Sage Therapeutics®

Corporate Presentation

October 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”, “vision”, “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 goals for ZURZUVAE to become first line therapy and standard of care in this indication, to expand the healthcare provider prescriber base, to support repeat prescribing, and to inspire women to discuss PPD and ZURZUVAE with their healthcare providers; our reimbursement and access expectations, and plans and goals related to other aspects of commercialization; 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; our clinical development plans and expectations, including expected timelines for data read-outs and other activities and our expectations as to potential results and next steps, if any, based on such results; our plans for evaluating opportunities across our early-stage pipeline; our belief in the potential profile and benefit of our product candidates, potential indications for our product candidates, the potential for success of our programs, and the opportunity to help patients in various indications; 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 for our business; the opportunity, mission, goals and vision for our business; and our expectations with respect to cash runway, 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, process-related or other 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, or meet our other goals for market access, sales and marketing, customer support, or distribution strategies.
  - Our clinical trials may not meet their primary endpoints or key secondary endpoints. For example, results of our ongoing DIMENSION Study of dalzanemdor in Huntington’s Disease may be negative like the results from the PRECEDENT Study evaluating dalzanemdor in Parkinson’s Disease and the LIGHTWAVE Study evaluating dalzanemdor in Alzheimer’s disease, even with the adjustments we made in the endpoints in the DIMENSION Study. 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 feasible or successful. We may experience slower than expected enrollment in our future clinical trials or may encounter delays or problems with ongoing or future clinical trials, 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 or gain regulatory approval of products beyond ZURZUVAE and ZULRESSO.
  - 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. Also, we may not achieve anticipated cost savings from our October 2024 reorganization at the levels we expect. 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. Additional funding 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

Fearlessly lead the way to *create a world with better brain health*.

OUR MISSION

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

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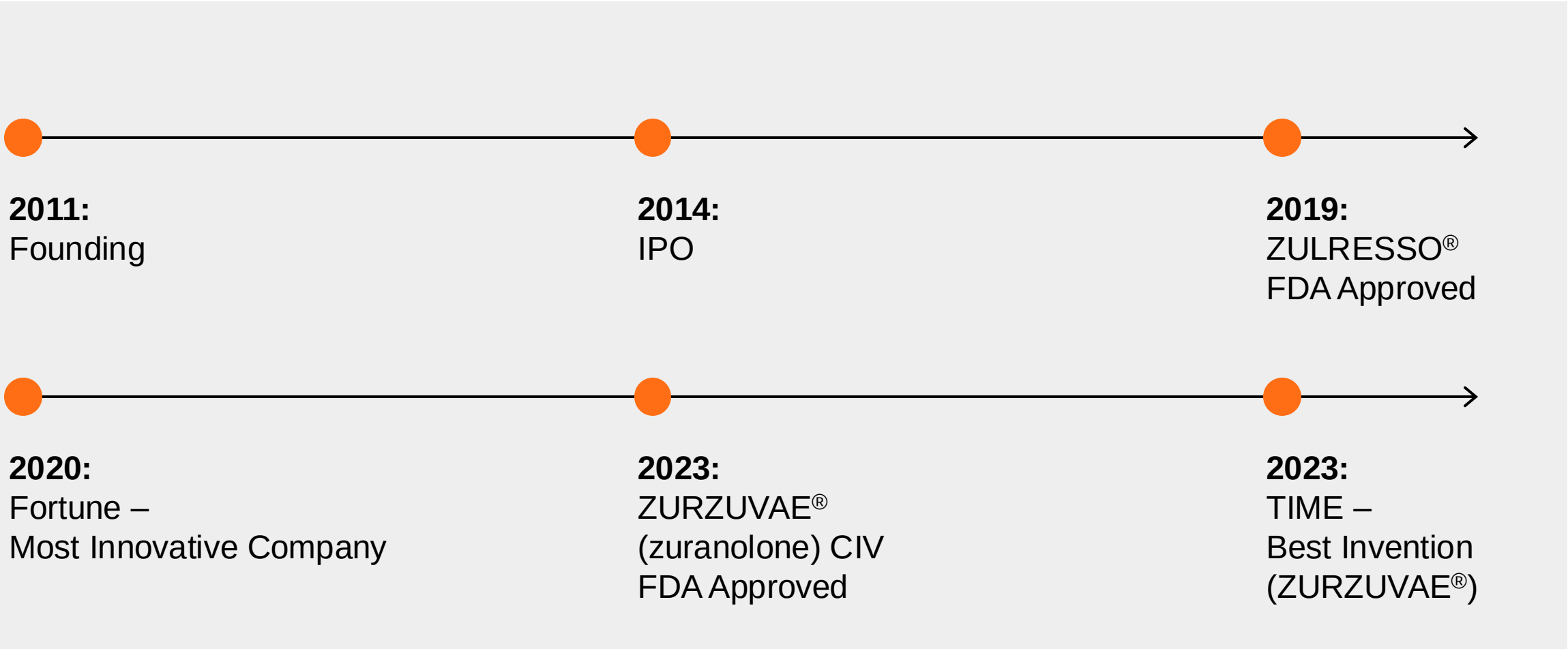
Business Milestones



