SEAPORT THERAPEUTICS

Corporate Presentation
June 2026

Turning the Tide on Mental Health

Disclaimer

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 in mid-2026 and 1H 2026, respectively, and the timing of initial data for both programs in 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 divest our noncore product candidates and 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. 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 U.S. Food and Drug Administration 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. Moreover, 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. Moreover, 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.

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.

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 a **top 3** cause of death in ages 10-34[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. Suicide Mortality in the United States, 2002–2022 | CDC. (2024). https://www.cdc.gov/nchs/data/databriefs/db509.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

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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

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

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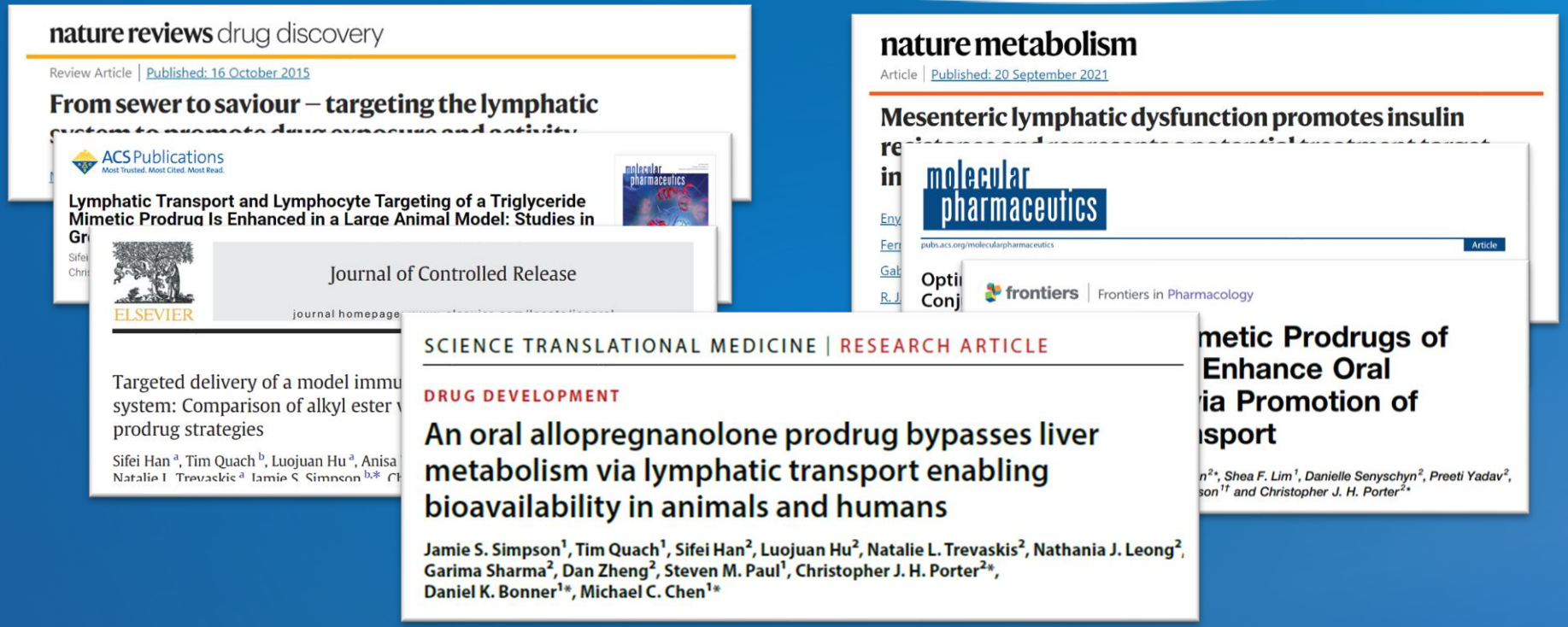
Glyph™ Platform: Transformative & Validated

