Sage Therapeutics®

# Corporate Presentation

April 2024

# Safe Harbor Statement

- The slides presented today and the accompanying oral presentations contain forward-looking statements, which may be identified by the use of words such as "may," "might," "will," "should," "can," "expect," "plan," "anticipate," "believe," "estimate," "project," "intend," "future," "opportunity", "goal", "mission", "potential," "target", or "continue," and other similar expressions.
- Forward-looking statements in this presentation include statements regarding: plans, expectations, strategy and goals for commercialization of ZURZUVAE as a treatment for women with PPD, including our goal for ZURZUVAE to become first line therapy and standard of care in this indication and our reimbursement, access and time to shipment goals; our belief in the potential benefit and profile of ZURZUVAE in the treatment of PPD; the potential for success of our commercialization of ZURZUVAE for women with PPD and our belief in the size of the potential market opportunity in PPD and the role of ZURZUVAE in unlocking such potential; the potential for success of our other product candidates in various indications, including the potential profile and benefit of our other product candidates; our clinical development plans, including expected timelines for activities and our expectations as to potential results; our estimates as to the number of patients with disorders and diseases of interest to us and that we hope to help; the potential drivers of value in our business and the potential for value creation; the opportunity, mission, goals and vision for our business; and our expectations with respect to cash, expenses and maintaining a strong financial foundation.
- These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risk that:
  - We may not be successful in our commercialization efforts with respect to ZURZUVAE in the treatment of women with PPD; the market size and market acceptance for ZURZUVAE as a treatment for women with PPD by healthcare professionals, patients and payors may be significantly smaller than we expect; we may encounter reimbursement, market access or other market-related issues in the course of our commercialization activities; early positive signs may not be a signal of future success; ZURZUVAE may not achieve the clinical benefit in the treatment of women with PPD that we expect; we may not generate revenue from sales of ZURZUVAE at the levels or on the timing we expect.
  - Our clinical trials may not meet their primary endpoints or key secondary endpoints. For example, results of our ongoing clinical studies of dalzanemdor in HD and AD may be negative like the results from the PRECEDENT study in MCI in PD. The possible distinctions among indications as a result of the underlying pathophysiology and symptomatology in PD may not prove to be relevant in the context of clinical trials of dalzanemdor. Success in nonclinical studies or in prior clinical trials of our product candidates may not be repeated or observed in ongoing, planned or future studies involving the same compound or other product candidates. Non-clinical and clinical results from ongoing or future trials may not support further development of the product candidate, our planned regulatory pathway, or filing for or obtaining regulatory approval on the timelines we expect or at all and we may be required to conduct additional clinical trials or nonclinical studies which may not be successful. We may experience slower than expected enrollment in our clinical trials or may encounter other delays or problems, including in analyzing data or requiring the need for additional analysis, data or patients, or due to timing and results of consultation with regulatory authorities, and such issues with any trial could cause delay in completion of the trial, availability of results and timing or success of future activities.
  - We may encounter unexpected safety or tolerability issues with respect to any of our product candidates or marketed products; we may encounter different or more severe adverse events at higher doses, different frequency or length of dosing or in new indications.
  - At any stage, regulatory authorities may ask for additional clinical trials, nonclinical studies or other data in order for us to proceed further in development or to file for or obtain regulatory approval. Other decisions or actions of the FDA or other regulatory authorities may affect the initiation, timing, design, size, progress and cost of clinical trials or development efforts and our ability to proceed with further development.
  - Even if our other product candidates are successfully developed and approved, the number of patients with the diseases or disorders our products treat or the subset of such patients we believe will use our products, the need for new treatment options, and the actual market for such products may be smaller than our current estimates.
  - The anticipated benefits of our collaborations, including our collaboration with Biogen, may never be achieved. The need to align with our collaborators may hamper or delay our development and commercialization efforts or increase our costs; our business may be adversely affected and our costs may increase if any of our key collaborators fails to perform its obligations or terminates our collaboration.
  - We may not be able to obtain and maintain adequate intellectual property protection or other forms of data and marketing exclusivity for our products, or to defend our patent portfolio against challenges from third parties.
  - We may face competition from others developing products or with approved products for similar uses as those for which our product candidates are being developed.
  - Our operating expenses may be higher than forecasted and we may face unexpected expenses which could cause us to use our cash faster or change our plans or both. Our revenues may be lower than we expect, including if we do not achieve market acceptance of ZURZUVAE in the treatment of women with PPD or if we do not achieve our access/reimbursement goals in this indication, or if our launch for other reasons is not as successful as we expect which may cause us to not achieve our cash runway expectations. We may not achieve expected milestones that trigger cash payments on the timing we expect, or at all. For these and other reasons, our expectations with respect to cash, expenses and financial strength may not prove to be accurate. We may need or choose to raise additional funding, which may not be available on acceptable terms, or at all.
  - We may not be able to establish and maintain key business relationships with third parties on acceptable terms or we may encounter problems with the performance of such third parties.
  - We may encounter technical and other unexpected hurdles in the manufacture, development or commercialization of our products.
  - Any of the foregoing or other factors may negatively impact our ability to achieve our goals, mission, opportunities, plans or expectations for our business and the potential for value creation.
- For additional disclosure regarding these and other risks Sage faces, see the disclosure contained in the "Risk Factors" section of our most recent report, and in our other public filings, with the Securities and Exchange Commission, available on the SEC's website at http://www.sec.gov. Any forward-looking statement represent our views only as of today, and should not be relied upon as representing our views as of any subsequent date. We undertake no obligation to update or revise the information contained in this presentation, whether as a result of new information, future events or circumstances or otherwise.

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**OUR VISION**: To fearlessly lead the way to create a world with *better brain health*

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# By The Numbers

## ADVANCING A LEADING BRAIN HEALTH PORTFOLIO

### RICH INNOVATIVE PIPELINE

**5** Clinical stage programs

### MARKETED PRODUCTS

**2** First-in-class treatments for postpartum depression

### SIGNIFICANT POTENTIAL PATIENT IMPACT

**+450** Million people living with a brain health disorder

## THIS IS SAGE

**+500** Total number of employees

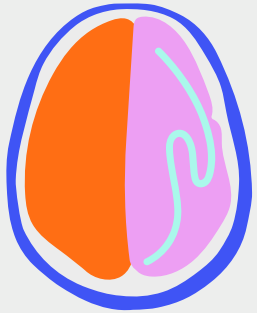
**43%** Employees in state of Massachusetts

**57%** Employees outside of Massachusetts

# Opportunity to become the leader in brain health

**Patient inspired, patient led, *patient first***

**ZURZUVAE™**
First and only oral product approved by the FDA specifically for postpartum depression *(second approved product)*



**Differentiated pipeline** driven by patient need, science, and external insights

**Scientific and therapeutic leadership** within GABA and NMDA opportunities – strong product engine

**Strong financial foundation** to help create value for sustained growth

**Values-driven culture** focused on doing what's right for patients

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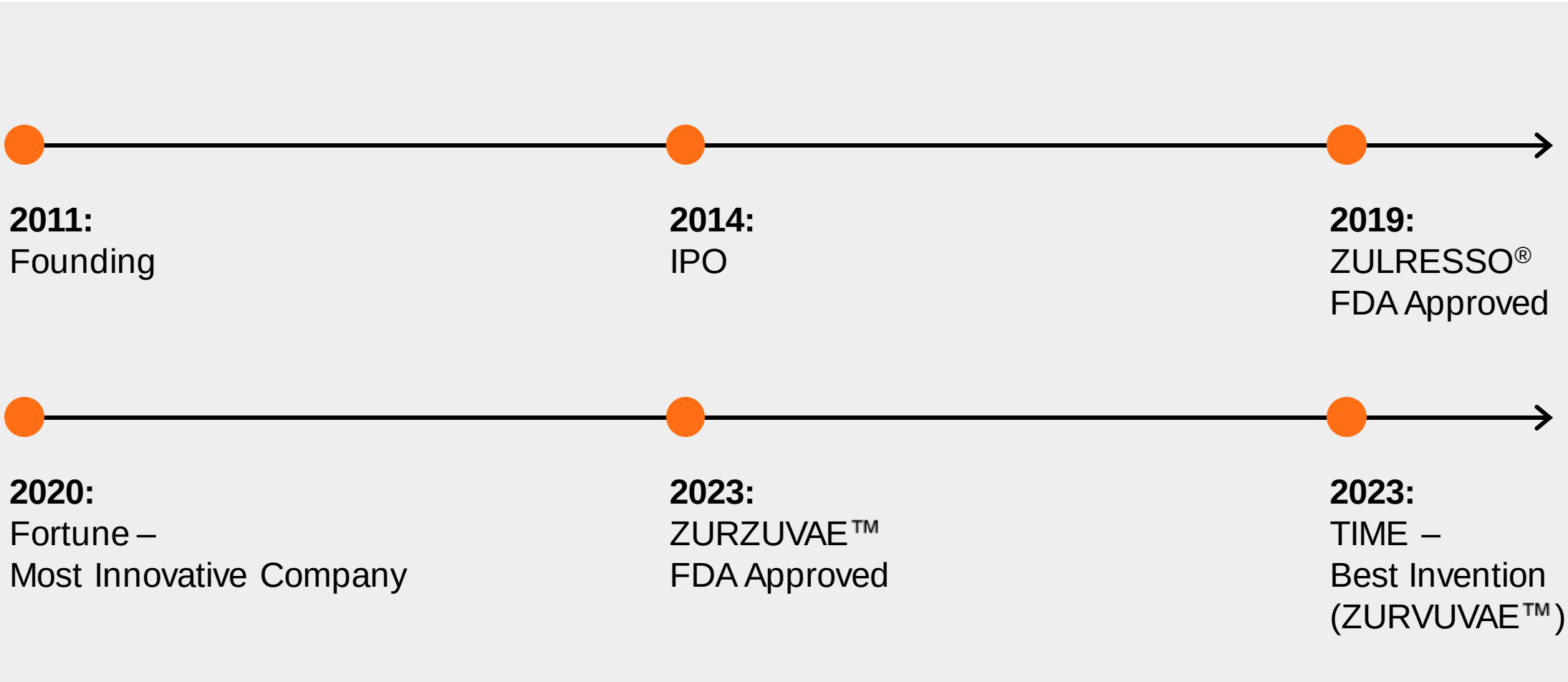
# Business Milestones



| COMPOUND | TARGET INDICATIONS | PHASE 1 | PHASE 2 | PHASE 3 | STATUS |
|---|---|---|---|---|---|
| **Postpartum Depression Commercial Products** | | | | | |
| ZURZUVAE™* (zuranolone) CIV | Postpartum Depression | | | | MARKETED |
| ZULRESSO® (brexanolone) CIV injection | Postpartum Depression | | | | MARKETED |
| **Pipeline** | | | | | |
| Zuranolone* (SAGE-217) | Major Depressive Disorder** | | | PHASE 3 | |
| Dalzanemdor (SAGE-718) | Huntington's Disease Cognitive Impairment | | IN PHASE 2 | | |
| | Alzheimer's Disease Mild Cognitive Impairment and Mild Dementia | | IN PHASE 2 | | |
| SAGE-324* | Essential Tremor | | IN PHASE 2 | | |
| **Programs In Evaluation** | | | | | |

SAGE-689
*Acute GABA Hypofunction*

SAGE-421
*NMDA Hypofunction*

SAGE-319
*GABA Hypofunction*

**Collaboration Partners: Biogen Inc. and Shionogi for zuranolone and Biogen Inc. for SAGE-324*
***The FDA issued a CRL on August 4, 2023, related to the NDA for the treatment of adults with MDD stating that the application did not provide substantial evidence of effectiveness to support the approval of zuranolone for the treatment of MDD and that an additional study or studies will be needed. No Phase 3 trials are currently ongoing.*

*Please refer to the U.S. Prescribing Information for ZULRESSO and the U.S. Prescribing Information for ZURZUVAE*
*Safety and efficacy for investigational uses or compounds have not been established. There is no guarantee that the outcome of these studies will be positive or result in approval by a health authority.*

# Multiple Expected Catalysts

1. Ongoing commercialization of **ZURZUVAE™** in the treatment of women with postpartum depression

2. Advance **dalzanemdor (SAGE-718)** with multiple topline data readouts expected in 2024

3. Advance **SAGE-324** with topline data expected in mid-2024

4. Progress earlier stage **pipeline**

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ZURZUVAE™
(zuranolone) capsules C IV
20 mg • 25 mg • 30 mg

# Is Now Available

ZURZUVAE (50mg) is approved for the treatment of postpartum depression in adults. A full course of ZURZUVAE includes 14 days of treatment.

Sage Therapeutics | Biogen

*Note: image does not represent actual size of blister pack*

**Important Safety Information**

ZURZUVAE may cause serious side effects, including decreased awareness and alertness, which can affect your ability to drive safely or safely do other dangerous activities. Do not drive, operate machinery, or do other dangerous activities until at least 12 hours after taking each dose. You may not be able to tell on your own if you can drive safely or tell how much ZURZUVAE is affecting you. ZURZUVAE may cause central nervous system (CNS) depressant effects including sleepiness, drowsiness, slow thinking, dizziness, confusion, and trouble walking. Taking alcohol, other medicines that cause CNS depressant effects such as benzodiazepines, or opioids while taking ZURZUVAE can make these symptoms worse and may also cause trouble breathing. ZURZUVAE is a federally controlled substance schedule IV because it contains zuranolone, which can be abused or lead to dependence. Tell your healthcare provider right away if you become pregnant or plan to become pregnant during treatment with ZURZUVAE. You should use effective birth control (contraception) during treatment with ZURZUVAE and for 1 week after the final dose. ZURZUVAE and other antidepressant medicines may increase the risk of suicidal thoughts and actions in people 24 years of age and younger. ZURZUVAE is not for use in children. The most common side effects of ZURZUVAE include sleepiness or drowsiness, dizziness, common cold, diarrhea, feeling tired, weak, or having no energy, and urinary tract infection.