Pipeline

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					
Dalzanemdor (SAGE-718)	Huntington's Disease Cognitive Impairment		IN PHASE 2		
Programs In Evaluation					

- SAGE-324*** *GABA Hypofunction*
- SAGE-689 *Acute GABA Hypofunction*
- SAGE-421 *NMDA Hypofunction*
- SAGE-319 *GABA Hypofunction*

**Collaboration Partners: Biogen Inc. and Shionogi for zuranolone.*
***Sage plans to discontinue commercial availability of ZULRESSO in the U.S. as of December 31, 2024.*
****In July 2024, we announced discontinuation of clinical development of SAGE-324 in essential tremor. Sage is evaluating next steps, if any, for other potential indications.*

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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.

ZURZUVAE®

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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 treatment course beginning as early as day 3 and maintained at day 45

14-day Treatment Course

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

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 $GABA_A$ receptor positive modulator with an MOA thought to be related to its positive allosteric modulation of $GABA_A$ 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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Goal to establish ZURZUVAE as the standard of care in PPD

1. Expand HCP prescriber base
2. Support repeat writing among existing prescriber base
3. Inspire women to discuss PPD symptoms with their HCP and ask about ZURZUVAE

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Please refer to the U.S. Prescribing Information for ZURZUVAE (https://documents.sage-biogen.com/us/zurzuvae/pi.pdf)

PPD poses a substantial burden to patients and their families

Estimated that about **1 in 8 women** with a recent live birth experience symptoms of PPD, or roughly ~500K women a year[1-2]

PPD symptoms are one of the **most common complications** of pregnancy and childbirth[1, 3]

Perinatal depression is **inconsistently diagnosed** and may be an undertreated condition[1, 4-6]

Mothers with perinatal depression often face **significant challenges** with functioning and infant-bonding[7-9]

The **economic burden** associated with perinatal depression is vast and impacts patients, their families, employers, and health care payers[10-11]

The **COVID-19 Pandemic** had a significant effect on perinatal mental health outcomes[12-14]

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):575-58 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. Screening and diagnosis of mental health conditions during pregnancy and postpartum. Clinical Practice Guideline No. 4. American College of Obstetricians and Gynecologists. Obstet Gynecol 2023;141:1232-61. 4. Ukatu N, et al. Psychosomatics. 2018;59(3):211-219. 5. Wang Z, et al. Transl Psychiatry. 2021;11(1):543. 6. Fonseca A, et al. J Affect Disord. 2020;274:167-173. 7. American Psychiatric Association. Depressive disorders. In: Diagnostic and Statistical Manual of Mental Disorders. 5th ed, text revision. American Psychiatric Association; 2022. 8. Saharoy R, Potdukhe A, Wanjari M, Taksande AB. Postpartum depression and maternal care: exploring the complex effects on mothers and infants. Cureus. 2023;15(7):e41381. 9. Slomian J, Honvo G, Emonts P, Reginster JY, Bruyère O. Consequences of maternal postpartum depression: a systematic review of maternal and infant outcomes. Womens Health. 2019;15:1745506519844044. 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. 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. 13. 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. 14. 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.