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



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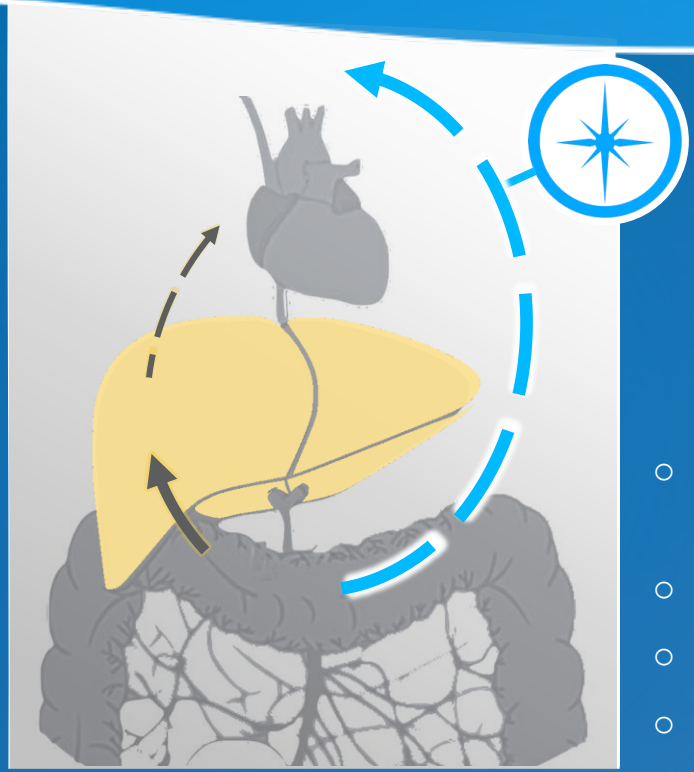
CoM = Composition of Matter

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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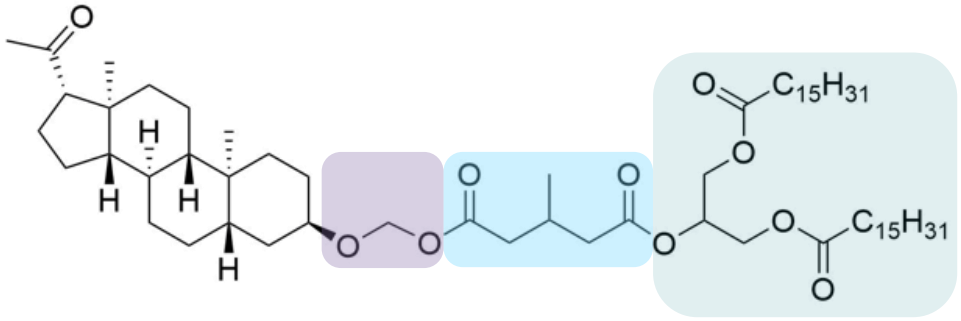
*PK = Pharmacokinetic

Design of Proprietary Prodrug Chemistry

Designed to avoid first-pass metabolism by promoting lymphatic uptake



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

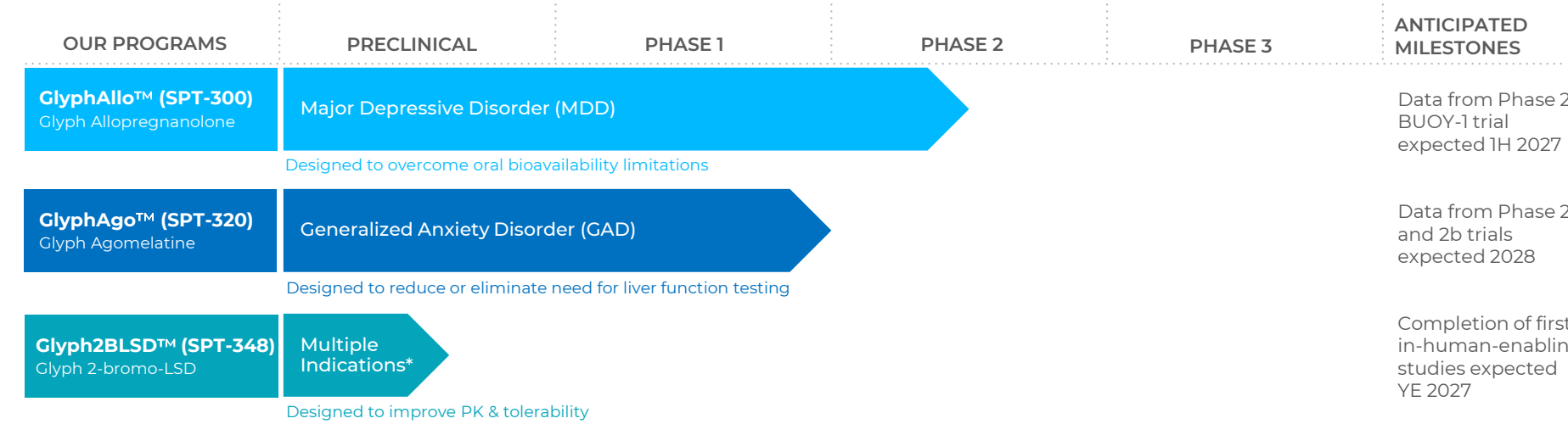
Self-Immolative (SI)
Allows controlled release of parent drug compound