# ZURZUVAE is the first and only oral treatment specifically indicated for the treatment of women with PPD

**Potential for Rapid & Sustained Improvement**

- In the SKYLARK and ROBIN Studies, an improvement in depressive symptoms vs. placebo was seen with a 14-day course treatment beginning as early as day 3 and maintained at day 45


**14-day Short Course**

- In the SKYLARK and ROBIN Studies, a statistically significantly greater improvement in depressive symptoms vs placebo was seen at day 15 following a 14-day short course treatment

**Flexible Approach**

- In clinical trials, ZURZUVAE was studied for use alone or as an adjunct to oral antidepressant therapy in the treatment of women with PPD

**Novel MOA & Class**

- ZURZUVAE is neuroactive steroid GABAA receptor positive modulator with an MOA thought to be related to its positive allosteric modulation of GABAA receptors

**Safety-related Information**

- The most common adverse reactions (incidence ≥5% and greater than placebo) are somnolence, dizziness, diarrhea, fatigue, nasopharyngitis, and urinary tract infection. See boxed warning and warnings & precautions for additional safety information.

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# PPD poses a substantial burden to patients and their families

PPD symptoms are one of the **most common complications** of pregnancy and childbirth[1]

Perinatal depression is **inconsistently diagnosed** and may be an undertreated condition[1-4]

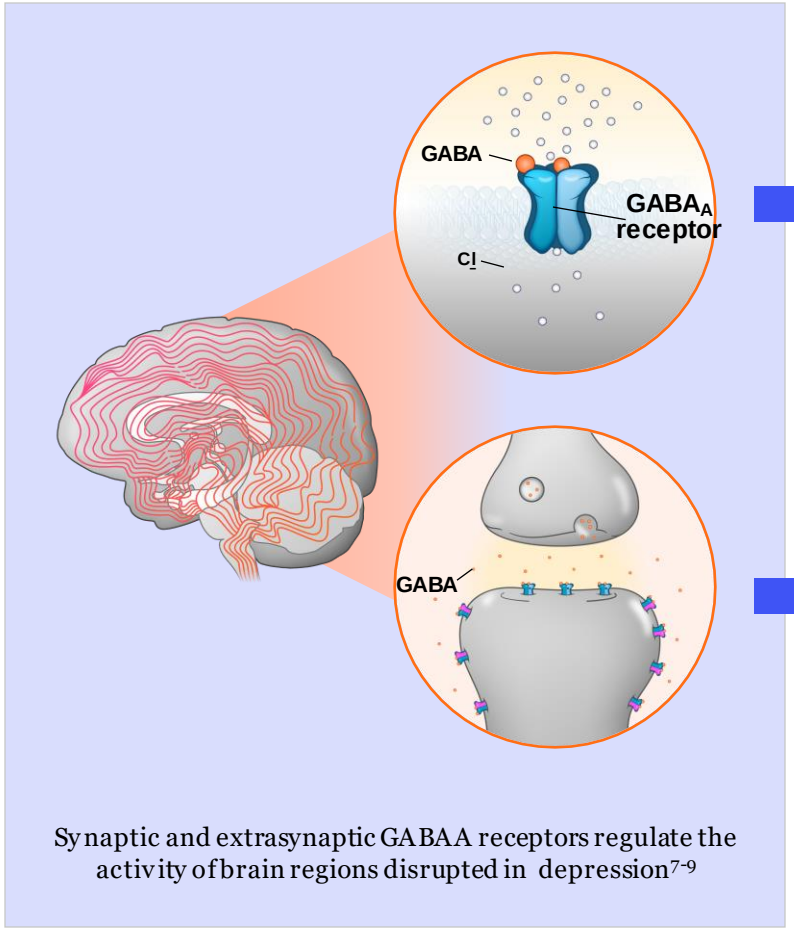
Mothers with perinatal depression often face **significant challenges** with functioning and infant-bonding[5-9]

The **economic burden** associated with perinatal depression is vast and impacts patients, their families, employers, and health care payers[10-12]

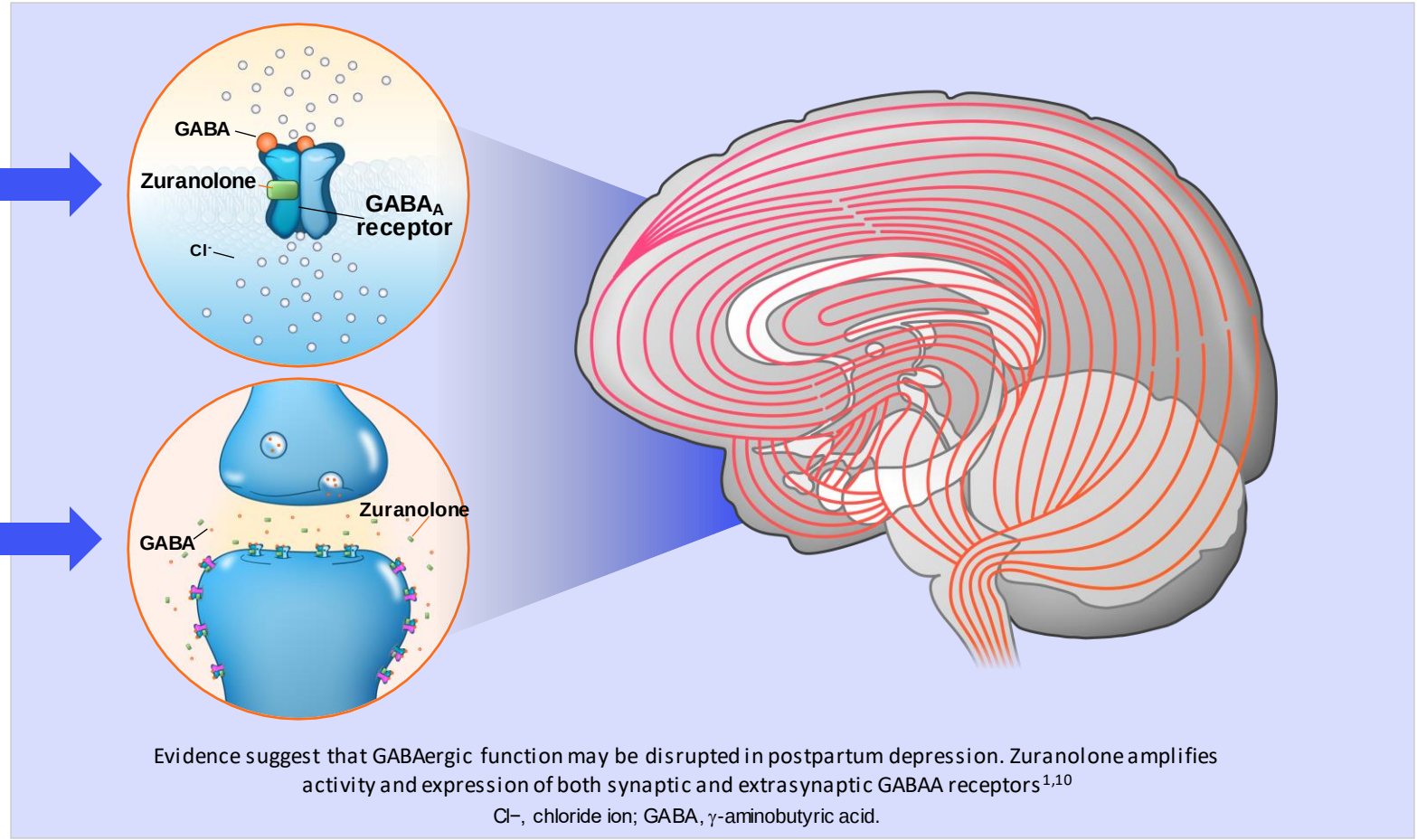
The **COVID-19 Pandemic** had a significant effect on perinatal mental health outcomes[13-15]

1. Bauman BL, Ko JY, Cox S, et al. MMWR Morb Mortal Wkly Rep. 2020;69(19):575-581 2. Ukatu N, et al. Psychosomatics. 2018;59(3):211-219. 3. Wang Z, et al. Transl Psychiatry. 2021;11(1):543. 4. Fonseca A, et al. J Affect Disord. 2020;274:167-173. 5. Beck CT, et al. Am J Nurs. 2006;106(5):40-50. 6. Wouk K, et al. Pediatrics. 2016;137(1). 7. Lilja G, et al. Scand J Caring Sci. 2012;26(2):245-253. 8. Gaglardi L, et al. Arch Dis Child. 2012;97(4):355-357. 9. Kerstis B, et al. Arch Womens Ment Health. 2016;19(1):87-94 10. Epperson CN et al. Curr Med Res & Opinion. 2020;36(10):1707-1716 11. Moore-Simas TA et al. J Med Economics. 2020; 23(2):174-183. 12. Luca DL et al. Math Pol Res. 2019. 13. Farewell CV, Jewell J, Walls J, Leiferman JA. A mixed-methods pilot study of perinatal risk and resilience during COVID-19. J Prim Care Community Health. 2020;11:2150132720944074. 14. Liu CH EC, Mittal L. Risk factors for depression, anxiety, and PTSD symptoms in perinatal women during the COVID-19 pandemic. Psychiatry Res. 2021;295:113552.15. Gustafsson HC, Young AS, Doyle O, et al. Trajectories of perinatal depressive symptoms in the context of the COVID-19 pandemic. Child Dev. Sep 2021;92(5):e749-e763.

# While not fully understood, the mechanism of action of ZURZUVAE is thought to be related to its positive allosteric modulation of GABAA receptors




Synaptic and extrasynaptic GABAA receptors regulate the activity of brain regions disrupted in depression[7-9]




Evidence suggest that GABAergic function may be disrupted in postpartum depression. Zuranolone amplifies activity and expression of both synaptic and extrasynaptic GABAA receptors[1,10]

Cl−, chloride ion; GABA, γ-aminobutyric acid.

1. Althaus AL, et al. Neuropharmacology. 2020;181:108333. 2. Fee C, et al. Biol Psychiatry. 2017;82(8):549-559. 3. Lener MS, et al. Biol Psychiatry. 2017;81(10):886-897. 4. Li YF. Pharmacol Ther. 2020;208:107494. 5. Northoff G, Sibille E. Mol Psychiatry. 2014;19(9):966-977. 6. Duman RS, et al. Neuron. 2019 Apr 3;102(1):75-90. 7. Bryson A, et al. Proc Natl Acad Sci U S A. 2020;117(6):3192-3202. 8. Antonoudiou P, et al. Biol Psychiatry. 2022;91(3):283-293. 9. Reddy DS, Estes WA. Trends Pharmacol Sci. 2016;37(7):543-561. 10. Fogaça MV, Duman RS. Front Cell Neurosci. 2019;13:87.

# ZURZUVAE clinical development program in PPD


**MONOTHERAPY or ADD-ON to existing ADT [1-3]**


**(217-PPD-301)[1,2]**

Evaluated efficacy and safety of ZURZUVAE 50 mg in women with PPD aged 18 to 45 years and ≤12 months postpartum

**Design:** Randomized, double-blind, placebo-controlled trial design
**Primary Endpoint:** CFB HAMD-17 total score at Day 15
**Population:** PPD Patients with HAMD-17 total score ≥26


**(217-PPD-201)[1,3]**

Evaluated efficacy and safety of another zuranolone capsule formulation (approximately equivalent to 40 mg of ZURZUVAE) in women with PPD aged 18 to 45 years and ≤6 months postpartum

**Design:** Randomized, double-blind, placebo-controlled trial design
**Primary Endpoint:** CFB HAMD-17 total score at Day 15
**Population:** PPD Patients with HAMD-17 total score ≥26

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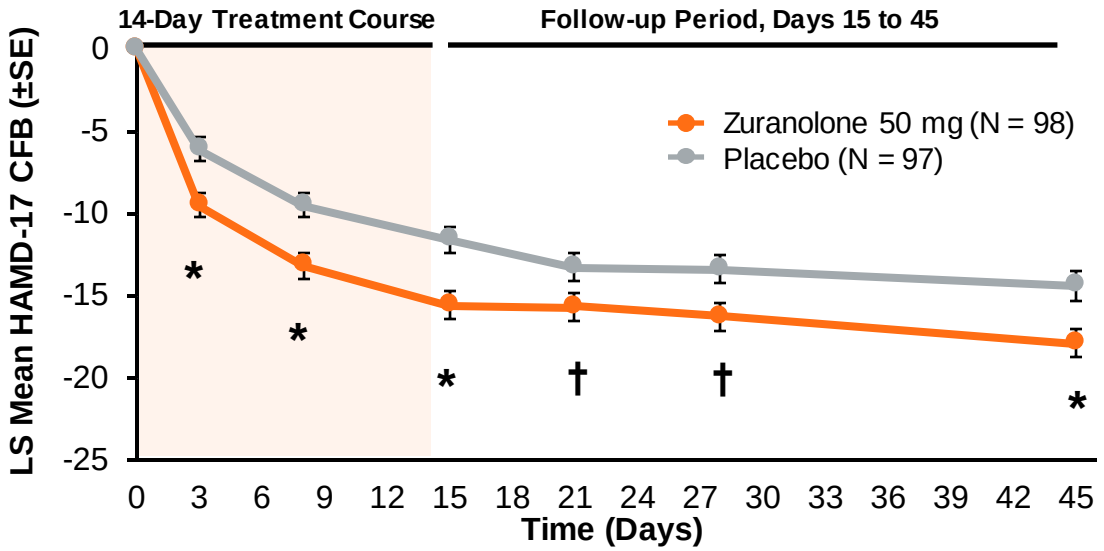
ADT = antidepressant therapy; CFB = change from baseline; HAMD-17 = 17-item Hamilton Rating Scale for Depression; PPD = postpartum depression

1. ZURZUVAE (zuranolone) [package insert]. Cambridge, MA: Sage Therapeutics, Inc and Biogen; 2023. 2. Deligiannidis KM et al. Am J Psychiatry; 2023. 3. Deligiannidis KM, et al. JAMA Psychiatry; 2021.

