SEAPORT THERAPEUTICS

Corporate Presentation
November 2026



Turning the Tide on Mental Health

Disclaimer

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. 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 "anticipate," "believe," "contemplate," "continue," "could," "design," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "seek," "should," "target," "will," "would," or the negative of these terms or other similar expressions are intended to identify forward-looking statements. These statements include, among other things, 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 topline data from the GlyphAllo Phase 2b BUOY-1 trial in 1H2027; the progress and enrollment of the GlyphAgo Phase 2a trial and topline data in early 2028, topline data from the GlyphAgo Phase 2b trial by the end of 2028, and the interpretation and clinical and regulatory implications of the previously reported topline results from the Phase 1 driving simulation trial of GlyphAllo in healthy volunteers, which we have submitted to the U.S. Food and Drug Administration ("FDA"), including the FDA's review of those results; the planned initiation of the GlyphAgo Phase 2/3 trial in the first half of 2027 and the anticipated timing of topline data by the end of 2028; the initiation timing, progress, and results of our research and development programs, preclinical studies, and future clinical trials, including preclinical and first-in-human-enabling activities for Glyph2BLSD, including the completion of first-in-human enabling studies by year-end 2027, and 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.

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, GlyphAgo 2a and planned Phase 2/3 trials; risks that result from earlier trials, including Phase 1 trials, or from third-party trials may not be predictive of future results, including with respect to liver safety; 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 our limited operating history and history of significant losses, our need for substantial additional funding, and our ability to raise capital when needed, on acceptable terms, or at all, to complete development activities and commercialize Seaport's 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 September 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. Seaport expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in its expectations or any changes in events, conditions, or circumstances on which any such statement is based, except as required by law, and claims the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

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. This presentation contains industry, market and prevalence data drawn from management's estimates and research and from third-party publications, studies and surveys, which we have not independently verified. These estimates, including prevalence data extrapolated to broader populations, involve assumptions and limitations and are subject to a high degree of uncertainty and risk.

Seaport uses and intends to continue to use its Investor Relations website (https://investors.seaporttx.com) as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD. Accordingly, investors should monitor the Company's Investor Relations website, in addition to following the Company's press releases, SEC filings, public conference calls, presentations, and webcasts.

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

SEAPORT THERAPEUTICS

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 Recipharm), Brammer Bio (acquired by Thermo Fisher for $1.7B)



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Over 1 Billion People Are Living with Mental Illness[1]

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 MDD[5]

Suicide is the **second leading** cause of death in ages 10-24[6]

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1. World Health Organization (2025): https://www.who.int/news/item/02-09-2025-over-a-billion-people-living-with-mental-health-conditions-services-require-urgent-scale-up; 2. Ruscio et al. (2017). Cross-sectional Comparison of the Epidemiology of DSM-5 Generalized Anxiety Disorder Across the Globe. JAMA Psychiatry, 74(5), 465-475; 3. Hopwood, M. (2023). Anxiety Symptoms in Patients with Major Depressive Disorder: Commentary on Prevalence and Clinical Implications. Neurol Ther. 12: 5-12; 4. World Health Organization, 2025; 5. American Association of Suicidology, 2009; 6. Deaths: Leading Causes for 2024 | CDC. (2026). https://www.cdc.gov/nchs/data/nvsr/nvsr75/nvsr75-07.pdf.; *MDD = Major Depressive Disorder.

Current Neuropsychiatry Medications

Widely prescribed but have limitations

Peak Sales

Zyprexa Olanzapine	>$5B[1]
Cymbalta chlorhydrate de duloxétine	~$5B[1]
Risperdal	>$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

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1. Global Data. Extraction Date: Jan 3, 2026; 2. Palmer, J. (2002). After the Boom, No Reason to Smile. Barron's. May 20; 3. Warden, D., et al.(2007). The STAR*D project results: A comprehensive review of findings. Current Psychiatry Reports, 9(6), 449–459. https://doi.org/10.1007/s11920-007-0061-3.

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

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Seaport Uniquely Positioned to Outperform in Neuropsychiatry Drug Development



Neuropsychiatry Challenges

Fundamental pathophysiology unknown

Poor drug-like properties

Challenging clinical studies

Seaport's Approach

>90% clinical trial failure rate[1] → Identify drugs with validated efficacy

Poor oral bioavailability and/or PK*, poor safety & tolerability → Overcome hurdles using Glyph™ platform & generate new IP

Difficult to demonstrate efficacy → Proven team leading better designed & executed trials

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1. BIO, PharmaIntelligence, QLS (2021) Clinical Development Success Rates and Contributing Factors 2011–2020; *PK = pharmacokinetic.