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



*Depressive disorders, including treatment-resistant depression (TRD), post-traumatic stress disorder (PTSD), 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; TRD = treatment-resistant depression; PTSD = post-traumatic stress disorder

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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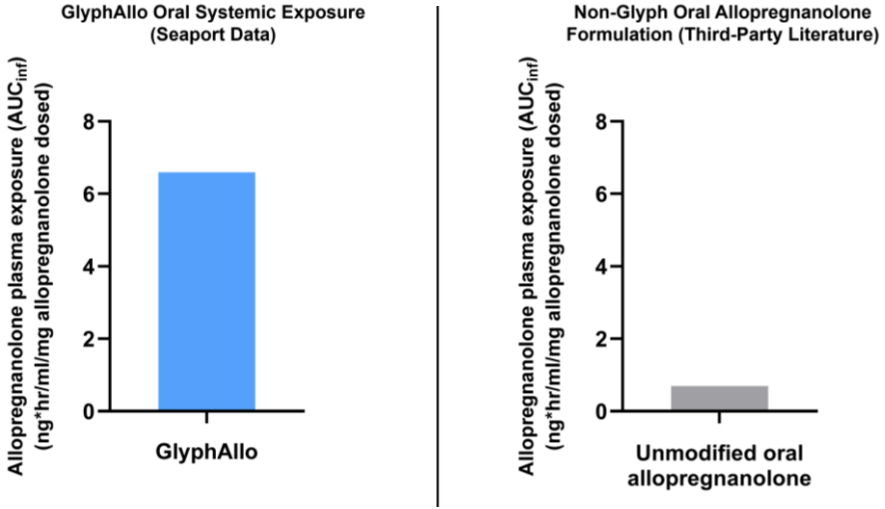
1. Paul, S.M., et al. (2020). Allopregnanolone: From molecular pathophysiology to therapeutics. A historical perspective. Neurobiol Stress, Mar 14, 12, 100215. 2. Epperson, C. N., et al. (2023). Effect of brexanolone on depressive symptoms, anxiety, and insomnia in women with postpartum depression: Pooled 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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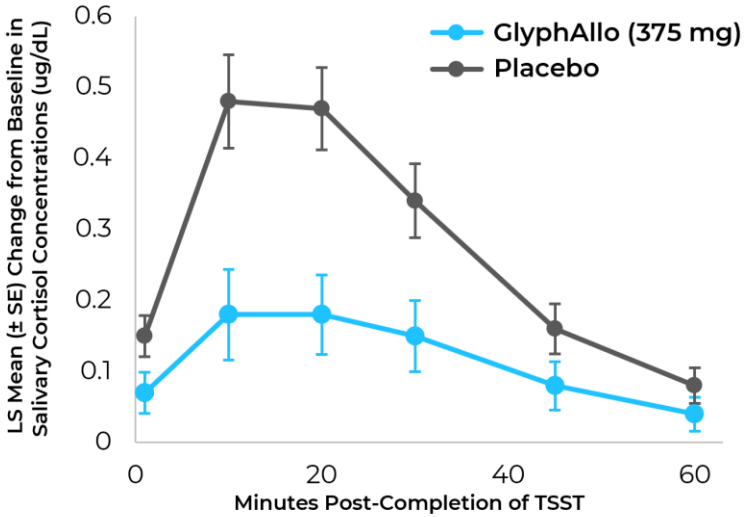
Phase 2a Results: GlyphAllo™ Significantly Reduced Stress Response Compared to Placebo (p=0.0001)[1]