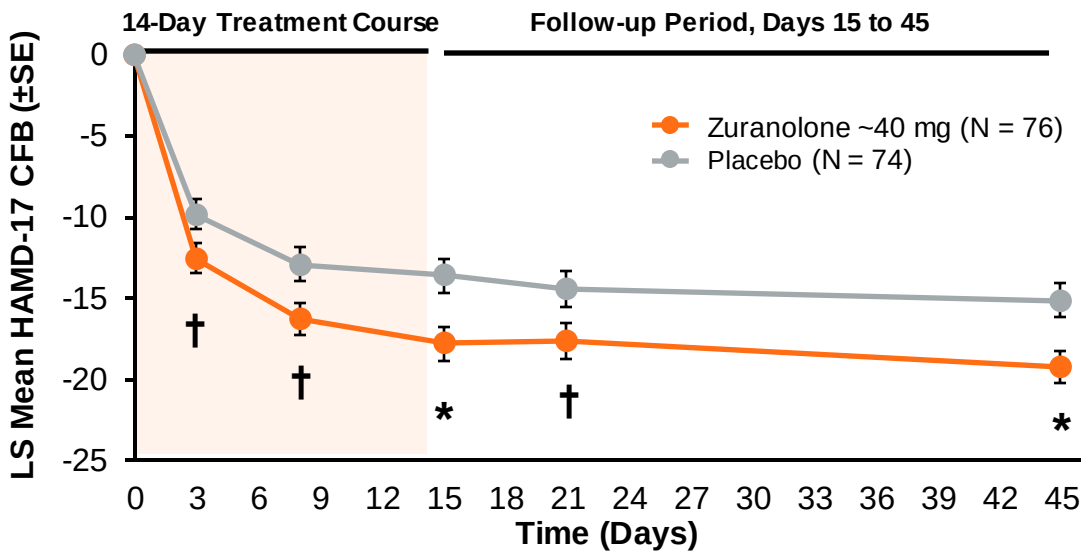
# Clinical studies in PPD

*See U.S. Prescribing Information for more information, including safety information and boxed warning*

**SKYLARK Study: Least Squares Mean Change from Baseline in HAM-D Total Score Over Time (Days) [1,2]**




**ROBIN Study: Least Squares Mean Change from Baseline in HAM-D Total Score Over Time (Days) [1,3]**




**LS Mean (SE) Change from Baseline in HAMD-17 Total Score Results from SKYLARK and ROBIN Studies**

| | Zuranolone | Placebo | P-value |
|---|---|---|---|
| **SKYLARK** [1,2] | | | |
| N | 98 | 97 | |
| Day 15 (Primary endpoint) | -15.6 (0.82) | -11.6 (0.82) | p < 0.001 |
| Day 3 | -9.5 (0.70) | -6.1 (0.71) | p < 0.001 |
| **ROBIN** [1,3] | | | |
| N | 76 | 74 | |
| Day 15 (Primary endpoint) | -17.8 (1.04) | -13.6 (1.07) | p < 0.01 |
| Day 3 | -12.5 (0.93) | -9.8 (0.95) | p < 0.05 |

* p <0.01; † p <0.05. Secondary analyses were not adjusted for multiplicity and were therefore considered nominally significant

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1. ZURZUVAE (zuranolone) [package insert]. Cambridge, MA: Sage Therapeutics, Inc and Biogen; 2023. 2. Deligiannidis KM et al. *Am J Psychiatry*; 2023. 3. Deligiannidis KM, et al. *JAMA Psychiatry;* 2021.

# ZURZUVAE, first and only oral treatment approved for women with PPD

**PPD**

In the US, an estimated **1 in 8** women experience symptoms of PPD[1]

**~477k** women with a live birth experience PPD symptoms annually[1,2]

**~50%** of PPD cases may go undiagnosed without appropriate screening[3,4] and less than **25%** of patients screened for PPD receive follow-up care[5-7]

## ZURZUVAE: Potential first-line treatment for women with PPD

***Launch Focus***

**Women diagnosed with PPD requiring treatment**

***Patient Profiles***

- **Newly diagnosed**
- **Partial response to current antidepressant treatment**

***Secondary Focus***

**Supporting efforts to appropriately diagnosis PPD**

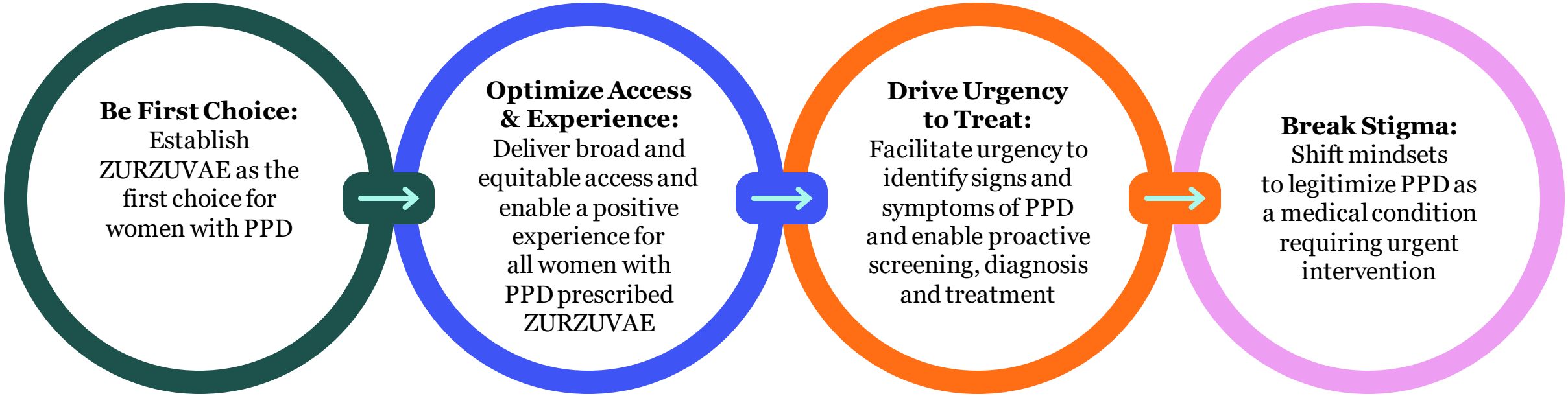
***Patient Profiles***

- **Increased screening and diagnosis for women with PPD who are symptomatic**

1. Bauman BL, Ko JY, Cox S, D'Angelo Mph DV, Warner L, Folger S, Tevendale HD, Coy KC, Harrison L, Barfield WD. Vital Signs: Postpartum Depressive Symptoms and Provider Discussions About Perinatal Depression—United States. Morb Mortal Wkly Rep. 2020; 69(19):575-581. 2. Centers for Disease Control and Prevention. National Vital Statistics Report. Volume 70, Number 17; February 7, 2022. https://www.cdc.gov/nchs/data/nvsr/nvsr70/nvsr70-17.pdf. 3. Georgiopoulos AM et al. J Fam Pract. 2001;50(2):117-122. 4. Evins GG et al. Am J Obstet Gynecol. 2000;182(5):1080-1082. 5. Byatt N et al. Arch Womens Ment Health. 2016;19:187-191. 6. Byatt N et al. Obstet Gynecol. 2015;126(5):1048-1058. 7. Goodman JH et al. J Womens Health (Larchmt). 2010;19:477-490.

# Focused on goal of establishing ZURZUVAE as first line therapy and standard of care for women with PPD

**ZURZUVAE KEY LAUNCH GOALS**

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**Katie – Caregiver,**
Huntington's Disease

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# Globally, disorders involving cognitive impairment continue to increase in prevalence.[1]

Cognitive impairment has devastating impacts on *patients, families, and society*[2]

## ~188K

### Huntington's Disease Global Prevalence[3,4*]

Cognitive Impairment in HD can occur up to 15 years before motor manifestation & is highly associated overall functional decline[5]

## ~134M

### Alzheimer's Disease Global Prevalence[3†]

Up to 50% of people with MCI due to AD progress to Alzheimer's dementia within 5-10 years, which may impact a person's ability to remain independent[6]

HD = Huntington's disease, AD = Alzheimer's disease

1.https://www.cdc.gov/aging/pdf/cognitive_impairment/cogimp_policy_final.pdf. Accessed Jan 10 2024. 2. Na, Kyoung-Sae. "Prediction of future cognitive impairment among the community elderly: A machine-learning based approach." Scientific reports 9.1 (2019): 3335. 3. Sage Therapeutics Data on file. 4. Pringsheim, Tamara, et al. "The incidence and prevalence of Huntington's disease: a systematic review and meta-analysis." Movement Disorders 27.9 (2012): 1083-1091. 5. Paulsen, Jane S. "Cognitive impairment in Huntington disease: diagnosis and treatment." Current neurology and neuroscience reports 11 (2011): 474-483. 6. Alzheimer's Facts and Figures. Alz Dement. Special Report. 2022.

# Cognitive impairment is prevalent and impacts people across the lifespan

**Executive Function**

Planning, decision-making, working memory, multitasking, flexibility

**Learning & Memory**

Recall, recognition. long-term memory, implicit learning

**Attention**

Sustained attention, divided attention, selective attention, processing speed

**Language**

Object naming, word finding, fluency, grammar and syntax, receptive language

**Visuospatial**

Visual perception. Visuo-constructional reasoning, perceptual-motor coordination

**DAILY LIFE**


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Sources: SSM Popul Health. 2020 Aug; 11: 100577. Published online 2020 Mar 31. doi: 10.1016/j.ssmph.2020.100577
https://altoida.com/blog/defining-the-6-key-domains-of-cognitive-function/

# Cognitive impairment affects ability to function every day and for many, ability to stay independent

## Executive Function

Individuals in early stages of HD[1]

"**There's zero multitasking** in my life. And what it causes is extreme anxiety"

"I wrote for websites and blogs, it used to take me maybe 20 or 30 minutes. **And now, it tends to take me a couple hours**"

## Memory & Learning

Caregiver and Individual with AD-MCI[2]

"She started making a sandwich, then walked away, sat down and spaced out. She left the water on stove boiling. **She forgets what she started**"

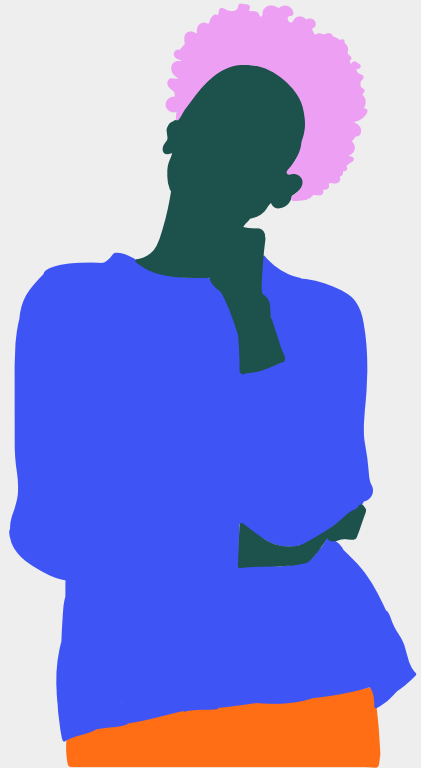
"He'll give me a task and I'll scratch my head. What was I supposed to do? **Not on drugs, not drinking, just a mental fog"**

## Concentration & Planning

Individuals with HD and AD-MCI[1,2]

**"**If I've got something planned and boss asks me to switch, it will literally **take me almost an hour to two hours to talk myself into doing it**."

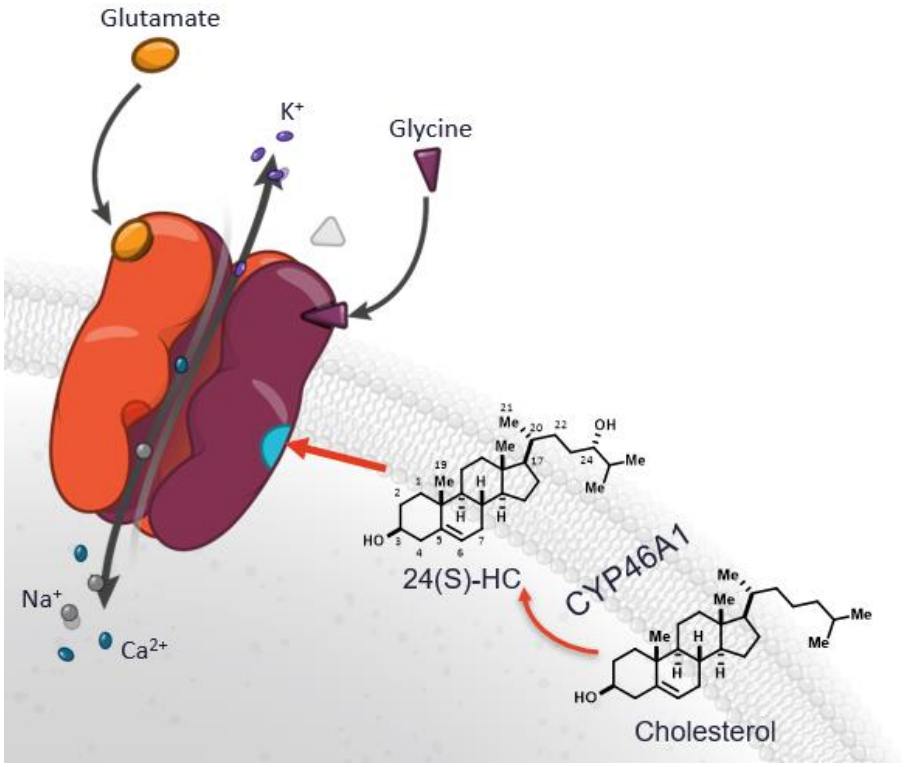
"**I have to put in a lot of effort to really focus** on where I'm going when driving, and even then I still end up turned around or at the wrong place."