Seaport's Proven Team & Approach

Karuna case study: Successful outcome for patients and shareholders

KARUNA THERAPEUTICS



STEVEN PAUL, MD
Former Board Chair & CEO, Karuna

DAPHNE ZOHAR
Co-founder of Karuna, originator of KarXT

COBENFY™
FDA-approved in 2024

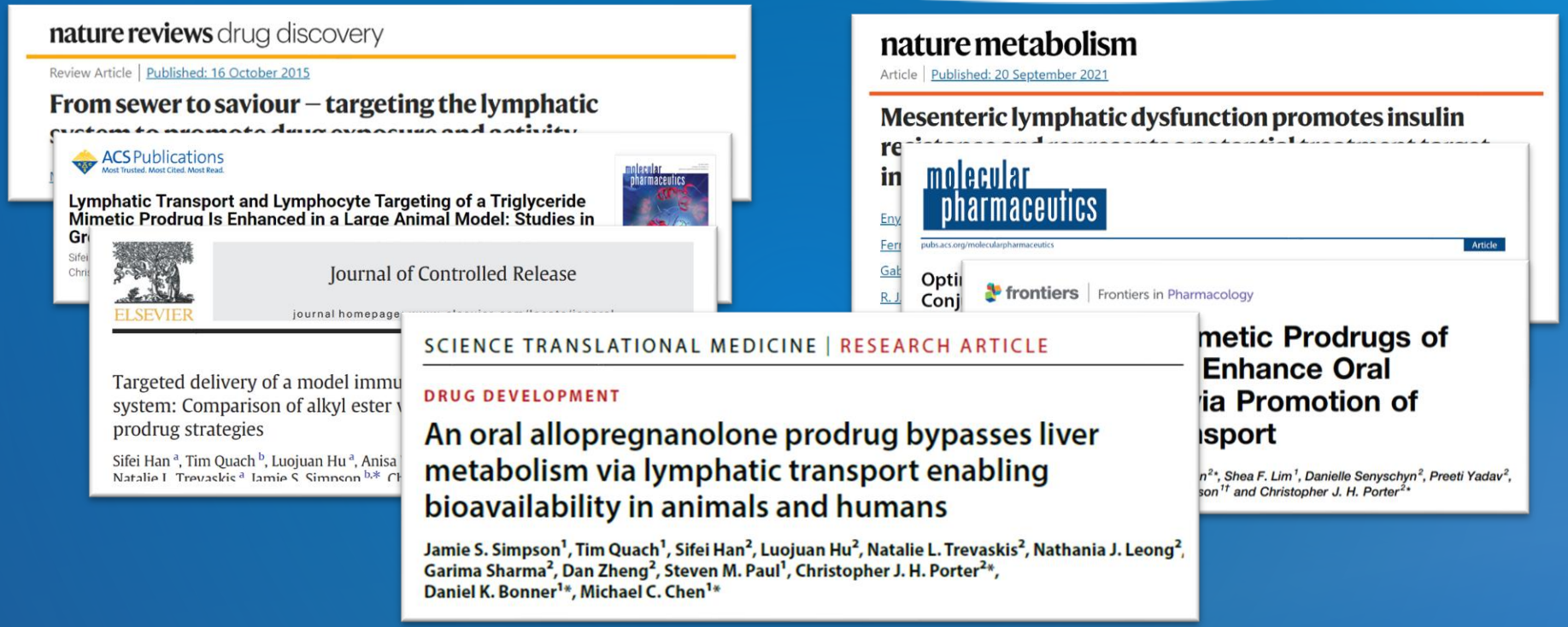


- Identified drug with validated efficacy (xanomeline)
- Overcame hurdles with Cobenfy™
- Proven team led better designed & executed trials

SEAPORT THERAPEUTICS

Glyph™ Platform: Transformative & Validated

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



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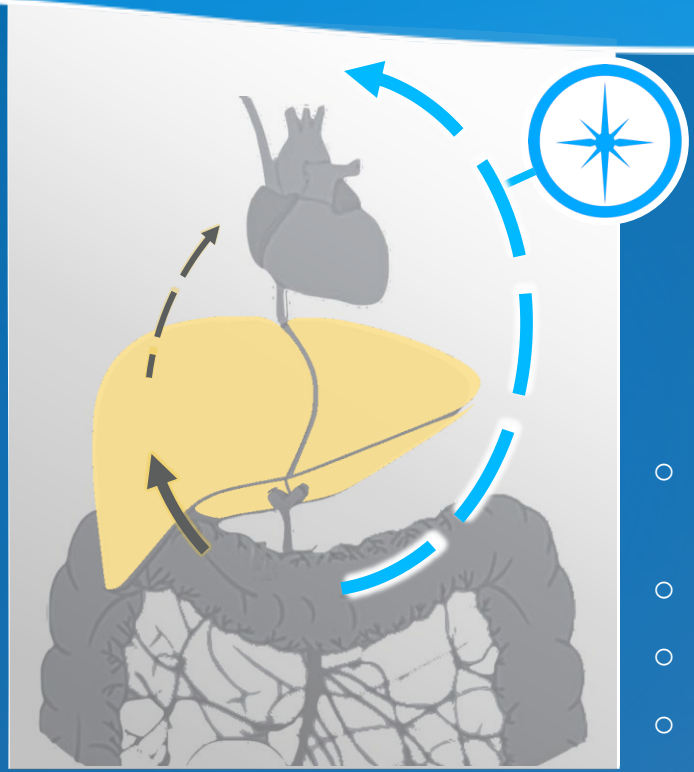
CoM = Composition of Matter

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**

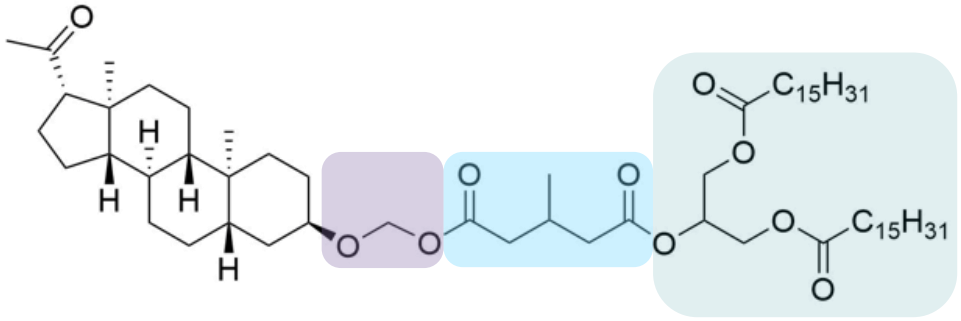
- **Reduces first-pass hepatotoxicity**
- **Enhances oral bioavailability**
- **Reduces PK* variability**
- **Reduces dose**
- **Generates new IP**