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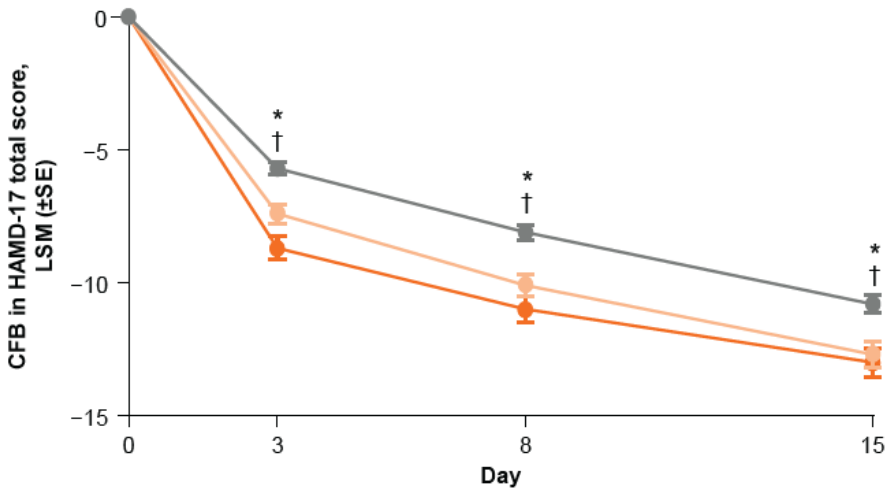
Zuranolone Showed Strong Early Efficacy in MDD, But Treatment Duration Was Only Two Weeks

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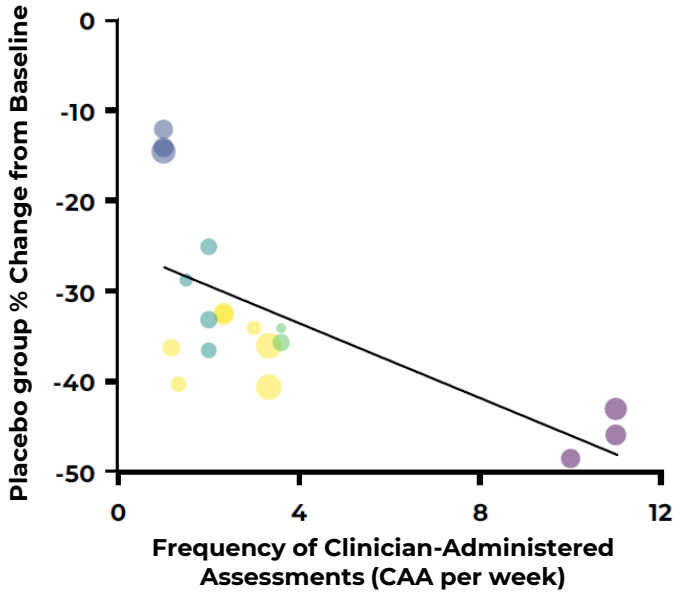
Number and Frequency of Clinical Assessments are Associated with Placebo Response in MDD Trials

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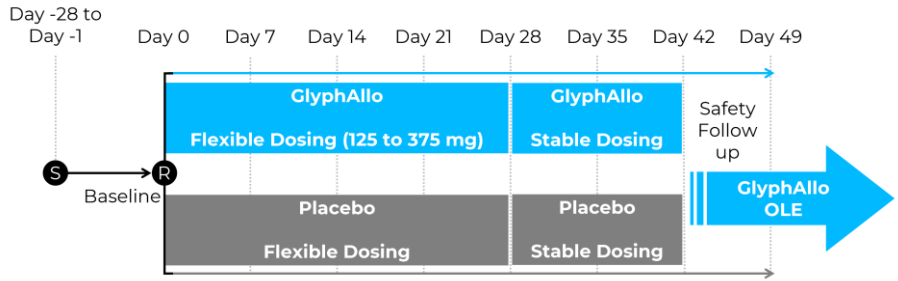
Design of Phase 2b BUOY-1 Trial of GlyphAllo™ in MDD With or Without Anxious Distress

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)

*ISM = Intensive Safety Monitoring

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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 (Topline Data Expected 2H 2026)

- Evaluating the impact of GlyphAllo on simulated driving 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 2b 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