AD: Alzheimer's disease; HD: Huntington's disease; MCI: Mild cognitive impairment;
1. Petrillo J. et. al. Patient Experiences in Early Huntington's Disease. Poster presented at American Academy of Neurology Annual Meeting. Seattle, WA. April 2-7, 2022 2. Sage Data on File;

# Sage's first-in-class NMDA receptor PAM

*Novel starting point for understanding NMDA receptor modulation*




## Emerging Science Drives New Thinking

- The neuroactive steroid, 24S-hydroxycholesterol (24S-HC), is an endogenous modulator of NMDA receptors
- NMDA receptors play a major role in excitatory transmission in the brain and influence cognition and other key brain functions
- NMDA receptor hypofunction has been implicated in cognitive impairment associated with disorders such as Huntington's disease and Alzheimer's disease

## Dalzanemdor (SAGE-718): NMDA Positive Allosteric Modulator (PAM)

- Dalzanemdor (SAGE-718) is a novel, positive allosteric modulator derived from our pharmacological understanding of 24S-HC
- Dalzanemdor (SAGE-718) is believed to bind to a novel neurosteroid site on the NMDA receptor
- Dalzanemdor (SAGE-718) has the potential to restore NMDA activity and improve cognitive functioning

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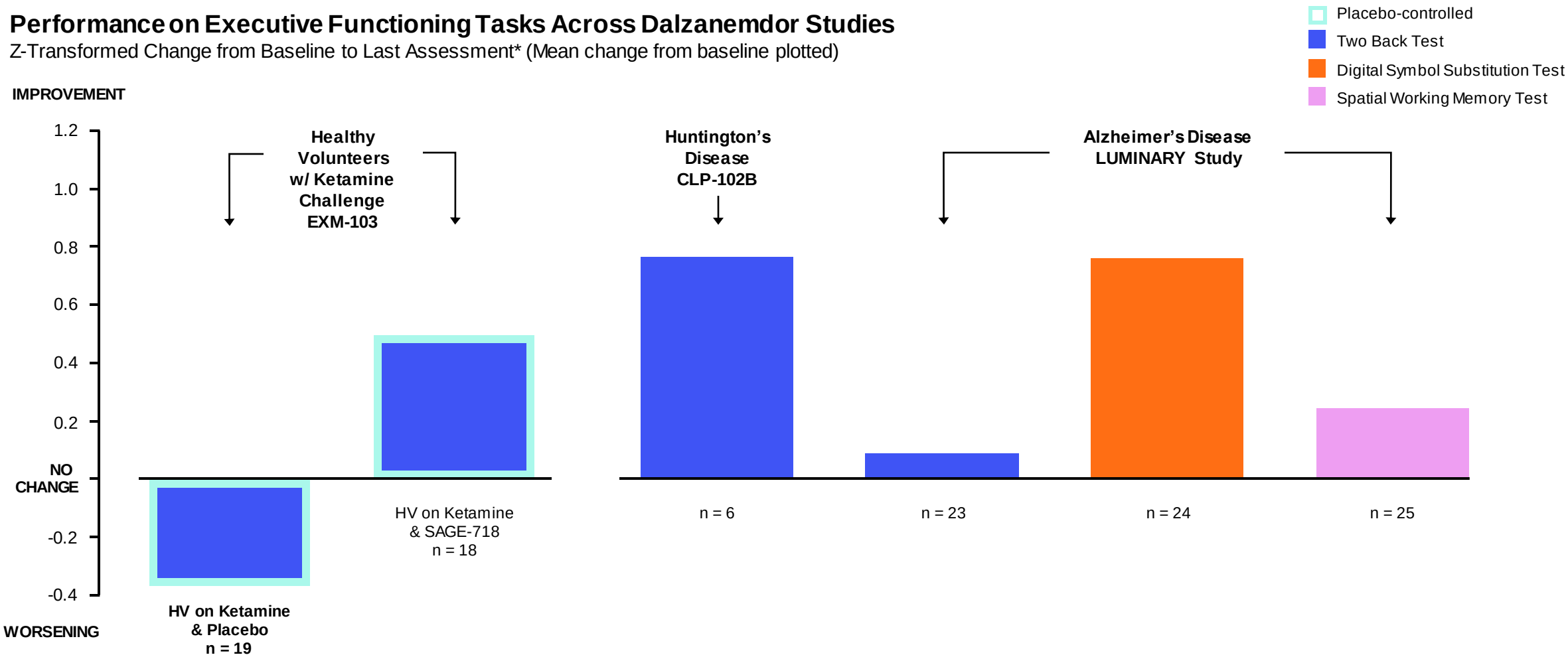
# Dalzanemdor (SAGE-718) clinical studies to date in Huntington's Disease and Alzheimer's Disease




HV = healthy volunteers

# Dalzanemdor Ongoing Clinical Development Program

## Huntington's Disease

FDA Fast-track & Orphan Drug Designations; EMA Orphan Drug Designation, UK ILAP Designation

PERSPECTIVE PROGRAM

**CLP-102-B**

Open-label MAD study in HD subjects.
To evaluate safety, tolerability, PK and preliminary efficacy in HD cognitive impairment.

Completed

**SURVEYOR (718-CIH-202)**

Randomized, placebo-controlled 4-week study in patients with HD cognitive impairment. Designed to facilitate clinical meaningfulness evidence.

Enrollment Complete

**DIMENSION (718-CIH-201)**

Randomized, placebo-controlled 12-week study in patients with HD cognitive impairment to evaluate efficacy and safety.

Enrolling

**PURVIEW (718-CIH-301)**

Long-term open-label safety study. Designed to evaluate the long-term safety profile.

Enrolling

## Alzheimer's Disease

LIGHTWAVE

LUMINARY (718-CNA-201)

Open-label 2-week study in AD-MCI and mild dementia designed to evaluate safety, tolerability, and preliminary efficacy.

Completed

LIGHTWAVE (718-CNA-202)

Randomized, placebo-controlled 12-week study in AD-MCI and mild dementia, designed to examine efficacy and safety.

Enrollment Complete

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# Phase 2 data expected for dalzanemdor (SAGE-718) in HD and AD indications in 2024

## EARLY 2024 (Q1/Q2)

- *Topline data from the **PRECEDENT Study in PD**[1]*

## MID 2024 (Q2/Q3)

- Topline data from the **SURVEYOR Study in HD**

## LATE 2024 (Q3/Q4)

- Topline data from the **LIGHTWAVE Study in AD**
- Topline data from the **DIMENSION Study in HD**

*PD = Parkinson's Disease, HD = Huntington's Disease, AD = Alzheimer's Disease*

1. See Sage Press Release dated April 17, 2024 for description of results in PD

# Multiple Expected Catalysts

1. Ongoing commercialization of ZURZUVAE™ in the treatment of women with postpartum depression

2. Advance **dalzanemdor (SAGE-718)** with multiple topline data readouts expected in 2024

3. Advance **SAGE-324** with topline data expected in mid-2024

4. Progress earlier stage **pipeline**

**Diann – Patient/Advocate**
Essential Tremor

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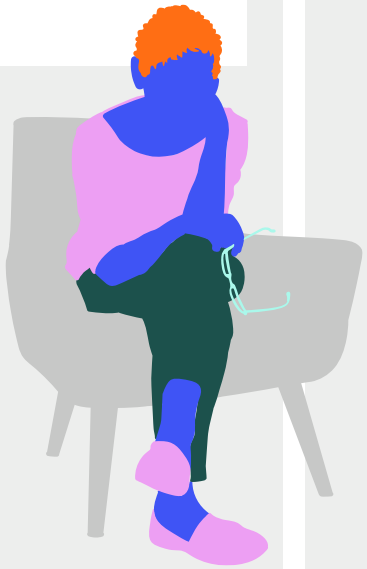
# Gaps remain in bringing effective treatments to people suffering from Essential Tremor

"I can't write. That's the worst thing in the world… I send my son to the bank for things. It's getting to the point where I'm going to have to let him do all the financial work, because I just can't do it… **My mind is okay, but my body is falling apart."**



An estimated 6.8M adults in the US have ET[1], **approximately 10-15% are diagnosed**[2]

ET impacts individuals' ability to perform a **wide range of activities of daily living** and their social-emotional well-being

In an interview study of ET patients and care partners with ET ranging **from mild to very severe** [3] :

- **100%** had difficulty writing and pouring liquids
- **≥80%** had difficulty drinking, performing grooming and hygiene activities, dressing, eating, and holding reading material
- **90%** had at least one emotional impact of ET
- ADL and social-emotional impacts **were greater** as severity of ET increased

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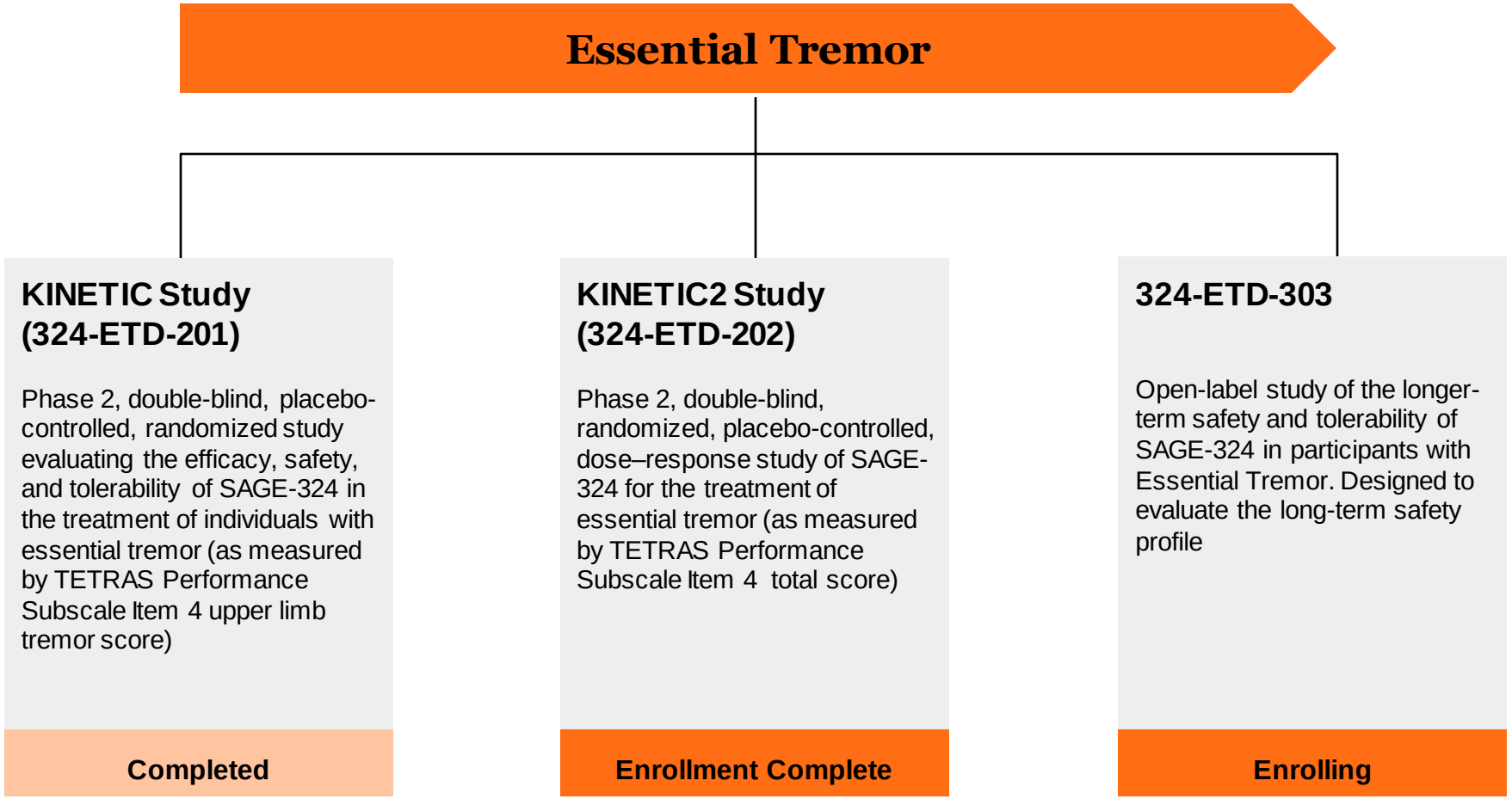
1. Furtado et al. Estimation of global age-specific prevalence of essential tremor by literature review of population-based studies. ICPE, 2023. 2. Saad et al. Diagnosed and drug-treated prevalence of essential tremor in adult patients: retrospective analyses of two US healthcare claims databases. MDS 2022. 3. Gerbasi et al. Patient experiences in essential tremor: Mapping functional impacts to existing measures using qualitative research. MDS 2023.