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*PK = Pharmacokinetic

Design of Proprietary Prodrug Chemistry

Designed to avoid first-pass metabolism by promoting lymphatic uptake



API **SI** **Linker** **Glyceride**

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

Pipeline of Novel Potential Treatments for Neuropsychiatric Disorders



OUR PROGRAMS	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	ANTICIPATED MILESTONES
GlyphAllo™ (SPT-300) Glyph Allopregnanolone	Major Depressive Disorder (MDD)				Data from Phase 2b BUOY-1 trial expected 1H 2027
Designed to overcome oral bioavailability limitations					
GlyphAgo™ (SPT-320) Glyph Agomelatine	Generalized Anxiety Disorder (GAD)				Data from Phase 2a and 2/3 trials expected 2028
Designed to reduce or eliminate need for liver function testing					
Glyph2BLSD™ (SPT-348) Glyph 2-bromo-LSD	Multiple Indications*				Completion of first-in-human-enabling studies expected YE 2027
Designed to improve PK & tolerability					

*Neuropsychiatric and headache disorders with significant unmet need

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

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The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our investigational product candidates are safe and effective. No regulatory agency has made any such determination that our investigational therapies are safe or effective for use by patients for any indication; *PK = pharmacokinetic.

GlyphAllo™ is Designed to Overcome Low Bioavailability of Allopregnanolone

Allopregnanolone Benefits

- Naturally occurring molecule that reduces stress[1]
- 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 MDD[4]

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

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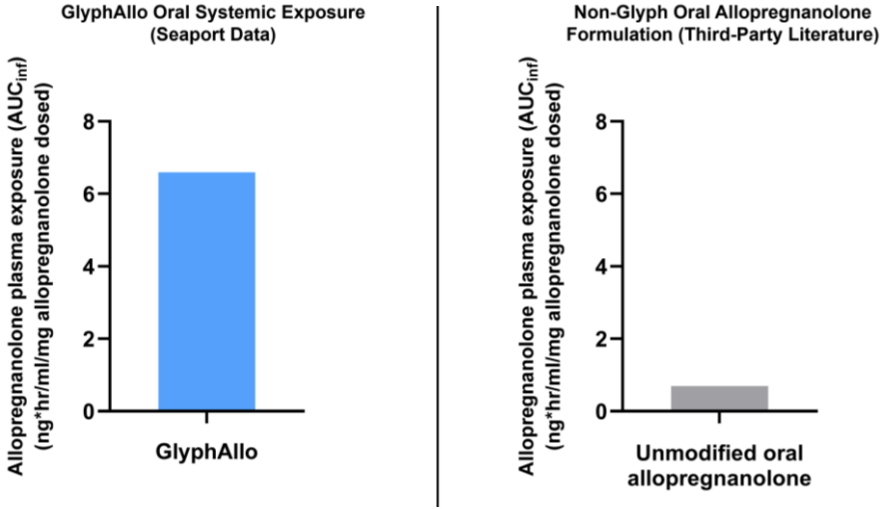
1. Paul, S.M., et al. (2020). Allopregnanolone: From molecular pathophysiology to therapeutics. A historical perspective. Neurobiol Stress, Mar 14, 12, 100215. 2. Epperson, C. N., et al. (2023). Effect of brexanolone on depressive symptoms, anxiety, and insomnia in women with postpartum depression: Pooled analyses from 3 double-blind, randomized, placebo-controlled clinical trials in the HUMMINGBIRD clinical program. J Affect Disord, Jan 1, 320, 353-359; 3. ZULRESSO (brexanolone) Prescribing Information, Revised 6/2022; 4. 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).

GlyphAllo™ Reaches Therapeutically Relevant Exposures with a Favorable Tolerability Profile

Key PK and Safety Data

- Bioavailability **>9X** vs. oral allopregnanolone[1]
- 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 1 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.

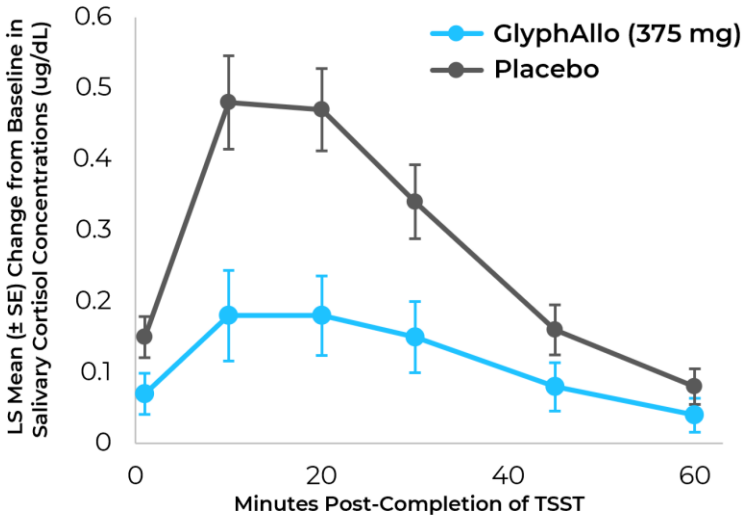
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Phase 2a Results: GlyphAllo™ Significantly Reduced Stress Response Compared to Placebo (p=0.0001)[1]

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.