*Depressive disorders, including treatment-resistant depression (TRD), post-traumatic stress disorder (PTSD), 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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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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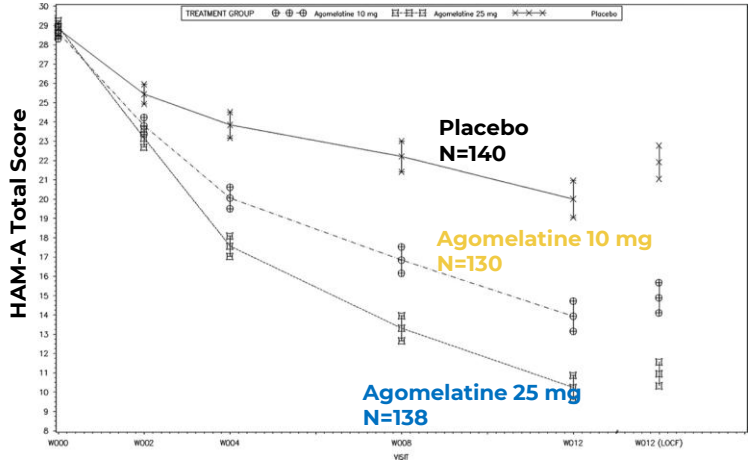
1. Stein, D.J., et al. (2008). Efficacy of agomelatine in generalized anxiety disorder: a randomized, double-blind, placebo-controlled study. J Clin Psychopharmacol, 28(5), 561-566; 2. Stein, D.J., et al. (2012). Agomelatine prevents relapse in generalized anxiety disorder: a 6-month randomized, double-blind, 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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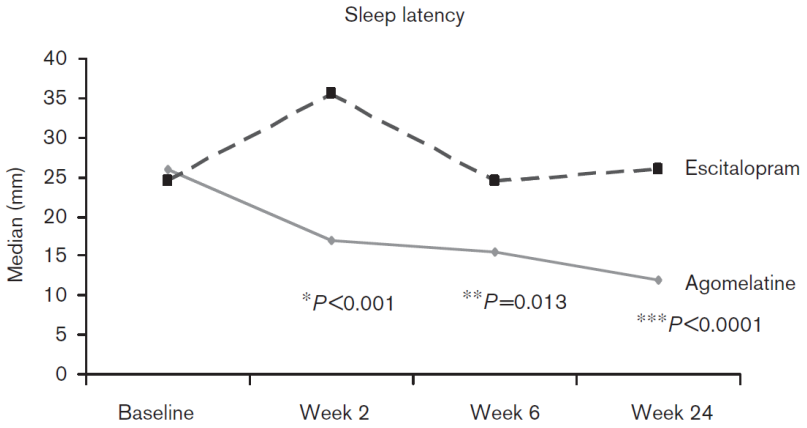
Agomelatine Improves Sleep in GAD and MDD

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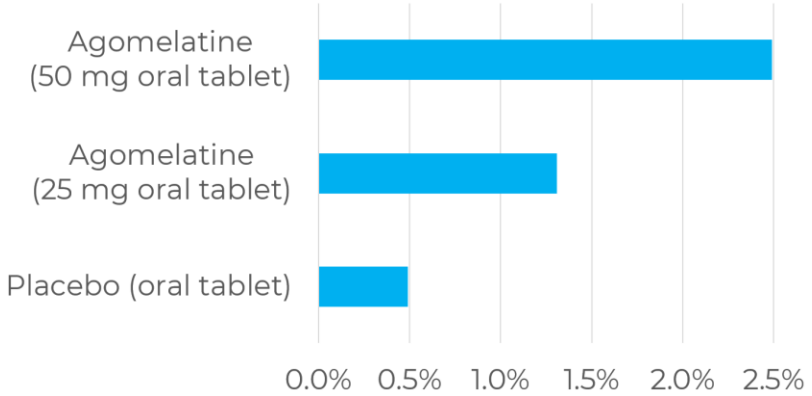
Despite Known Efficacy, Agomelatine Has Been Held Back by Need for Liver Function Testing