Dalzanemdor (SAGE-718)

Sage Therapeutics

Cognitive impairment in HD is a significant unmet need

~188,000

Huntington's Disease Global Prevalence[1]

~40,000

Individuals in the US are diagnosed and currently live with HD, **and an additional 200,000 people** who carry the genetic mutation are at risk for developing HD[2]

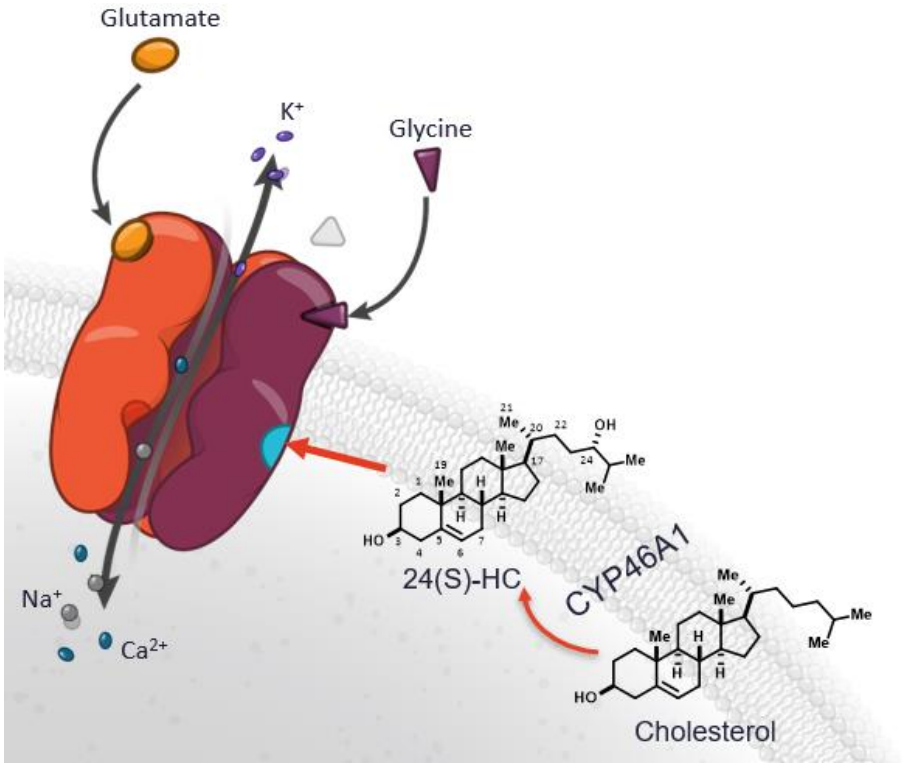
~10-15 years

Cognitive and behavioral symptoms can appear before perceptible motor symptoms[3]

1. Pringsheim T, Wiltshire K, Day L, Dy keman J, Steev es T, Jette N. The incidence and prev alence of Huntington's disease: a sy stematic rev iew and meta-analy sis. Mov Disord. 2012 Aug;27(9):1083-91. doi: 10.1002/mds.25075. Epub 2012 Jun 12. PMID: 22692795 2. Yohrling G, Raimundo K, Crowell V, et al. Prevalence of Huntington's disease in the US (954). Neurology 2020; 94, Number 15 Supplement. DOI: 10.1212/WNL.94.15_supplement.954.; Overview of Huntington's Disease: Huntington's Disease Society of America, https://hdsa.org/what-is-hd/overview-of-huntingtons-disease/ 3. Paulsen JS. Cognitive impairment in Huntington disease: diagnosis and treatment. Curr Neurol Neurosci Rep 2011; 11: 474-483. DOI: 10.1007/s11910-011-0215-x; Ross CA, Pantelyat A, Kogan J, et al. Determinants of functional disability in Huntington's disease: role of cognitive and motor dysfunction. Mov Disord 2014; 29: 1351-1358. DOI: 10.1002/mds.26012.

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.

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 Ongoing Clinical Development Program

Huntington's Disease

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

CLP-102-B

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

Completed

PERSPECTIVE PROGRAM

SURVEYOR (718-CIH-202)

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

Completed

DIMENSION (718-CIH-201)

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

Enrollment Complete

PURVIEW (718-CIH-301)