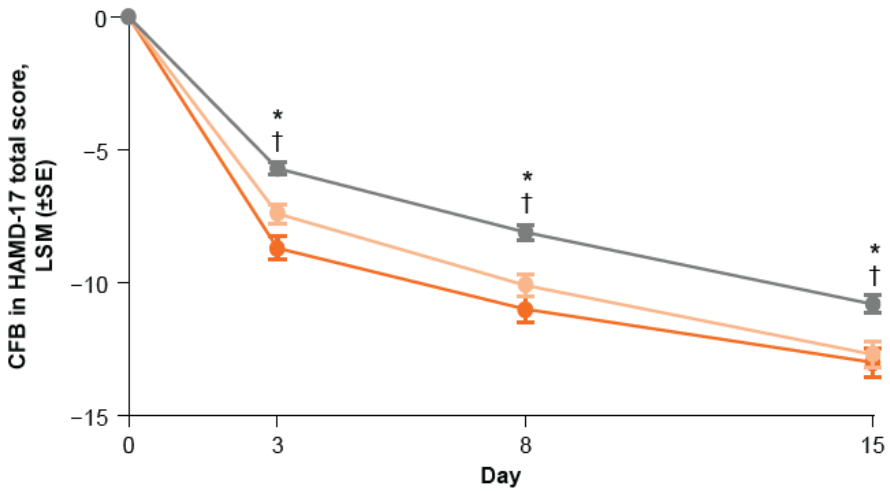
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Zuranolone Showed Strong Early Efficacy in MDD, But Treatment Duration Was Only Two Weeks

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 endpoint[1]

Zuranolone Had a Continuing Response in MDD Over Two-Week Treatment Period[2]



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

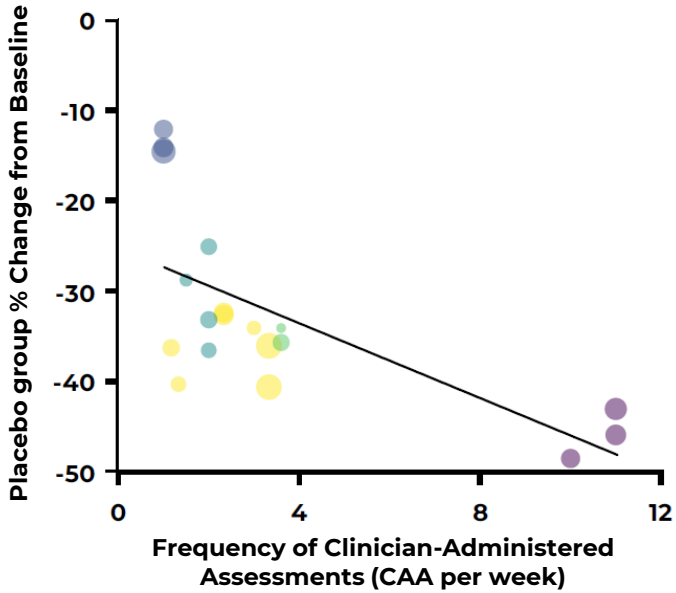
1. Phase 2 MDD-201B, Phase 3 WATERFALL, Phase 3 CORAL, Phase 3 MOUNTAIN, Phase 2 trial in Japan (JapicCTI-205276), Phase 3 trial in Japan (jRCT2031210577).; 2. Clayton, A., Parikh, S., Iovin, R., Vera, T., Li, S., Forrestal, F., Motomiya, T., Baba, T., Czzysz, A. (2023 Sept 6-10) Improvements in Depressive Symptoms in Patients With Major Depressive Disorder: Analysis of Zuranolone Efficacy From 4 Randomized, Placebo-Controlled Trials. Psych Congress, 2023, Nashville TX, United States.

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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



Gold, M., Bisson, B., Zhu, H., Chen, M. (2025 Feb 19-21) Clinician-administered assessments and impact on placebo response in recent major depressive disorder (MDD) clinical trials. International Society for CNS Clinical Trials and Methodology (ISCTM) Conference, 2025, Washington, D.C., United States; Clinician-Administered Assessments (CAAs) include all assessments conducted by clinicians, including HAM-D, MADRS, HAM-A, CGI-I, CGI-S.

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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

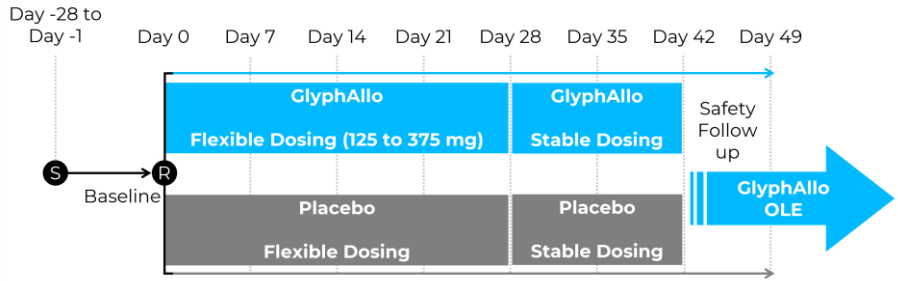
GlyphAllo was well tolerated: most AEs were mild and transient, no serious AEs were reported

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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*

*ISM = Intensive Safety Monitoring

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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 Rates[3]

GlyphAllo Potential Benefit

- Provide More Rapid Efficacy
- Deliver a Differentiated Tolerability Profile
- Show Benefit for Patients with Anxious Distress

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1. Turner, E.H., et al. (2008). Selective Publication of Antidepressant Trials and Its Influence on Apparent Efficacy. NEJM, 388: 252-260; 2. Turner E.H., et al. (2022). Selective Publication of Antidepressant Trials and Its Influence on Apparent Efficacy: Updated Comparisons and Meta-analyses of Newer Versus Older Trials. PLoS Med, 19(1): e1003886; 3. Fava, M., et al. (2008). Difference in Treatment Outcome in Outpatients With Anxious Versus Nonanxious Depression: A STAR*D Report. Am J Psychiatry, 165: 342-351.