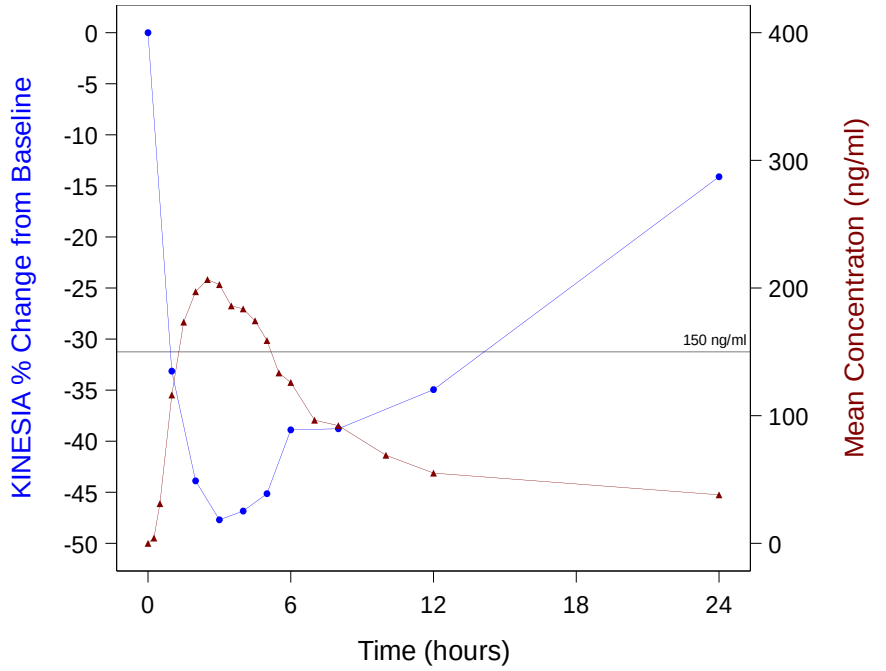
# SAGE-324 clinical development program



# SAGE-324: Novel potential treatment for movement disorders
## *Predictable PD effects and PK profile with long half-life*

- SAGE-324 is well-suited for development in essential tremor (ET):
  - Last pharmacological treatment for ET was approved in 1967
  - High unmet need; 50% of treated patients do not respond or have sub-optimal response to standard of care
- In an open-label, phase 1 study, a single dose of SAGE-324 resulted in nearly 50% tremor reduction in ET patients, demonstrated on measure most closely associated with disability
- Good oral bioavailability and long halflife provides flexibility in dosing paradigms

Total upper limb combined score after single dose in 6 people with ET as measured by accelerometer




PK over time in 6 people with ET dosed with SAGE-324

- Clear PK/PD relationship
- Promising signals of tremor reduction, consistent with those observed previously for brexanolone and Zuranolone
- Most common AEs (≥5%) included somnolence, dizziness, and feeling of relaxation

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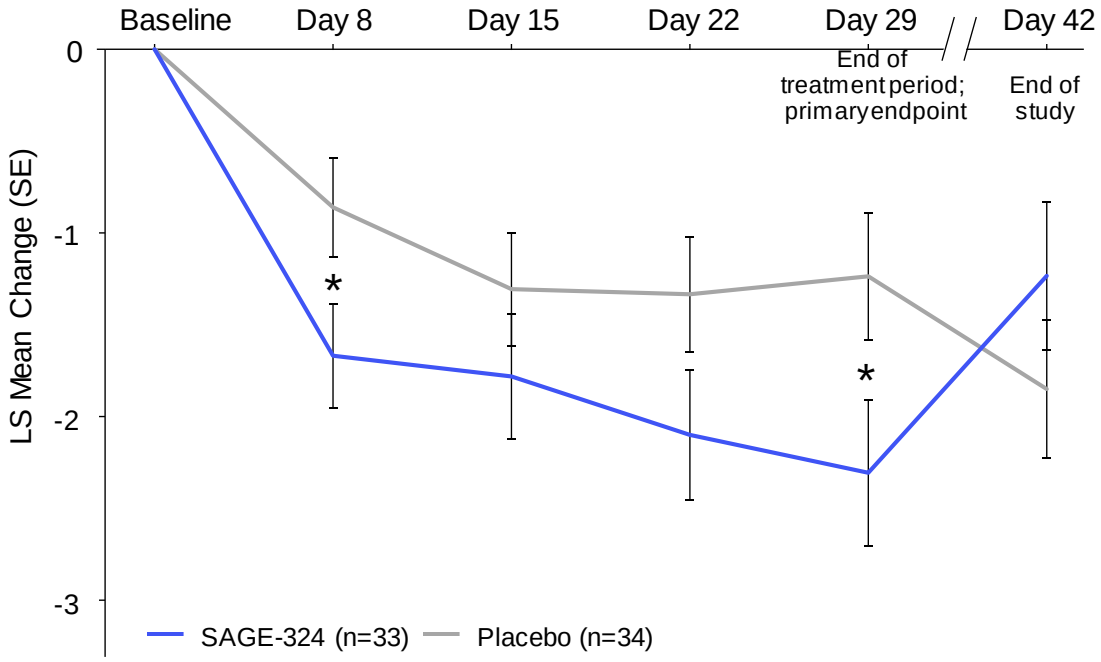
SAGE-324 is being developed in collaboration with Biogen.

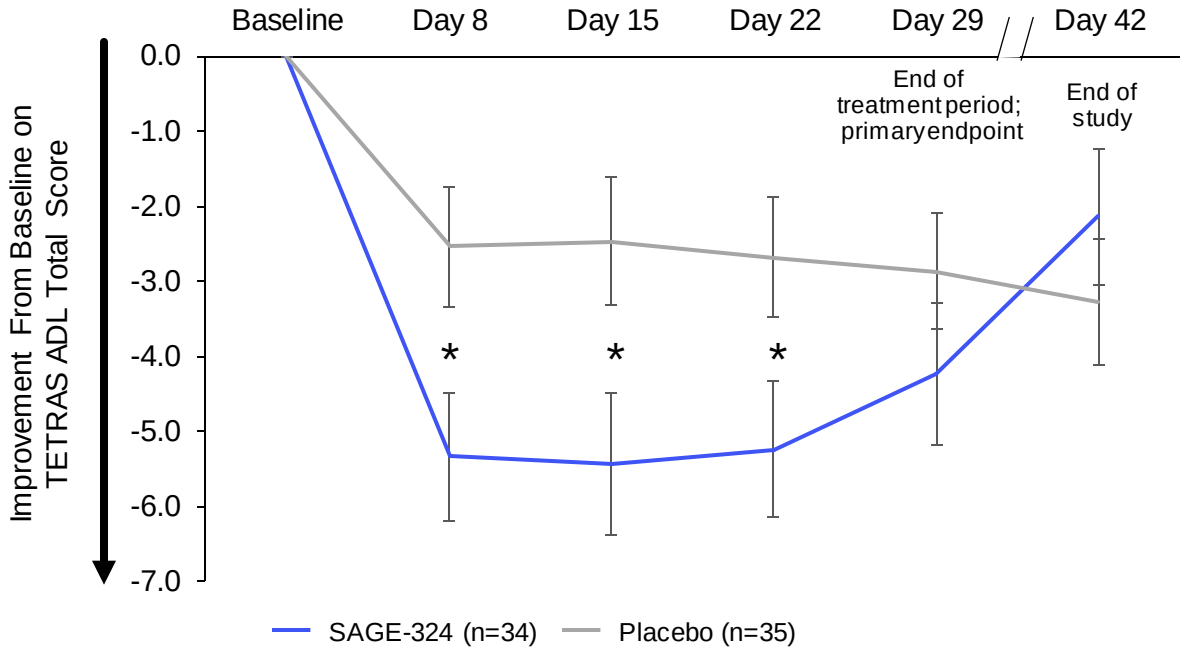
# Improvement in tremor control and ADL score observed in KINETIC Study

**Change From Baseline for TETRAS Performance Subscale Upper Limb Tremor Total Score in SAGE-324 and Placebo Treatment Groups**




Baseline mean (SD) TETRAS Performance Subscale Upper Limb Tremor Total Score: placebo 12.28 (1.69); SAGE-324 12.82 (1.73)

**Change From Baseline for TETRAS ADL Subscale Total Score in SAGE-324 and Placebo Treatment Groups**




Baseline mean (SD) TETRAS ADL Subscale Total Score: placebo 26.7 (6.84); SAGE-324 26.3 (8.50)

The most frequently reported adverse events reported by at least 10% of participants on SAGE-324 in the KINETIC Study were somnolence (68%), dizziness (38%), balance disorder (15%), fatigue (15%), diplopia (12%), dysarthria (12%), and gait disturbance (12%).

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*p<0.05 (Secondary/other endpoints were not adjusted for multiplicity; p-values are nominal)
Sage Therapeutics, Inc. Data on file.
SAGE-324 is being developed in collaboration with Biogen.

# Multiple Expected Catalysts

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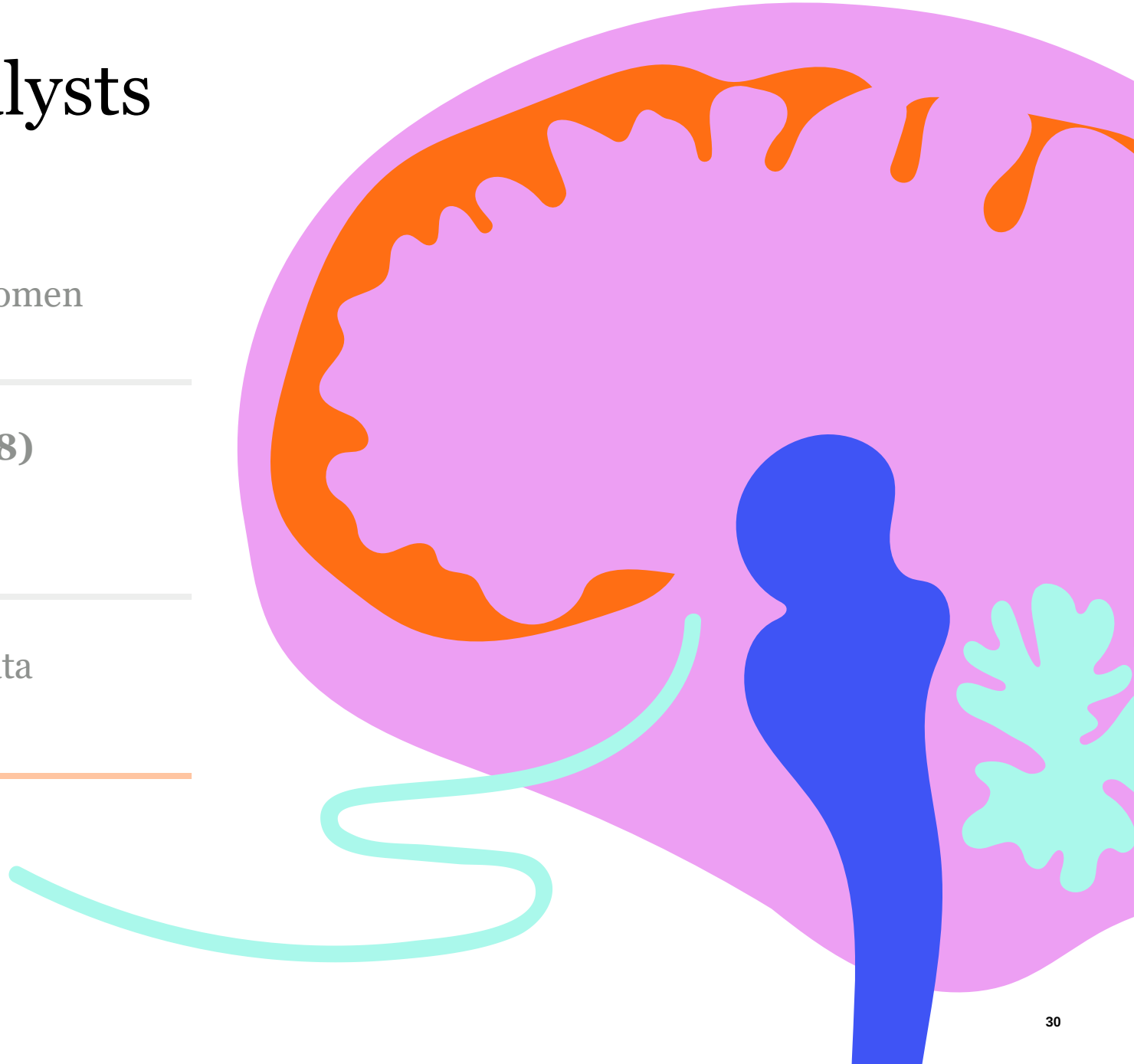

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# Other potential areas of growth within GABA and NMDA platforms

## Profile of SAGE-319

*GABA Receptor PAM*

- Extra-synaptic $GABA_A$ receptor preferring positive allosteric modulator
- Profile intended to support daily, oral, chronic dosing
- Differentiated clinical EEG signature compared to zuranolone and SAGE-324

Potential indications:

**NEURODEVELOPMENTAL / MOTOR DISORDERS**

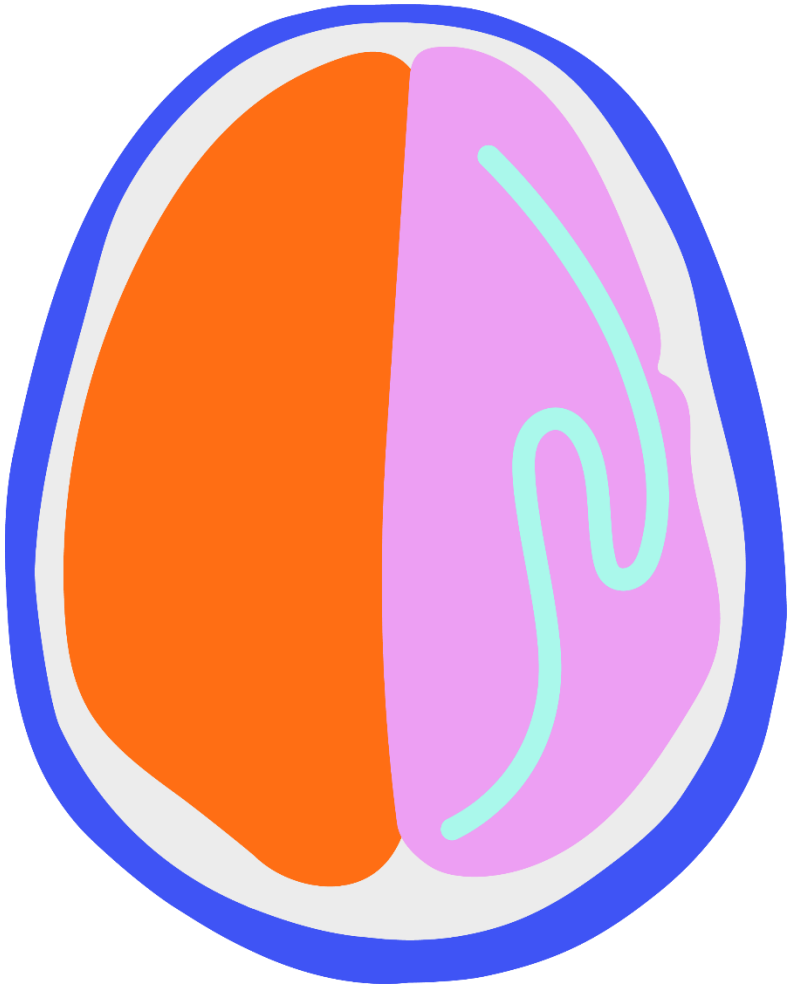
## Preclinical profile of SAGE-421

*NMDA Receptor PAM*

- NMDA receptor positive allosteric modulator
- Profile intended to support daily, oral, chronic dosing

Potential indications:

**COGNITIVE IMPAIRMENT, SCHIZOPHRENIA**



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# Potential Value Creating Catalysts

| Anticipated Events | | |
|---|---|---|
| ZURZUVAE* | Ongoing commercialization of ZURZUVAE in the treatment of women with PPD | 2024 |
| | Present additional analyses of data from NEST clinical program, including health economics and patient reported outcomes | 2024 |
| Dalzanemdor (SAGE-718) | *Topline data from the PRECEDENT Study in PD* | EARLY 2024 – COMPLETED |
| | Topline data from the SURVEYOR Study in HD | MID 2024 |
| | Topline data from the LIGHTWAVE Study in AD | LATE 2024 |
| | Topline data from the DIMENSION Study in HD | LATE 2024 |
| | Present additional analyses of data from clinical development program as well as disease state and burden of disease research in HD, PD and/or AD | 2024 |
| SAGE-324* | Topline data from Phase 2 KINETIC 2 Study in ET | MID 2024 |
| | Present additional analyses of data from clinical development program as well as disease state and burden of disease research in ET | 2024 |
| **Additional Expected Milestones** | | |
| Cash Balance | Maintain strong financial foundation | 2024 |

*PPD = postpartum depression, ET = essential tremor, HD = Huntington's disease, PD = Parkinson's disease, AD = Alzheimer's disease*

**Collaboration Partners: Biogen Inc. and Shionogi for zuranolone and Biogen Inc. for SAGE-324*

**OUR MISSON**: Pioneer solutions to deliver life-changing brain health medicines, *so every person can thrive*

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# Appendix

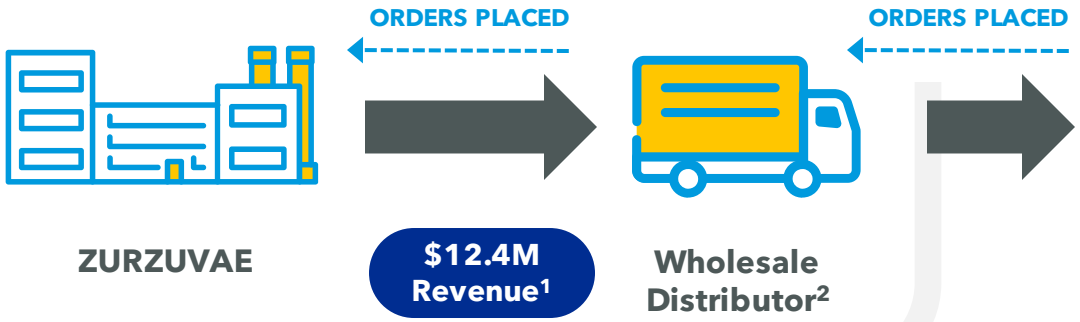
# ZURZUVAE Distribution Diagram

## (All metrics are Q1 2024 results*)

HCP and woman with PPD discuss ZURZUVAE; HCP sends prescription to SP

Patient + HCP

Wholesale Distributor orders ZURZUVAE




Patient receives ZURZUVAE at home from SP

Patient

*All metrics are Q1 2024 results
1. Net revenues Biogen reports for ZURZUVAE; Sage records 50% as collaboration revenue ($6.2M)
2. Inventory
3. Tracked by outside sources (i.e. IQVIA); Data does not reflect all shipments of ZURZUVAE (e.g. free drug shipments not included)

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# Prescribing information for ZURZUVAE

## U.S. Prescribing Information

### Indication

- ZURZUVAE is indicated for the treatment of adults with postpartum depression (PPD)

### Dosing and Administration

- 50 mg taken orally once daily in the evening for 14 days with fat-containing food
- Dosage may be reduced to 40mg once daily if CNS depressant effects occur with the 14-day period
- Can be used alone or as an adjunct to oral antidepressant therapy

### Available Dose Strengths

- 20 mg, 25 mg and 30 mg capsules

### Contraindications

- None

## Important Safety Information

ZURZUVAE may cause serious side effects, including decreased awareness and alertness, which can affect your ability to drive safely or safely do other dangerous activities. Do not drive, operate machinery, or do other dangerous activities until at least 12 hours after taking each dose. You may not be able to tell on your own if you can drive safely or tell how much ZURZUVAE is affecting you. ZURZUVAE may cause central nervous system (CNS) depressant effects including sleepiness, drowsiness, slow thinking, dizziness, confusion, and trouble walking. Taking alcohol, other medicines that cause CNS depressant effects such as benzodiazepines, or opioids while taking ZURZUVAE can make these symptoms worse and may also cause trouble breathing. ZURZUVAE is a federally controlled substance schedule IV because it contains zuranolone, which can be abused or lead to dependence. Tell your healthcare provider right away if you become pregnant or plan to become pregnant during treatment with ZURZUVAE. You should use effective birth control (contraception) during treatment with ZURZUVAE and for 1 week after the final dose. ZURZUVAE and other antidepressant medicines may increase the risk of suicidal thoughts and actions in people 24 years of age and younger. ZURZUVAE is not for use in children. The most common side effects of ZURZUVAE include sleepiness or drowsiness, dizziness, common cold, diarrhea, feeling tired, weak, or having no energy, and urinary tract infection.

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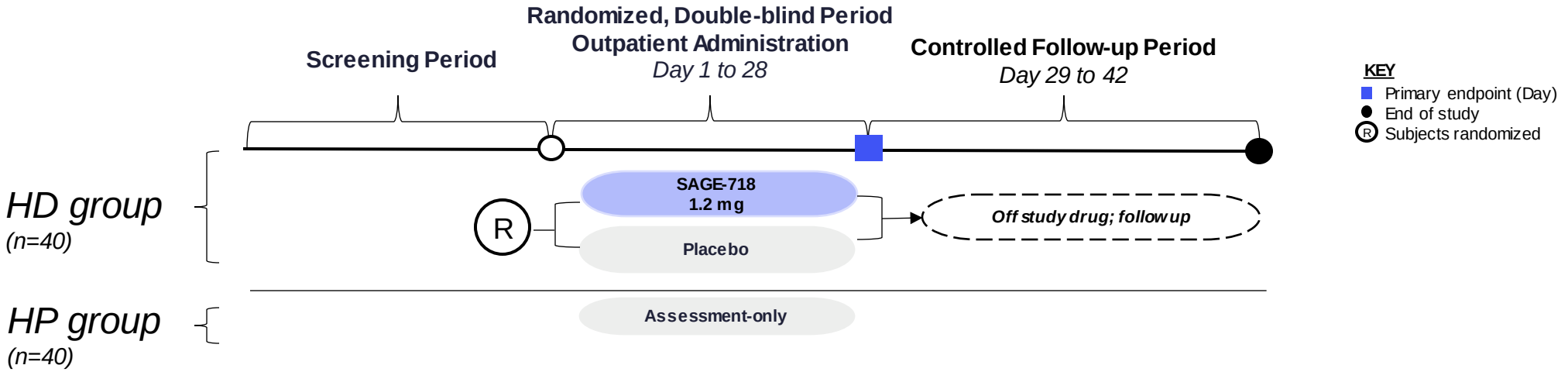
# SURVEYOR Study - SAGE-718

*PBO-controlled study in patients with early HD, with Healthy Participant (HP) Comparator Arm*

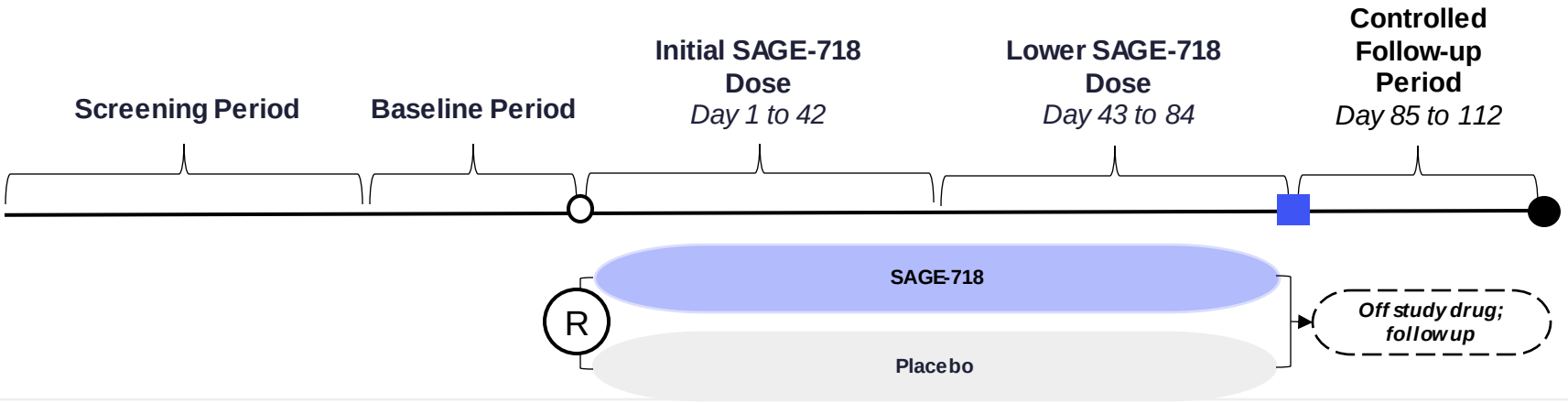



## STUDY OVERVIEW

| | | | |
|---|---|---|---|
| **Status** | Enrollment Complete | **Objectives** | • To assess the magnitude of the baseline difference between participants with early Huntington's Disease (HD) and healthy participants (HP) with respect to measures of cognitive performance.<br>• To evaluate the effect of SAGE-718 on cognition and functioning outcomes in participants with HD |
| **Indication** | Huntington's disease<br>Cognitive Impairment | **Primary Endpoint** | • Baseline measures of the Huntington's disease Cognitive Assessment Battery (HD-CAB) cognitive composite score. |
| **Phase** | Phase 2 | **Secondary Endpoints** | • Change from Baseline to Day 28 on HD-CAB, VRFCAT, other endpoints.<br>• Safety and tolerability of SAGE-718 |
| **Arms** | Double-blind, randomized: 1:1 (HD)<br>• SAGE-718, placebo<br>Assessment-only comparator arm (HP) | **Inclusion Criteria (HD Participants)** | • Be at least 25 years old but no older than 65 years of age at Screening<br>• Meet all the following criteria for HD:<br>– Genetically confirmed disease with huntingtin gene CAG expansion ≥36<br>– UHDRS-Total Functional Capacity (TFC) score >6 and <13<br>– No features of juvenile HD<br>• Score <26 on the Montreal Cognitive Assessment (MoCA) at screening<br>• Be willing to invite a study partner, if available, who is reliable, competent, and able to participate in the study |
| **Dosing Regimen** | 1.2 mg oral daily | **Exclusion Criteria (HD Participants)** | • Have participated in a previous clinical study of SAGE-718, have participated in a previous gene therapy study, or have received study treatment in any other drug, biologic, or device trial within 90 days or 5 half-lives (whichever is longer), unless the patient participated solely in the placebo arm of the study<br>• Have a diagnosis of an ongoing neurodegenerative condition other than HD, including but not limited to, Alzheimer's disease, vascular dementia, dementia with Lewy bodies, or Parkinson's disease |

# LIGHTWAVE Study - SAGE-718

*Placebo-controlled study in patients with MCI or Mild Dementia due to Alzheimer's Disease*