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

Enrolling

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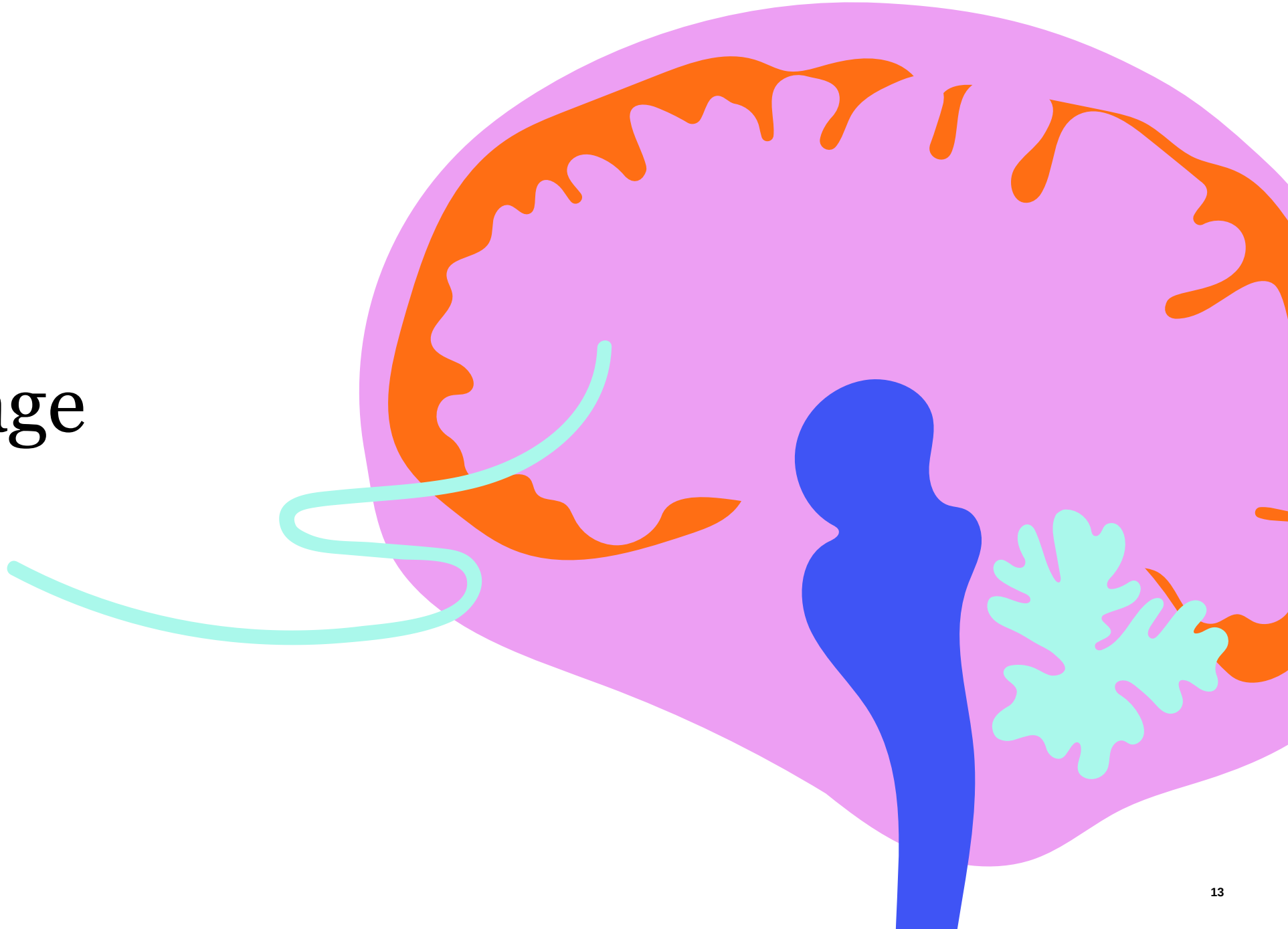
Earlier Stage Pipeline



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Other potential areas of growth within GABA and NMDA platforms