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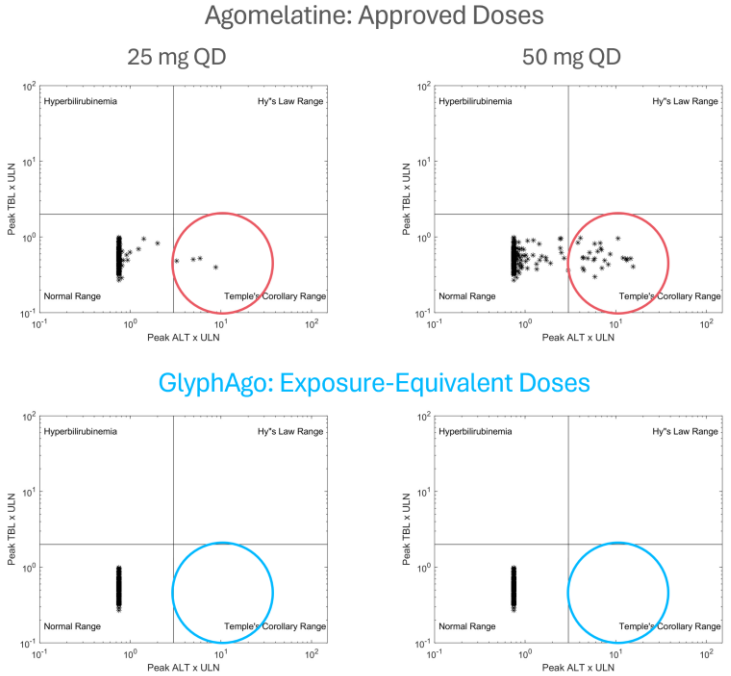
DILIsym Simulations Demonstrate that GlyphAgo™ is Not Projected to Cause Liver Enzyme Elevations

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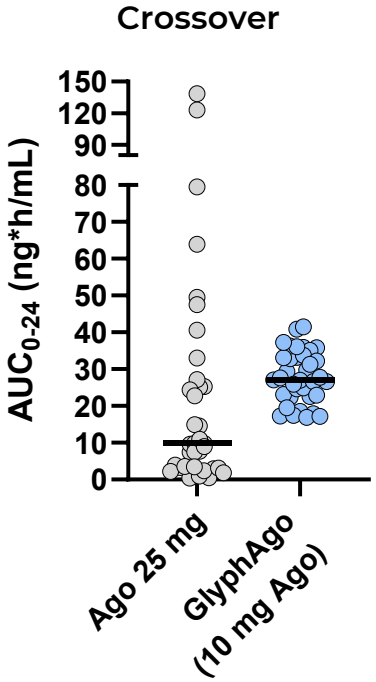
Phase 1 Topline: GlyphAgo™ Provided Therapeutic Exposures at Doses Projected to Avoid Liver Issues

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



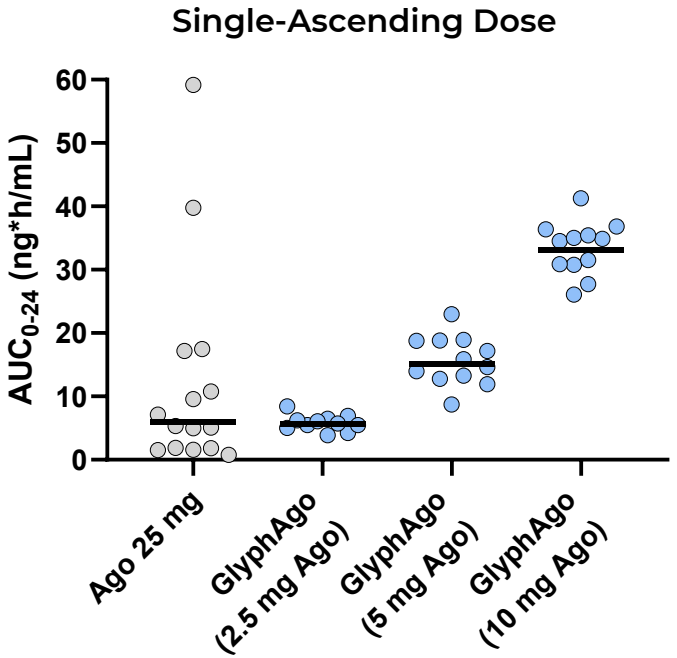
SEAPORT THERAPEUTICS

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 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 2b 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 2b 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				