GlyphAllo™ Clinical Development Plan Overview

Completed and ongoing trials

Phase 1 and 2a Trials in Healthy Volunteers (Completed)

- ✓ Phase 1: Demonstrated therapeutically relevant allopregnanolone exposures, dose-dependent PD*, and a favorable tolerability profile that supports chronic dosing
- ✓ Phase 2a: Demonstrated initial proof-of-concept by blunting physiological stress response in a validated clinical model of anxiety (TSST*)

Phase 1 Driving Simulation Trial (Completed)

- ✓ GlyphAllo did not impair next-morning driving performance in healthy volunteers

Phase 2b BUOY-1 Trial in MDD (Topline Data Expected 1H 2027)

- Evaluating the efficacy, safety, and tolerability of GlyphAllo in adults with MDD, with or without anxious distress

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*PD= pharmacodynamic; TSST = Trier Social Stress Test.

Pipeline of Novel Potential Treatments for Neuropsychiatric Disorders



OUR PROGRAMS	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	ANTICIPATED MILESTONES
GlyphAllo™ (SPT-300) Glyph Allopregnanolone	Major Depressive Disorder (MDD) Designed to overcome oral bioavailability limitations				Data from Phase 2b BUOY-1 trial expected 1H 2027
GlyphAgo™ (SPT-320) Glyph Agomelatine	Generalized Anxiety Disorder (GAD) Designed to reduce or eliminate need for liver function testing				Data from Phase 2a and 2/3 trials expected 2028
Glyph2BLSD™ (SPT-348) Glyph 2-bromo-LSD	Multiple Indications* Designed to improve PK & tolerability				Completion of first-in-human-enabling studies expected YE 2027

*Neuropsychiatric and headache disorders with significant unmet need

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

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The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our investigational product candidates are safe and effective. No regulatory agency has made any such determination that our investigational therapies are safe or effective for use by patients for any indication; *PK = pharmacokinetic.

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 GAD[1-4]
- 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 testing[5]

GlyphAgo™ Approach

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

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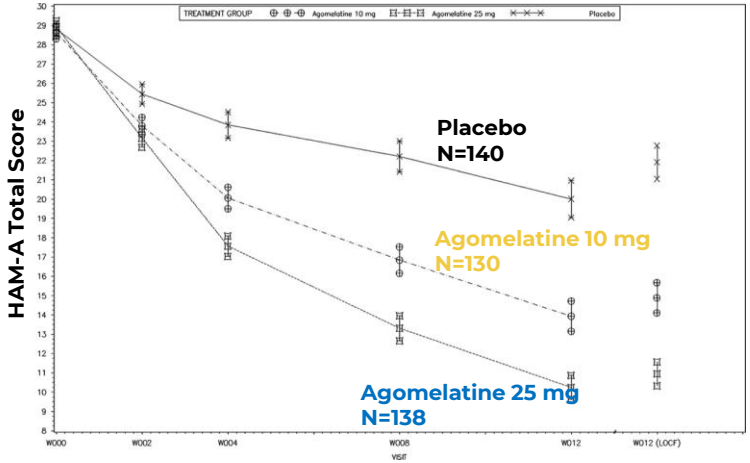
1. Stein, D.J., et al. (2008). Efficacy of agomelatine in generalized anxiety disorder: a randomized, double-blind, placebo-controlled study. J Clin Psychopharmacol, 28(5), 561-566; 2. Stein, D.J., et al. (2012). Agomelatine prevents relapse in generalized anxiety disorder: a 6-month randomized, double-blind, 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. VALDOXAN (agomelatine) – Australian Product Information; *PK = pharmacokinetic

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 GAD[1-4]
- Better efficacy and tolerability compared to SSRIs and benzodiazepines in GAD[5]

Agomelatine Significantly Reduces Anxiety in Patients with GAD[4]



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.

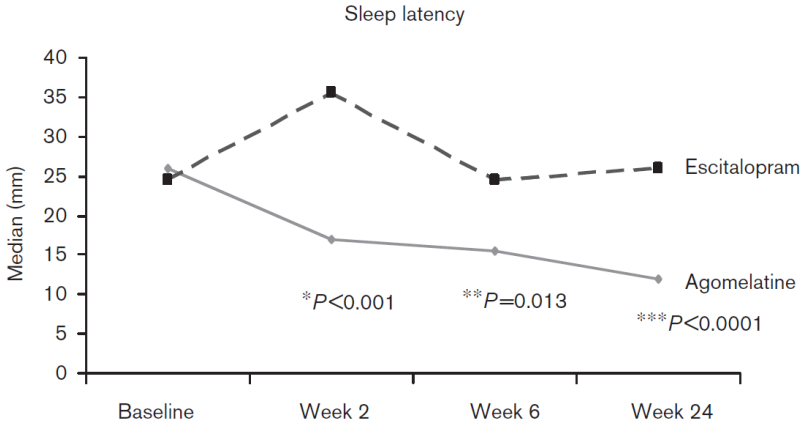
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Agomelatine Improves Sleep in GAD and MDD

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 MDD[3]
- No hangover effects, unlike other 5-HT2C antagonists

Agomelatine Improves Sleep Compared to SSRIs[1]



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.