KEY
- Primary endpoint (Day)
- End of study
- Ⓡ Subjects randomized

Target enrollment = 150

## STUDY OVERVIEW

| | |
|---|---|
| **Status** | Enrollment Complete |
| **Indication** | MCI or Mild Dementia due to Alzheimer's disease |
| **Phase** | Phase 2 |
| **Arms** | Double-blind, randomized: 1:1<br>• SAGE-718, placebo |
| **Dosing Regimen** | Initial Dose (Days 1 to 42), then Lower dose (Days 43 to 84) |

**Objectives**
- To evaluate the effect of SAGE-718 on cognitive performance in participants with Mild Cognitive Impairment (MCI) or mild dementia due to Alzheimer's (AD)
- To evaluate the safety and tolerability of SAGE-718 oral capsule in participants with MCI or mild dementia due to AD

**Primary Endpoint**
- Change from Baseline to Day 84 in the Wechsler Adult Intelligence Scale-IV (WAIS-IV) Coding test

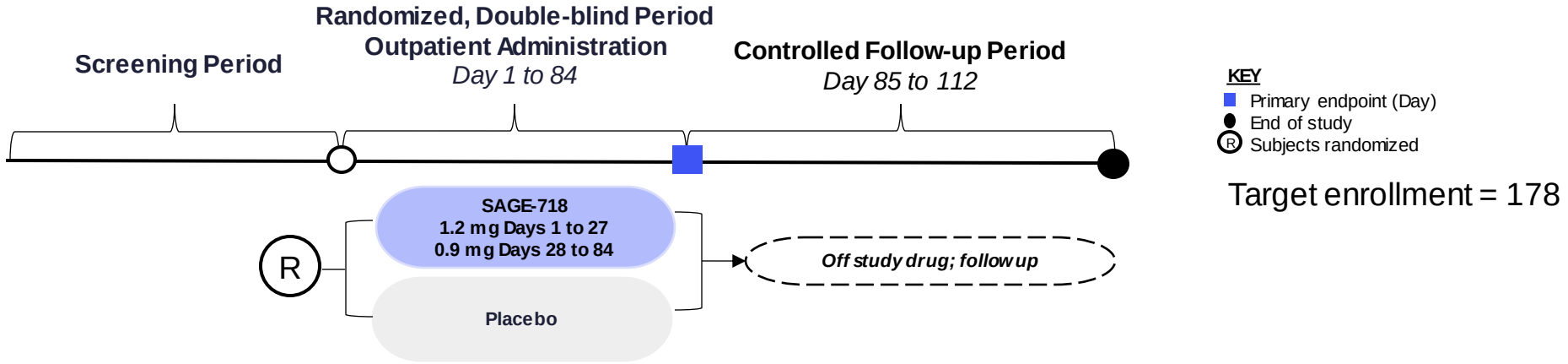
**Key Secondary Endpoint**
- Additional endpoints to assess the effects of SAGE-718 on cognitive performance and functioning, including CGI-C, MoCA, CANTAB, and the Amsterdam Instrumental Activity of Daily Living questionnaire
- Proportion of participants experiencing treatment emergent adverse events (TEAEs) and severity of TEAEs
- Number of participants who withdraw due to adverse events (AEs)

**Inclusion Criteria**
- Be between the ages of 50 and 80 at Screening
- Meet all the following criteria for MCI or mild dementia due to AD:
  - A memory complaint reported by the participant or their study partner
  - A CDR score of 0.5 to 1.0 (inclusive) with a memory box score ≥0.5
  - Essentially preserved activities of daily living, in the opinion of the investigator
  - Brain MRI report, obtained within the 2 years preceding the Baseline Period, which is consistent with the diagnosis of AD and with no clinically significant findings of non-AD pathology that could account for the observed cognitive impairment
- Have a MoCA score of 15 to 25 (inclusive) at Screening
- Have a study partner who, in the opinion of the investigator, is willing and able to provide informed consent, reliably support study-specific activities including IP adherence, be available by phone, and accompany the participant to study visits as needed
- If on concomitant medication, stable for at least 4 weeks prior to the first administration of study drug, and ~~is~~ expected to remain stable for duration of the study

**Exclusion Criteria**
- Have participated in a previous clinical study of SAGE-718, have participated in a previous gene therapy study, or have received study treatment in any other drug, biologic, or device trial within 180 days or 5 half-lives (whichever is longer), unless the patient participated solely in the placebo arm of the study
- Have a medical or neurological condition (other than AD) that may be contributing to their cognitive impairment or history of cognitive decline

# DIMENSION Study - SAGE-718

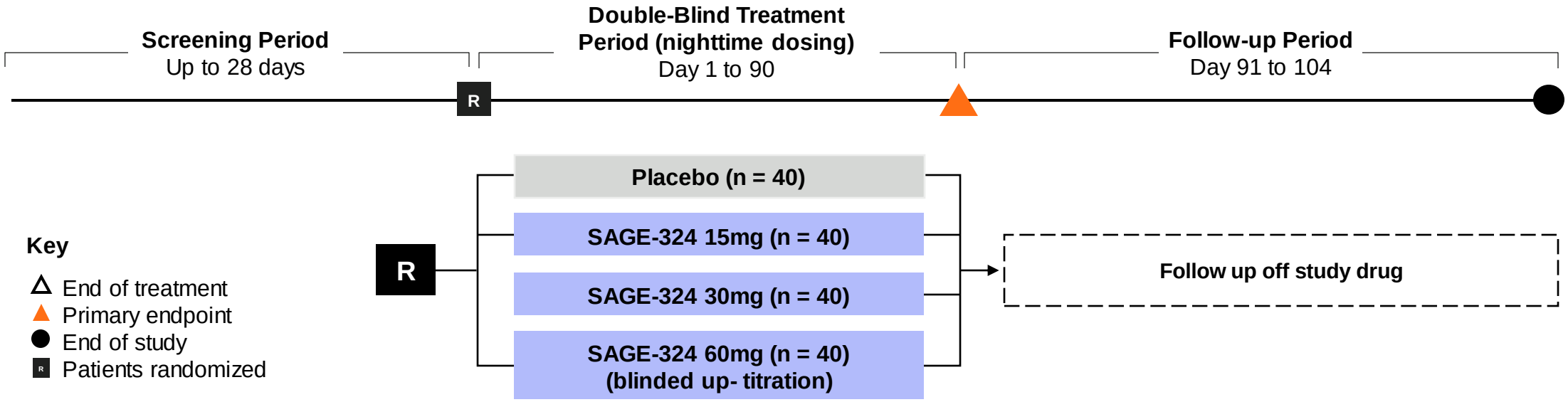
*Placebo-controlled study in patients with early Huntington's disease*




**STUDY OVERVIEW**

| | | | |
|---|---|---|---|
| **Status** | Enrolling | **Primary Endpoint** | • Change from baseline in Composite score of the Huntington's Disease Cognitive Assessment Battery (HD-CAB) |
| **Indication** | Huntington's disease<br>Cognitive Impairment | **Key Secondary Endpoint** | • UHDRS Independence Scale |
| **Phase** | Phase 2 | **Inclusion Criteria** | • Be at least 25 years old but no older than 65 years of age at Screening<br>• Meet all the following criteria for HD:<br>– Genetically confirmed disease with huntingtin gene CAG expansion ≥36<br>– UHDRS-Total Functional Capacity (TFC) score >6 and <13<br>– No features of juvenile HD<br>• Score <26 on the Montreal Cognitive Assessment (MoCA) at screening<br>• Be willing to invite a study partner, if available, who is reliable, competent, and at least 18 years of age to participate in the study<br>• Be ambulatory (use of assistance devices such as a walker or cane is acceptable; individuals requiring a wheelchair are excluded), able to travel to the study center, and, as judged by the investigator, is likely to be able to continue to travel to the study center to complete study visits for the duration of the study |
| **Arms** | Double-blind, randomized: 1:1<br>• SAGE-718, placebo | | |
| **Dosing Regimen** | 1.2 mg oral daily from days 1 to 27; 0.9 mg oral daily from days 28 to 84 | **Exclusion Criteria** | • Have participated in a previous clinical study of SAGE-718, have participated in a previous gene therapy study, or have received study treatment in any other drug, biologic, or device trial within 180 days or 5 half-lives (whichever is longer), unless the patient participated solely in the placebo arm of the study<br>• Have a diagnosis of an ongoing neurodegenerative condition other than HD, including but not limited to, Alzheimer's disease, vascular dementia, dementia with Lewy bodies, or Parkinson's disease |

# 324-ETD-202: Phase 2 double-blind, randomized, placebo-controlled, dose–response study of SAGE-324 for the treatment of patients with essential tremor

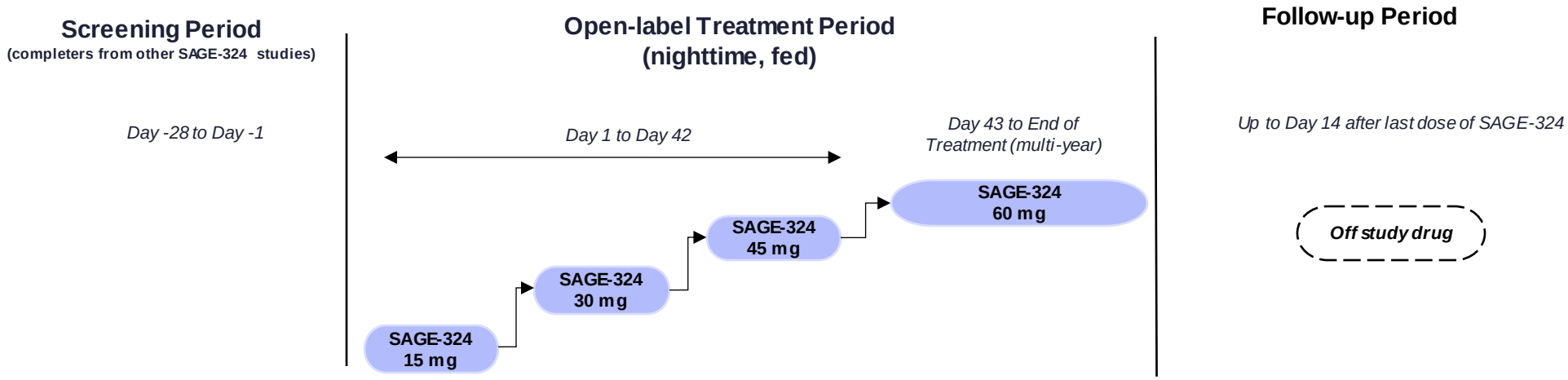



- Patients with moderate to severe essential tremor
- Primary aim is to identify a dose-response
- Primary endpoint is change from baseline in TETRAS Performance Subscale Item 4 total score at Day 91
- Dose(s) selected for potential pivotal studies will balance efficacy with tolerability

SAGE-324 is being developed in collaboration with Biogen.

# SAGE-324 Long-Term Open Label Safety Study (ETD-303)

*A Long-term, Open-Label Safety and Tolerability Study of SAGE-324 in Participants with Essential Tremor*




## STUDY OVERVIEW

| | |
|---|---|
| **Status** | Initiated |
| **Indication** | Essential Tremor |
| **Phase** | Phase 2 |
| **Arms** | Open-label<br>• SAGE-324 |
| **Dosing Regimen** | Up titration in 15mg increments to 60mg<br>Nighttime, fed |