*Depressive disorders, including treatment-resistant depression (TRD), post-traumatic stress disorder (PTSD), 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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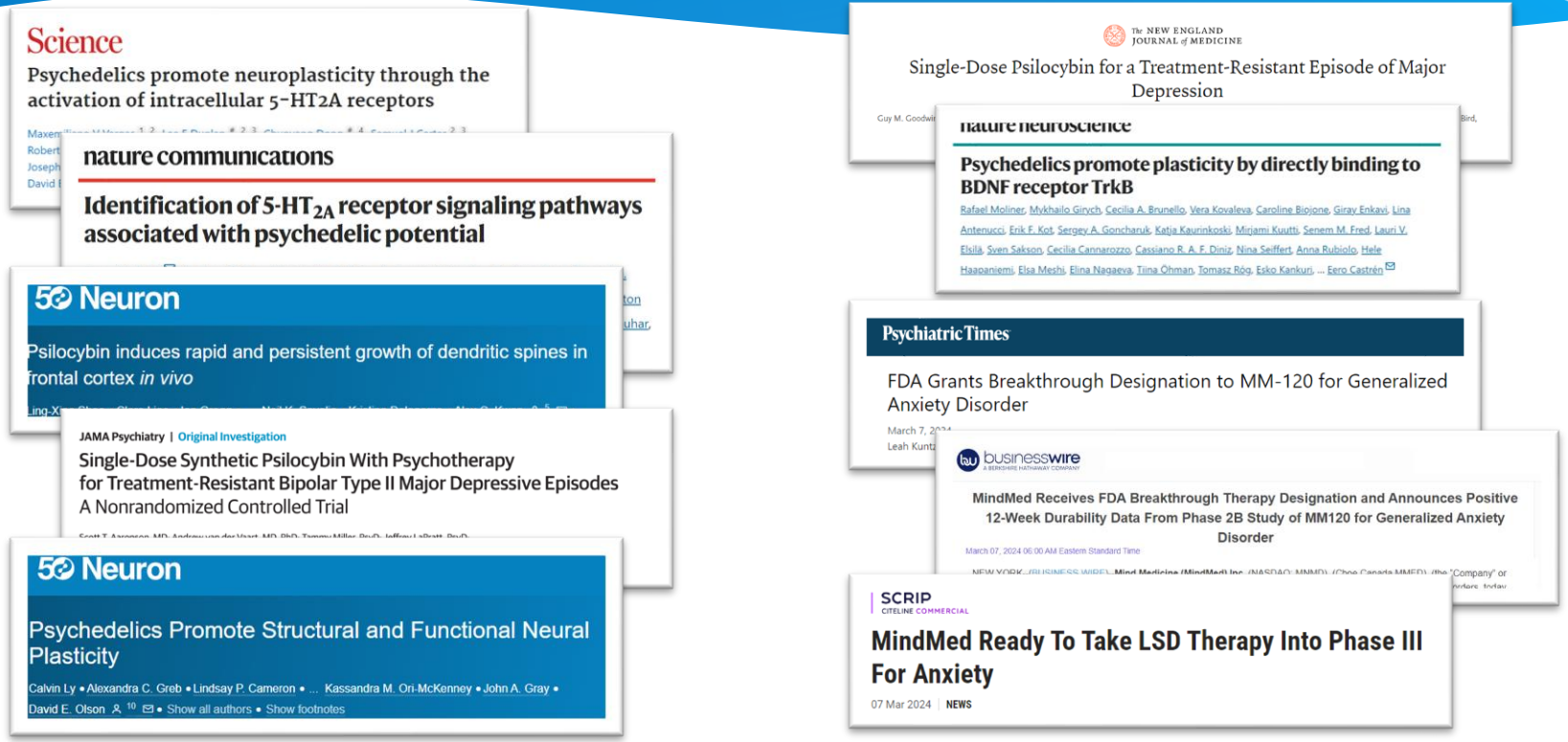
The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our investigational product candidates are safe and effective. No regulatory agency has made any such determination that our investigational therapies are safe or effective for use by patients for any indication; *PK = pharmacokinetic; TRD = treatment-resistant depression; PTSD = post-traumatic stress disorder

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	★ **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

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

★ = Key Readout

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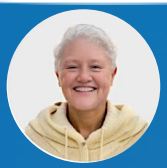