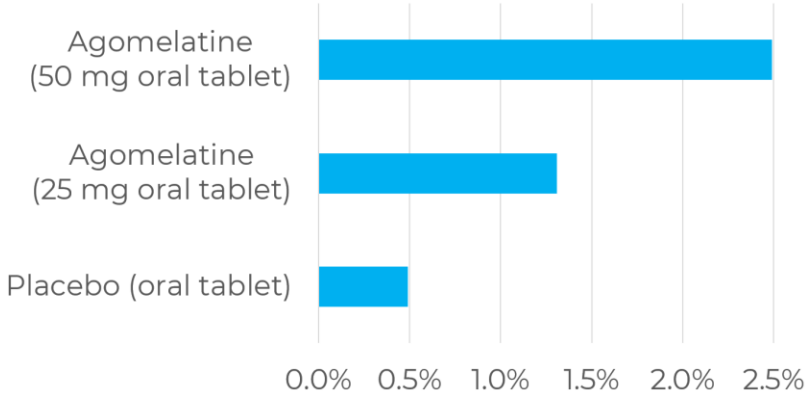
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Despite Known Efficacy, Agomelatine Has Been Held Back by Need for Liver Function Testing

Agomelatine Treatment Requires Frequent Liver Function Tests[2]

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

Agomelatine Can Cause Dose-Dependent Liver Enzyme Elevations[1]



% of Patients with Serum Transaminase Increase >3x the Upper Limit of Normal

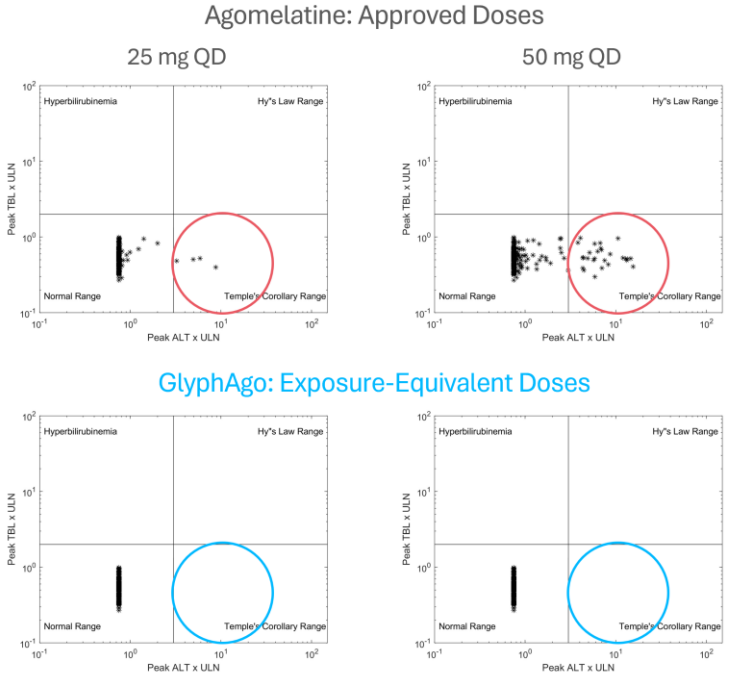
1. Perlemuter, Gabriel, et al. "Characterisation of Agomelatine-Induced Increase in Liver Enzymes: Frequency and Risk Factors Determined from a Pooled Analysis of 7605 Treated Patients." CNS Drugs 30.9 (2016): 877-888. Significant increase in transaminase levels defined as an increase to >3x the upper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

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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



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

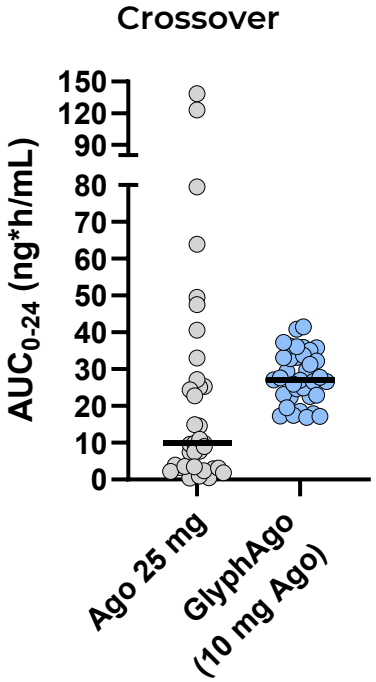
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Phase 1 Topline: GlyphAgo™ Provided Therapeutic Exposures at Doses Projected to Avoid Liver Issues

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 Cmax 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



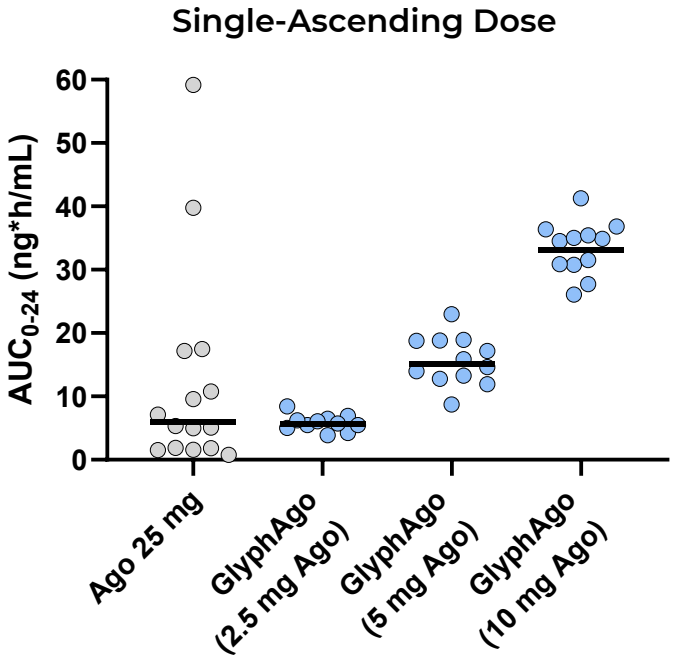
SEAPORT THERAPEUTICS

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



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GlyphAgo™ Clinical Development Plan Overview

