Sage Business Update

August 7, 2023

Sage Therapeutics®

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: the completion of DEA scheduling, commencement of planned launch, availability and commercialization of ZURZUVAE, and potential timing of such activities; our belief in our readiness for commercial launch of ZURZUVAE and our commercialization plan; our goals of enabling access to ZURZUVAE for women with PPD; our plans to review FDA feedback with respect to zuranolone for the treatment of MDD and evaluate next steps; the potential for regulatory approval of zuranolone for the treatment of MDD; our belief in the potential benefit of ZURZUVAE in the treatment of adults with PPD; our belief in the potential of ZURZUVAE to be successful and to meet an unmet need in the treatment of women with PPD; the number of women with PPD and the potential market for ZURZUVAE for the treatment of women with PPD; the goals, opportunity, mission and vision for business; our expectations with respect to cash, cash runway, asset prioritization, restructuring, expenses and the potential receipt of milestone payments; and our views with respect to our financial strength.

- 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:

- Our launch and commercialization efforts in the U.S. with respect to ZURZUVAE for the treatment of women with PPD may not occur on the timelines we expect and may not be successful, and we may be unable to generate revenues at the levels or on the timing we expect or at levels or on the timing necessary to support our goals. The number of women with PPD, the unmet need for additional treatment options, and the potential market for ZURZUVAE in this indication may be significantly smaller than we expect. ZURZUVAE may not achieve the clinical benefit, clinical use or market acceptance we expect in the treatment of women with PPD or we may encounter reimbursement-related or other market-related issues that impact the success of our commercialization efforts.

- We may never achieve regulatory approval of zuranolone in MDD. The FDA has taken the position that an additional clinical trial or clinical trials of zuranolone are required to support approval in MDD and may not change that position. Such trial or trials could be time-consuming, significantly increase our expenses, and may not be feasible; even if we conduct such clinical trials, they may not be successful; the FDA may decide that the design, conduct or results of such clinical trials, even if positive, are not sufficient for approval in MDD or may find other deficiencies in our development program, data, processes, or manufacturing sites, or we may encounter delays in initiation, conduct, completion of enrollment or completion of any such clinical trials, including as a result of slower than expected site initiation, slower than expected enrollment, the need or decision to expand the trials or other changes, that may impact our ability to meet our expected timelines and increase our costs. Even if we receive regulatory approval of zuranolone for the treatment of MDD, the FDA may approve zuranolone for only a subset of MDD patients or with limitations or restrictions.

- 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.

- Our operating expenses may be higher than forecasted and we may face unexpected expenses which could cause us to change our plans. Our revenues may be lower than we expect, including if we do not receive approval of zuranolone in MDD in the future or if our launch of ZURZUVAE in PPD is not as successful as we expect. We may not receive expected milestones payments on the timing we expect, or at all. For these and other reasons, our expectations with respect to cash, cash runway, expenses and our 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.

- Our clinical trials may not meet their primary endpoints or key secondary endpoints. Success in non-clinical 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 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, and such issues with any trial could cause delay in completion of the trial, availability of results and timing of future activities.

- We may encounter unexpected safety or tolerability issues with respect to any of our product candidates or marketed products that could negatively impact commercialization, if approved, and the potential for regulatory approval. We may encounter different or more severe adverse events at higher doses, different frequency or length of dosing or in new indications we are studying or may study in ongoing or planned trials.

- 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 and our ability to proceed with further development.

- 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.

- 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.

- 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.

Sage Call Participants

Barry Greene

Chief Executive Officer,
Sage Therapeutics

Laura Gault

Chief Medical Officer,
Sage Therapeutics

Chris Benecchi

Chief Business Officer,
Sage Therapeutics

Kimi Iguchi

Chief Financial Officer,
Sage Therapeutics

Jim Doherty

Chief Development Officer,
Sage Therapeutics

Opening Remarks

Barry Greene – Chief Executive Officer

ZURZUVAE™

(zuranolone) capsules Ⓒ

20 mg • 25 mg • 30 mg

Is Now FDA Approved

DEA scheduling is pending

Sage Therapeutics® | Biogen

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 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

Generally Well-Tolerated

- 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.

