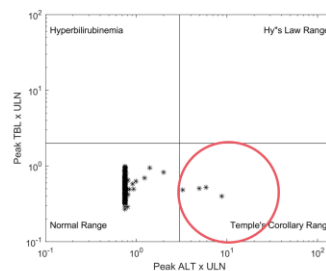


DILIsym: Model Used to Predict and Explain DILI*

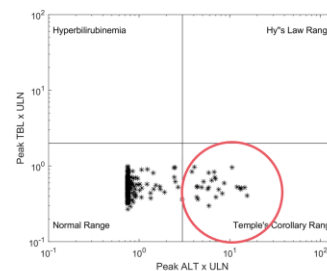
- Liver enzyme elevations observed in previous clinical trials of agomelatine are recapitulated with DILIsym
- GlyphAgo doses designed to generate comparable systemic exposures of agomelatine are not projected to cause liver enzyme elevations

Agomelatine: Approved Doses

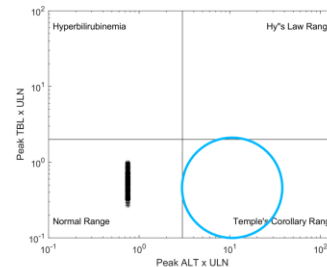
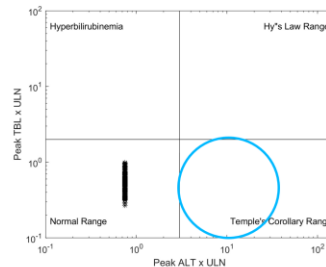
25 mg QD



50 mg QD



GlyphAgo: Exposure-Equivalent Doses



Internal Seaport data; * DILI = Drug-Induced Liver Injury

Glyph™ Platform: Transformative & Validated

Successfully applied to create over 24 different small molecules – novel CoM IP



nature reviews drug discovery

Review Article | Published: 16 October 2015

From sewer to saviour – targeting the lymphatic system to promote drug exposure and activity



Lymphatic Transport and Lymphocyte Targeting of a Triglyceride Mimetic Prodrug Is Enhanced in a Large Animal Model: Studies in

Gr
Sifei
Chri



Journal of Controlled Release

journal homepage

Targeted delivery of a model immunization system: Comparison of alkyl ester and prodrug strategies

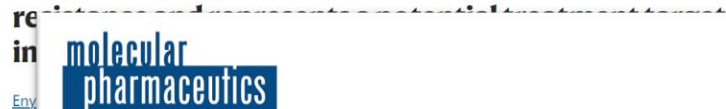
Sifei Han^a, Tim Quach^b, Luojuan Hu^a, Anisa
Natalie L. Trevaskis^a, Jamie S. Simpson^{b,*}



nature metabolism

Article | Published: 20 September 2021

Mesenteric lymphatic dysfunction promotes insulin resistance and represents a potential treatment target



Env

Fer

Gat

R.J

Opti
Conj



Frontiers in Pharmacology

Article

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

DRUG DEVELOPMENT

An oral allopregnanolone prodrug bypasses liver metabolism via lymphatic transport enabling bioavailability in animals and humans

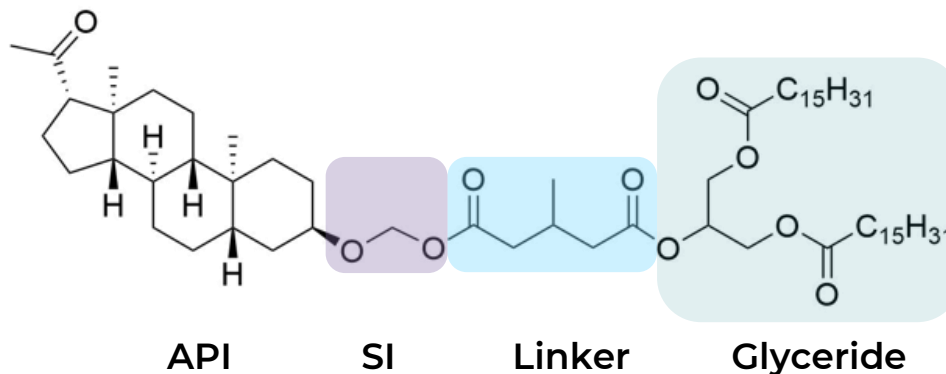
Jamie S. Simpson¹, Tim Quach¹, Sifei Han², Luojuan Hu², Natalie L. Trevaskis², Nathania J. Leong²,
Garima Sharma², Dan Zheng², Steven M. Paul¹, Christopher J. H. Porter^{2*},
Daniel K. Bonner^{1*}, Michael C. Chen^{1*}

Mimetic Prodrugs of Enhance Oral via Promotion of Transport

n^{2*}, Shea F. Lim¹, Danielle Senyschyn², Preeti Yadav²,
son^{1†} and Christopher J. H. Porter^{2*}

Design of Proprietary Prodrug Chemistry

Designed to avoid first-pass metabolism by promoting lymphatic uptake



Self-Immolative (SI)

Allows controlled release of parent drug compound

Linker

Tunes stability to gut esterases and recognition for triglyceride resynthesis

Glyceride

Integrates prodrug into chylomicrons for lymphatic transport

Distinct composition of matter IP for each new candidate and multiple layers of coverage