Completed, ongoing, and near-term trials

Phase 1 Proof-of-Concept Trial in Healthy Volunteers (Completed)

- ✓ GlyphAgo™ provided therapeutic exposures of agomelatine at doses projected to avoid liver issues, and was generally well-tolerated, with no serious or severe AEs, and no liver-related AEs

Phase 2a Proof-of-Pharmacology Trial in GAD (Topline Data Expected Early 2028)

- Randomized, double-blind trial of two dose levels of GlyphAgo designed to evaluate the potential sleep benefit of GlyphAgo in patients with GAD and sleep disturbance

Phase 2/3 Trial in GAD (Topline Data Expected YE 2028)

- Randomized, double-blind, placebo-controlled, potentially registration-enabling trial designed to evaluate efficacy and safety of GlyphAgo in adults with GAD

Pipeline of Novel Potential Treatments for Neuropsychiatric Disorders



OUR PROGRAMS	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	ANTICIPATED MILESTONES
GlyphAllo™ (SPT-300) Glyph Allopregnanolone	Major Depressive Disorder (MDD)				Data from Phase 2b BUOY-1 trial expected 1H 2027
	Designed to overcome oral bioavailability limitations				
GlyphAgo™ (SPT-320) Glyph Agomelatine	Generalized Anxiety Disorder (GAD)				Data from Phase 2a and 2/3 trials expected 2028
	Designed to reduce or eliminate need for liver function testing				
Glyph2BLSD™ (SPT-348) Glyph 2-bromo-LSD	Multiple Indications*				Completion of first-in-human-enabling studies expected YE 2027
	Designed to improve PK & tolerability				

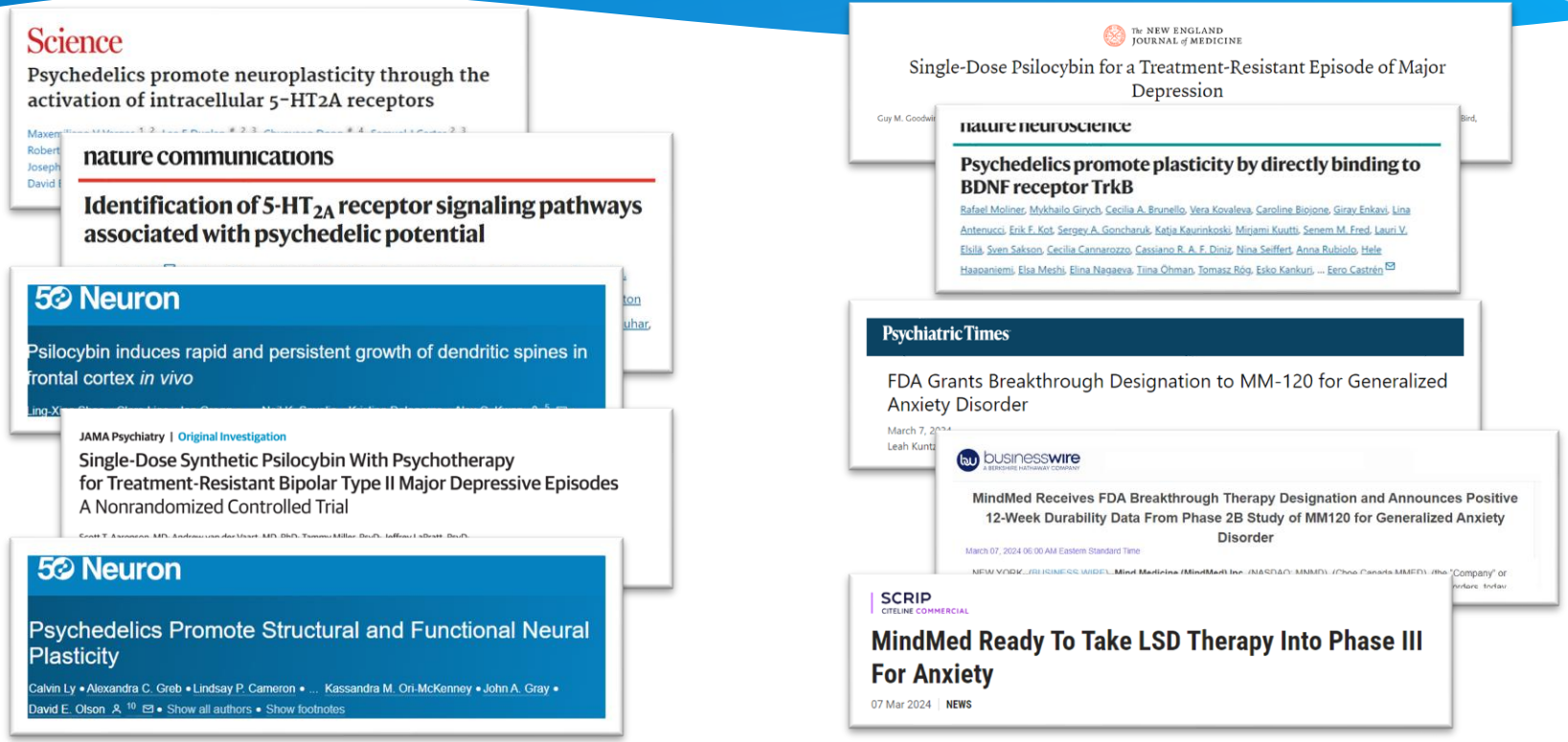
*Neuropsychiatric and headache disorders with significant unmet need

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

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The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our investigational product candidates are safe and effective. No regulatory agency has made any such determination that our investigational therapies are safe or effective for use by patients for any indication; *PK = pharmacokinetic.