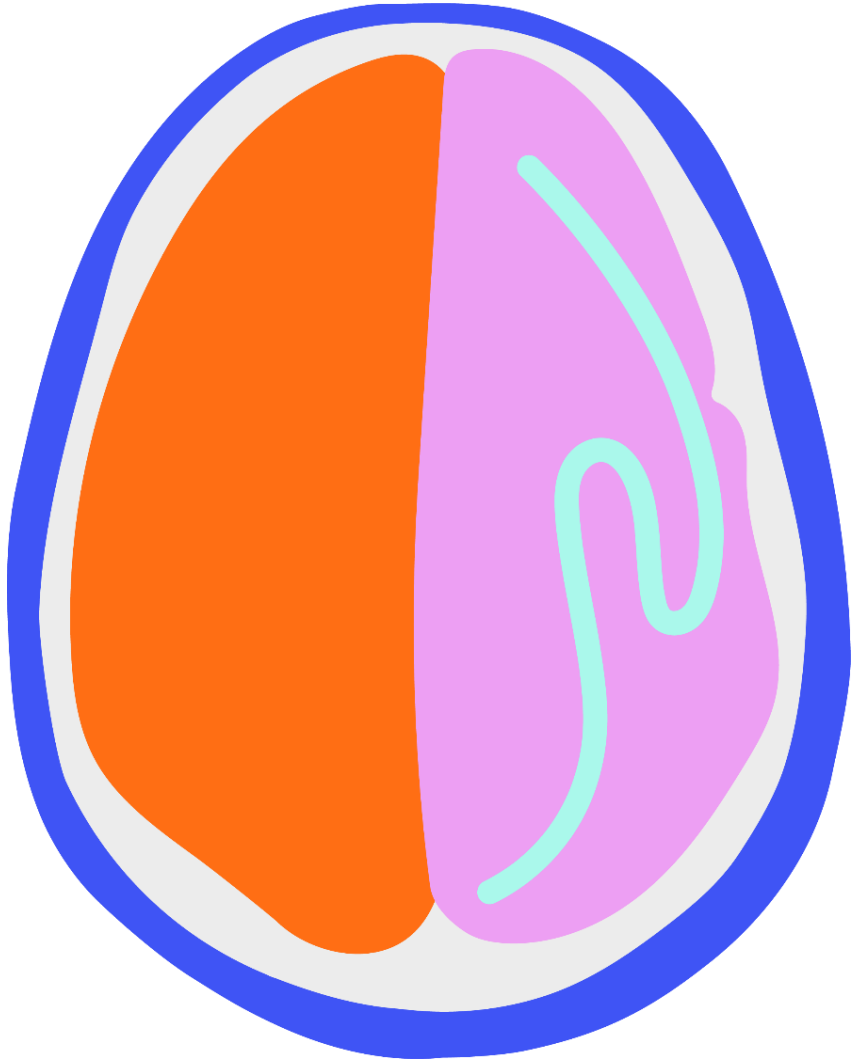
Preclinical profile of SAGE-319

$GABA_A$ Receptor PAM

- Extra-synaptic $GABA_A$ receptor preferring positive allosteric modulator

Potential indications:

NEURODEVELOPMENTAL / MOTOR DISORDERS



Preclinical profile of SAGE-421

NMDA Receptor PAM

- NMDA receptor positive allosteric modulator

Potential indications:

COGNITIVE IMPAIRMENT

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OUR VISION

Fearlessly lead the way to *create a world with better brain health*.

OUR MISSION

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

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Appendix

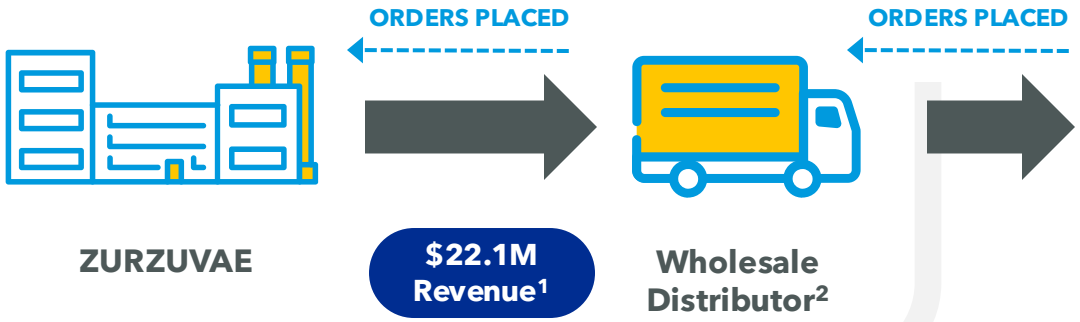
ZURZUVAE Distribution Diagram

(All metrics are Q3 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 Q3 2024 results
1. Net revenues Biogen reports for ZURZUVAE; Sage records 50% as collaboration revenue ($11M)
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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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.

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Seeing the brain differently *makes a world of difference*

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