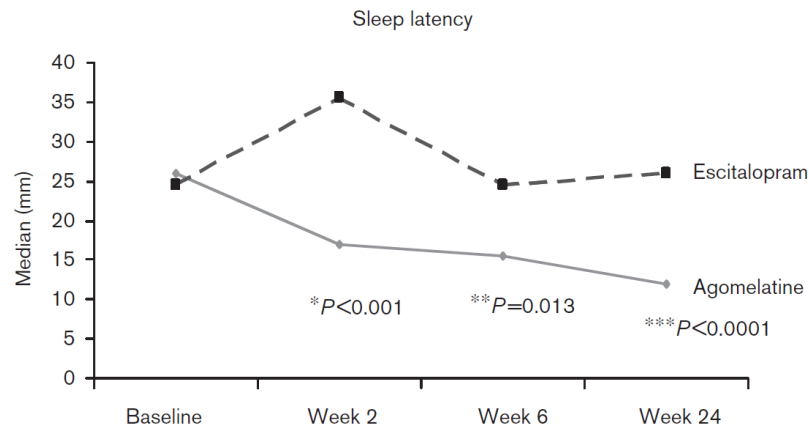
Agomelatine Improves Sleep in GAD and MDD



Sleep Disturbances: a Core Feature of Mood Disorders

- Agomelatine improves sleep latency, sleep architecture, and daytime sleepiness compared to SSRIs^{1,2}
- SSRIs can exacerbate insomnia and sleep problems in MDD³
- No hangover effects, unlike other 5-HT_{2C} antagonists

Agomelatine Improves Sleep Compared to SSRIs¹



Sleep latency after 2, 6, and 24 weeks of treatment. * $P < 0.001$, ** $P = 0.013$, *** $P < 0.001$ (Mann-Whitney test).

1. Quera-Salva, Maria-Antonia, et al. (2011) Comparison of agomelatine and escitalopram on nighttime sleep and daytime condition and efficacy in major depressive disorder patients. *International clinical psychopharmacology*, 26(5), 252-262; 2. Demyttenaere, K. (2014) Agomelatine in treating generalized anxiety disorder. *Expert Opin Investig Drugs*, 23(6), 857-864; 3. Peterson, M., and Benca, R. (2008) Sleep in mood disorders. *Sleep Medicine Clinics*, 3(2), 231-249.

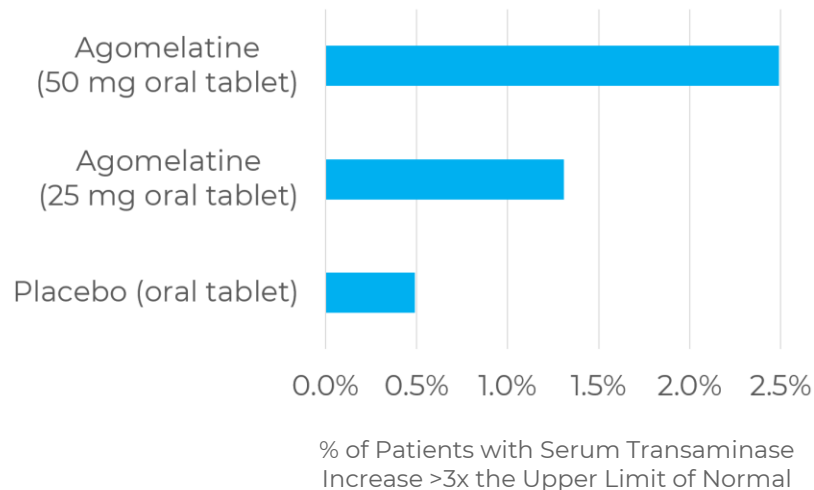
Despite Known Efficacy, Agomelatine Has Been Held Back by Need for Liver Function Testing



Agomelatine Treatment Requires Frequent Liver Function Tests²

- Before starting treatment
- After 3, 6, 12, and 24 weeks
- When increasing dose
- Thereafter when clinically indicated

Agomelatine Can Cause Dose-Dependent Liver Enzyme Elevations¹



1. Perlemuter, Gabriel, et al. "Characterisation of Agomelatine-Induced Increase in Liver Enzymes: Frequency and Risk Factors Determined from a Pooled Analysis of 7605 Treated Patients." CNS Drugs 30.9 (2016): 877-888. Significant increase in transaminase levels defined as an increase to >3x the upper limit of normal. 2. Agomelatine (Valdoxan) Summary of Product Characteristics <https://www.ema.europa.eu/en/medicines/human/EPAR/valdoxan>

Phase 1 Topline: GlyphAgo™ Provided Therapeutic Exposures at Doses Projected to Avoid Liver Issues



Data from SAD and MAD Portions of Trial

- SAD: GlyphAgo demonstrated 9.6-14.5-fold increase in bioavailability compared to agomelatine
- MAD: 7-day GlyphAgo dosing confirmed favorable safety, tolerability, and PK observed across Phase 1 program; agomelatine exposures were consistent with data from the SAD and crossover
- Well-tolerated; no serious or severe AEs, no liver-related AEs

GlyphAgo™ Exceeded Target of Two-Fold Increase in Bioavailability Compared to Unmodified Agomelatine