Neuroplastogens are Poised to Transform Psychiatric Treatment



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

Neuroplastogen Benefits

- Offer potential to enhance neuroplasticity in brain circuits implicated in neuropsychiatric disorders[1]
- Demonstrated clinical efficacy for depression and other disorders[2]

Key Limitations

Functional unblinding of clinical trials, need for supervised administration, concerns over long-term safety[2]

Glyph2BLSD™ Approach

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

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1. Ly, C., et al.(2018). Psychedelics promote structural and functional neural plasticity. Cell Reports, 23(11), 3170–3182; 2. McIntyre, R., et al. (2025). Psychedelics for the Treatment of Psychiatric Disorders: Interpreting and Translating Available Evidence and Guidance for Future Research. Am J Psychiatry, 182, 21-32.

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 ✓ **2H 2026:** Initiated Phase 2a trial	• **1H 2027:** Initiate Phase 2/3 trial ★ **Early 2028: Phase 2a trial topline data** ★ **YE 2028: Phase 2/3 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 2/3 trial of GlyphAgo, as well as through initiation of the Phase 3 program of GlyphAllo

MDD = Major Depressive Disorder; POC = Proof-of-Concept; FIH = First-in-Human

★ = Key Readout

Seaport Board of Directors



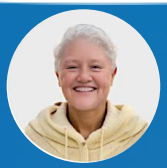
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Former Chair & CEO of Karuna



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Corporate Presentation
November 2026

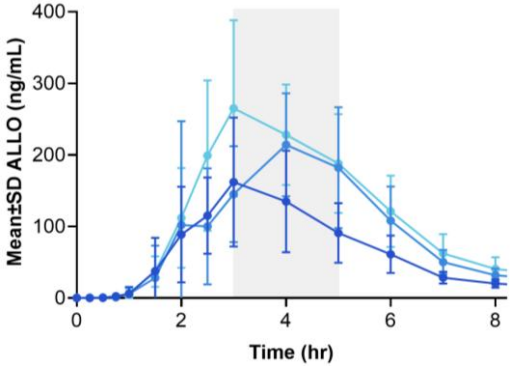


Unlocking Better Days™

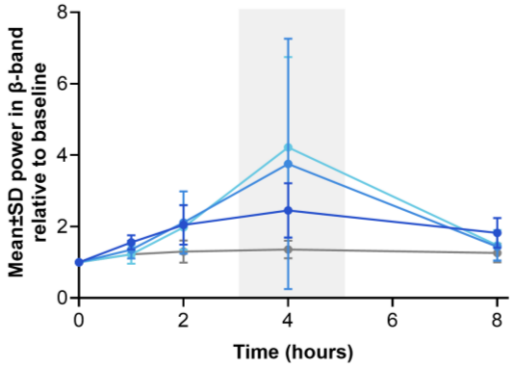
Appendix

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

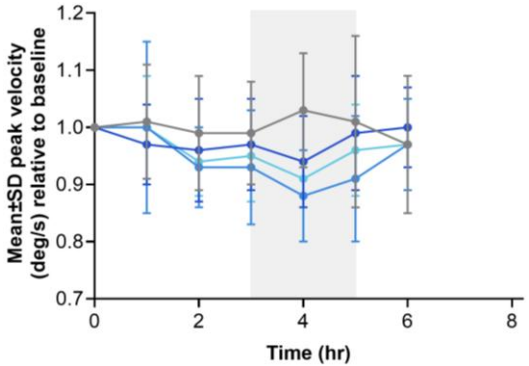
Pharmacokinetics



Beta EEG Power



Saccadic Eye Velocity



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

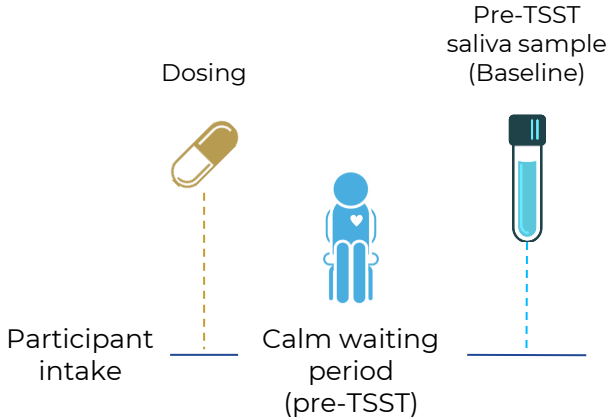
Allopregnanolone Levels and PD Signals Peaked 3-5 Hours Post-Dose and Declined by 6-8 Hours

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Simpson, J.S., et al. (2026). An oral allopregnanolone prodrug bypasses liver metabolism via lymphatic transport enabling bioavailability in animals and humans. Sci Transl Med, 18(842):eadu2352;
EEG = Electroencephalogram; PD = Pharmacodynamic.

Design of Phase 2a Trial of GlyphAllo™

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

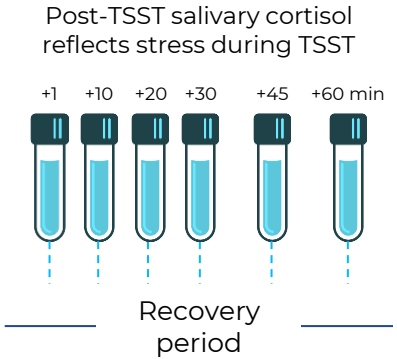


1. Anticipation: prepare a speech
2. Public speaking to a panel
3. Live math test to a panel



Trier Social Stress Test:

Validated model of acute anxiety



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