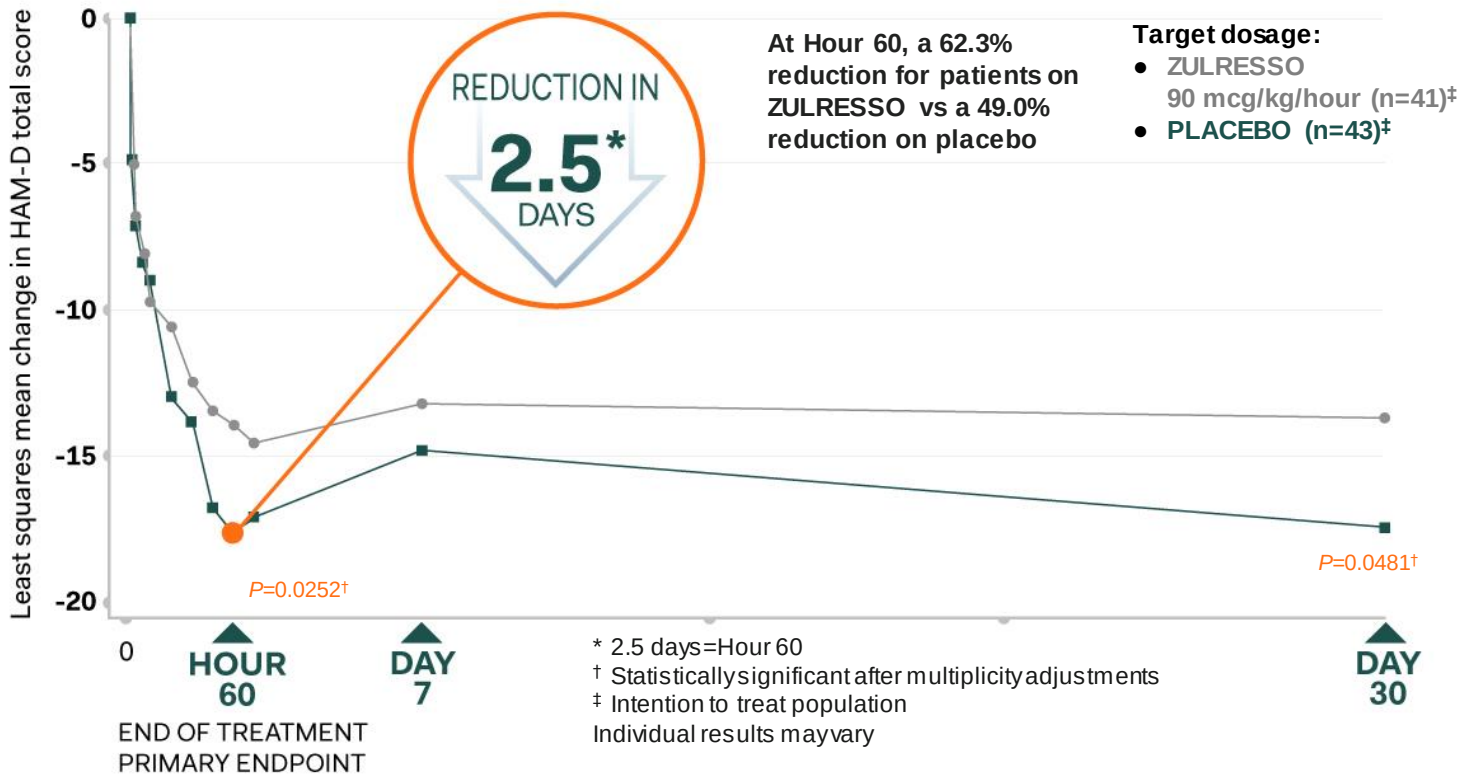
| | |
|---|---|
| **Objectives** | • To assess the long-term safety and tolerability of SAGE-324 |
| **Primary Endpoint** | • Incidence of treatment-emergent adverse events (TEAEs) |
| **Key Secondary Endpoint** | • Change from baseline in vital signs, electrocardiogram (ECG) and clinical laboratory parameters, Epworth Sleepiness Scale (ESS), Physician Withdrawal Checklist (PWC-20), and Columbia-Suicide Severity Rating Scale (C-SSRS) responses |
| **Inclusion Criteria** | • Be between the ages of 18 and 80 at Screening<br>• Participant has a clinician-confirmed diagnosis of ET in compliance with all the following criteria:<br>a. Duration of at least 3 years<br>b. Absence of other neurological signs, such as dystonia, ataxia, parkinsonism, task- and position-specific tremors, sudden tremor onset, or evidence of stepwise deterioration of tremor<br>c. Absence of historical or clinical evidence of tremor with psychogenic origin<br>• Participant has successfully completed participation in another SAGE-324 study |
| **Exclusion Criteria** | • Participant has presence of alcohol withdrawal state.<br>• Participant has had direct or indirect injury or trauma to the nervous system within 3 months before the onset of tremor.<br>• Participant is taking and unable to discontinue the use of primidone at least one month prior to administration of first dose of SAGE-324. |

SAGE-324 is being developed in collaboration with Biogen.

# ZULRESSO® (brexanolone) CIV Injection

*Treated patients experienced rapid improvement of depressive symptoms*

**Change from baseline in HAM-D total score over time in Study 1 with the recommended target dosage of ZULRESSO (90 mcg/kg/h)[i,ii]**




**Durable therapeutic effect**

A prespecified secondary efficacy endpoint was the mean change from baseline in HAM-D total score at Day 30[i]

In Study 1, significantly greater symptom reduction vs placebo was observed at Day 30[i,ii]

In Study 2, the 90 mcg/kg/hour arm maintained therapeutic effect at Day 30, but did not show a greater reduction vs placebo

**The most common adverse reactions** (incidence of ≥5% and at least twice the rate of placebo):

- Sedation/somnolence
- Dry mouth
- Loss of consciousness
- Flushing/hot flush

ZULRESSO is only available through the ZULRESSO Risk Evaluation and Mitigation Strategy (REMS), a safety program to manage the risk of serious harm resulting from excessive sedation and sudden loss of consciousness during the ZULRESSO infusion. To administer ZULRESSO, sites of care must be certified in the ZULRESSO REMS[iii]

**Please see full Prescribing Information, including Boxed Warning available with this presentation**

Sage Therapeutics





*Sources: i. ZULRESSO Prescribing Information. Cambridge, MA: Sage Therapeutics, Inc., ii. Meltzer-Brody S et al. Lancet. 2018;392(10152):1058-1070, iii. ZULRESSO REMS. https://zulressorems.com/#Public*

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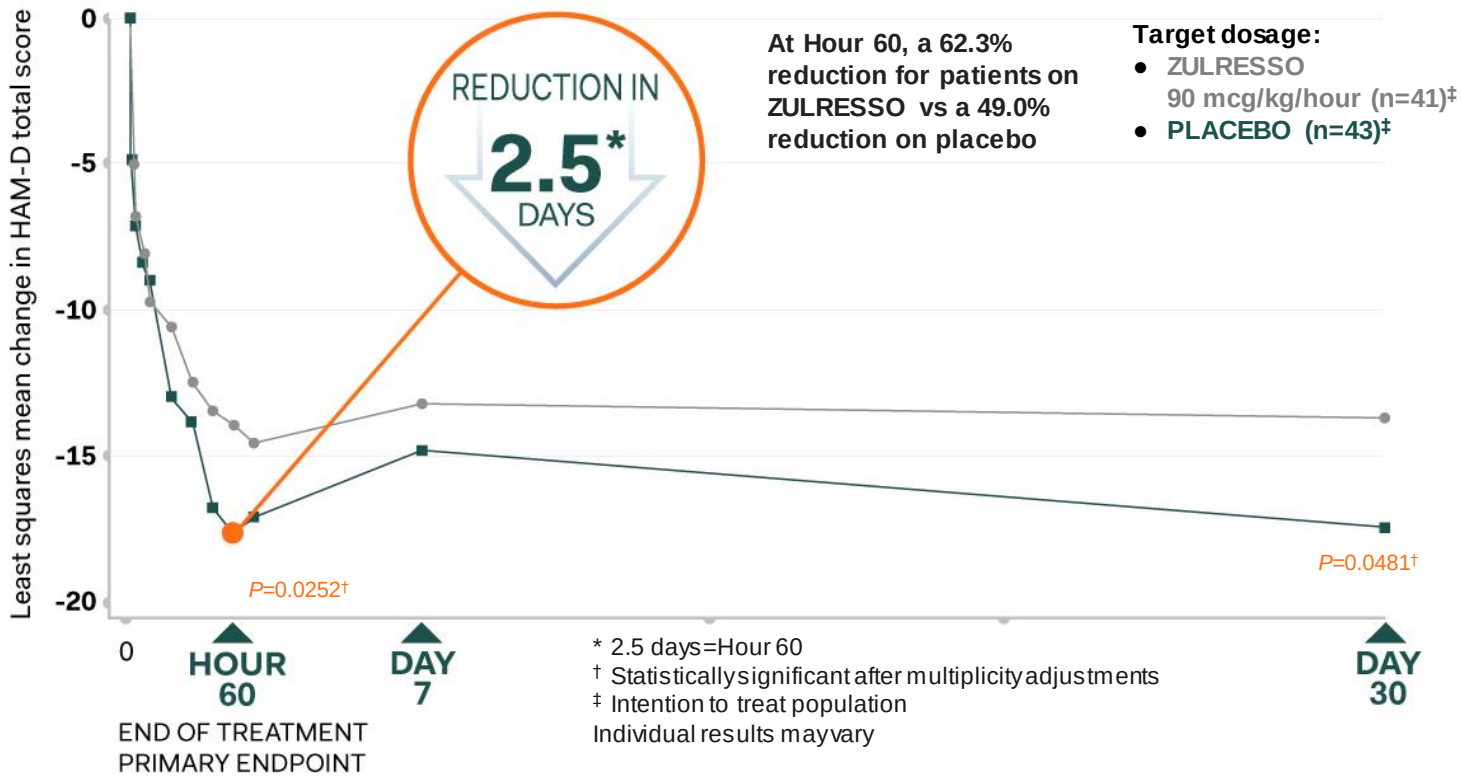


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- Loss of consciousness
- Flushing/hot flush

ZULRESSO is only available through the ZULRESSO Risk Evaluation and Mitigation Strategy (REMS), a safety program to manage the risk of serious harm resulting from excessive sedation and sudden loss of consciousness during the ZULRESSO infusion. To administer ZULRESSO, sites of care must be certified in the ZULRESSO REMS[iii]

**Please see full Prescribing Information, including Boxed Warning available with this presentation**

Sage Therapeutics





*Sources: i. ZULRESSO Prescribing Information. Cambridge, MA: Sage Therapeutics, Inc., ii. Meltzer-Brody S et al. Lancet. 2018;392(10152):1058-1070, iii. ZULRESSO REMS. https://zulressorems.com/#Public*

# ZULRESSO® (brexanolone) CIV Injection
*Boxed warning*

**WARNING: EXCESSIVE SEDATION AND SUDDEN LOSS OF CONSCIOUSNESS**

*See full prescribing information for complete boxed warning.*

- Patients are at risk of excessive sedation or sudden loss of consciousness during administration of ZULRESSO. (5.1)
- Because of the risk of serious harm, patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring. Patients must be accompanied during interactions with their child(ren). (5.1)
- ZULRESSO is available only through a restricted program called the ZULRESSO REMS. (5.1, 5.2)

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# ZULRESSO® (brexanolone) CIV injection

## *Select Important Safety Information*

These are not all the side effects of ZULRESSO.

**ZULRESSO can cause serious side effects, including:**

- **Excessive sedation and sudden loss of consciousness.** ZULRESSO may cause you to feel very sleepy (excessive sedation) or pass out (loss of consciousness). Your healthcare provider should check you for symptoms of excessive sleepiness every 2 hours while you are awake.
  - During your infusion, tell your healthcare provider right away if you feel like you cannot stay awake during the time you are normally awake or if you feel like you are going to pass out. Your healthcare provider may lower your dose or stop the infusion until symptoms go away
  - You must have a caregiver or family member with you to help care for your child(ren) during your infusion
- Because of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness, ZULRESSO is only available through a restricted program called the ZULRESSO REMS.

**ZULRESSO can cause other serious side effects, including:**

- **Increased risk of suicidal thoughts or actions.** ZULRESSO and other antidepressant medicines may increase suicidal thoughts and actions in some people 24 years of age and younger. **Pay close attention to and tell your healthcare provider right away if you have any of the following symptoms, especially if they are new, worse, or worry you:**
  - Attempts to commit suicide, thoughts about suicide or dying, new or worse depression, other unusual or sudden changes in behavior or mood
  - Keep all follow-up visits and call your healthcare provider between visits as needed, especially if you have concerns about symptoms.

**The most common side effects of ZULRESSO include:**

- Sleepiness, dry mouth, passing out, flushing of the skin or face.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**Before receiving ZULRESSO, tell your healthcare provider about all your medical conditions** including if you drink alcohol, have kidney problems, are pregnant or think you may be pregnant, or are breastfeeding or plan to breastfeed. It is not known if ZULRESSO will harm your unborn baby. If you become pregnant during treatment, talk with your healthcare provider about enrolling with the National Pregnancy Registry for Antidepressants at 1-844-405-6185.

**While receiving ZULRESSO, avoid the following:**

- Driving a car or doing other dangerous activities after your ZULRESSO infusion until your feeling of sleepiness has completely gone away
- Do not drink alcohol

**Tell your healthcare provider about all the medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements. ZULRESSO and some medicines may interact with each other and cause serious side effects.

**Especially tell your healthcare provider if you take** other antidepressants, opioids, or Central Nervous System (CNS) depressants (such as benzodiazepines).

**Please see the patient Medication Guide, including information about serious side effects, for ZULRESSO in the full Prescribing Information.**

Sage Therapeutics®

# Strategic Zuranolone Collaboration with Shionogi

- **Expansion of Global Footprint**
  - Goal of collaboration to accelerate development of a potentially groundbreaking medicine to patients in key Asian markets
  - Sage maintains exclusive rights to develop and commercialize zuranolone outside of those geographies
- **Expert Partner in Key Asian Markets**
  - Shionogi is responsible for clinical development and commercialization of zuranolone in Japan, Taiwan, and South Korea
  - Shionogi has strong presence in Asia in developing & commercializing therapeutics for CNS disorders
- **Attractive Terms**
  - Sage to receive tiered royalties on sales averaging in the greater than 20% range, if commercialized
  - Shionogi has also granted Sage certain rights to co-promote zuranolone in Japan across all indications

Sage Therapeutics™ + SHIONOGI

**$90M**

Upfront payment

**$485M**

Potential development & commercial milestones

# Strategic Zuranolone and SAGE-324 Collaboration with Biogen

- **50:50 joint development and commercialization of zuranolone and SAGE-324 in the United States**
  - Opportunity to expand the number of indications, patient impact and thereby the commercial value of zuranolone and SAGE-324, assuming successful development
- **Enables expansion and acceleration of pipeline**
  - Financial and operational flexibility from collaboration allows Sage to fully evaluate the potential of existing programs and fuels product engine enabling continued identification and development of product candidates
- **Attractive terms, with potential total deal value of more than $3.1 billion**
  - Sage to receive tiered royalties on sales outside of the United States in the high teens to low twenties percentage if commercialized
  - 50:50 cost and profit sharing within the United States

Sage Therapeutics™ + Biogen®

**$1.5B**

Upfront payment and equity investment

**$1.6B**

Potential development & commercial milestones*

**$1.6B in potential development and commercial milestones amount to total milestone payments over the life of the collaboration including the $75M payment which we received in January 2024 related to first commercial sale of ZURZUVAE for PPD which we achieved in December 2023.*

# Seeing the brain differently *makes a world of difference*

Sage Therapeutics®