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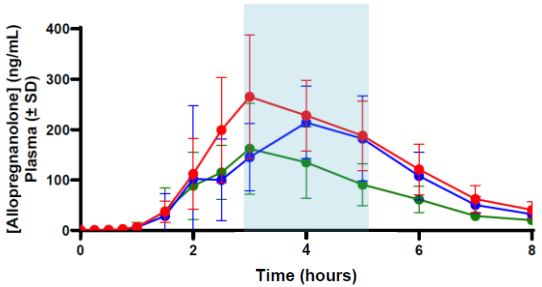
Corporate Presentation
June 2026

Unlocking Better Days™

Appendix

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

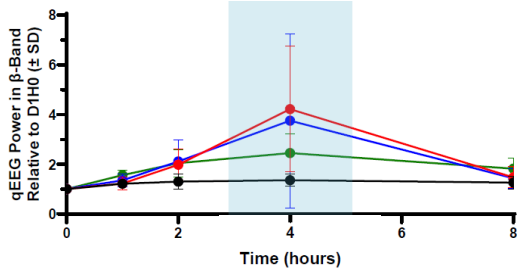
PK



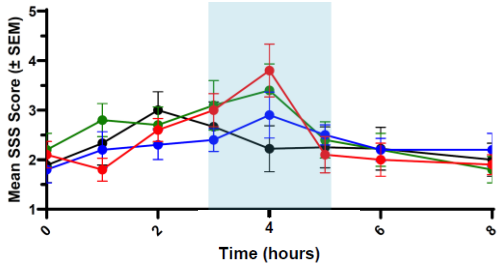
- Pooled Placebo (N=15)
- GlyphAllo 250 mg (N=9)
- GlyphAllo 375 mg (N=9)
- GlyphAllo 500 mg (N=9)

PD

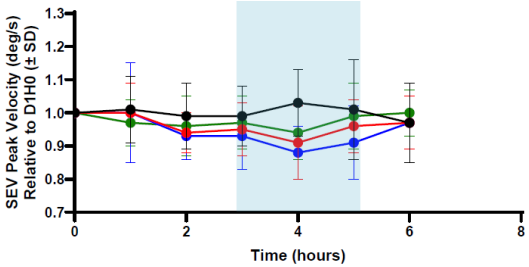
Beta EEG Power



Stanford Sleepiness Score (SSS)



Saccadic Eye Velocity (SEV)



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

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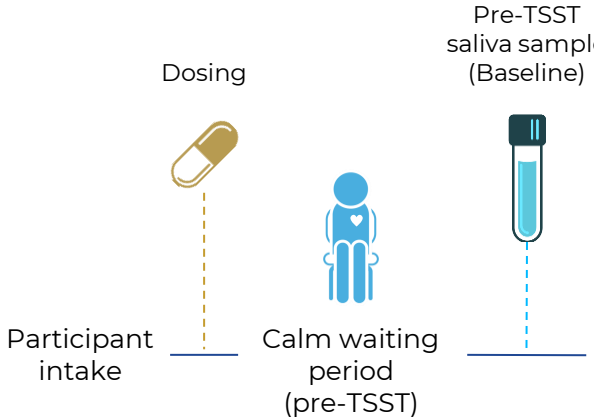
1. Bonner, D., Garg, V., Gold, M., Loebel, A., Chen, M. (2024 Dec 8-11) GlyphAllo (SPT-300), a First-in-Class Orally Bioavailable Prodrug of the Neurosteroid Allopregnanolone: Safety, Tolerability, and Clinical Pharmacology in Healthy Volunteers. American College of Neuropsychopharmacology (ACNP) Annual Meeting, 2024, Phoenix, AZ, United States; PK = Pharmacokinetics; PD = Pharmacodynamics.

Design of Phase 2a Trial of GlyphAllo™

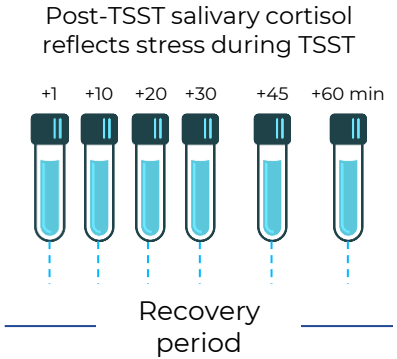
Randomized, placebo-controlled trial using the Trier Social Stress Test (TSST)



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