PPD is a critical medical condition requiring urgent treatment; left untreated, PPD can be devastating to mom, baby and family

Mothers with PPD often face significant **challenges with functioning and infant-bonding**[1-5]

A mother's PPD can be associated with **short-term and long-term developmental, psychological, cognitive and physical ramifications** in her children[6]

Women with PPD are at **higher risk for substance abuse and suicidality**[7-10]

Unresolved PPD may continue beyond a year postpartum which can lead to **prolonged maternal morbidity and mortality**[11-13]

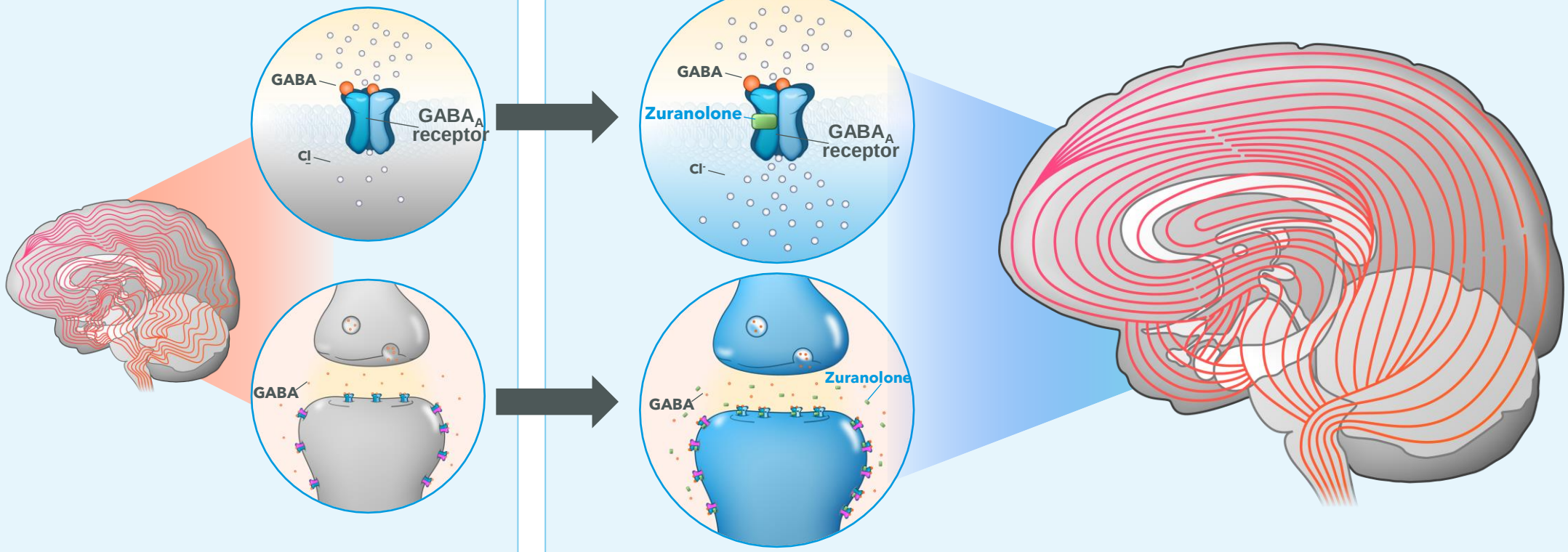
Women affected by PPD have significantly **higher healthcare resource utilization and costs** than women not affected by PPD[14-17]

1. Beck CT, et al. Am J Nurs. 2006;106(5):40-50. 2. Wouk K, et al. Pediatrics. 2016;137(1). 3. Lilja G, et al. Scand J Caring Sci. 2012;26(2):245-253. 4. Gaglardi L, et al. Arch Dis Child. 2012;97(4):355-357. 5. Kerstis B, et al. Arch Womens Ment Health. 2016;19(1):87-94. 6. Moore Simas et al. Curr Med Res Opin. 2019;35(3):383-393. 7. Fitelson E, et al. Int J Womens Health. 2010;3:1-14. 8. Moses-Kolko EL, et al. Am J Psychiatry. 2016;173(6): 559-561.e203550. 9. Gressier F, et al. J Psychiatr Res. 2017;84:284-291. 10. Bodnar-Deren S, et al. J Womens Health. 2016;25(12):1219-1224. 11. Vliegen N et al. 2014 Harv Rev Psychiatry;22(1):1-22. 12. Putnik DL, et al. Pediatrics. 2020;146(5):e20200857.13. Netsi E, et al. JAMA Psychiatry. 2018;75(3):247-253. 14. Epperson CN et al. CMRO, 2020;36 (10):1707-1716. San Diego, CA. March 25-28, 2019. 15. Dagher RK et al. J Occup Environ Med. 2012;54(2):210-215. 16. Le HN et al. J Paediatr Child Health. 2016;52(4):402-409. 17. Paul IM et al. Pediatrics. 2013;131(4):e1218-e1224.

ZURZUVAE Clinical Development in PPD

Laura Gault – Chief Medical Officer

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



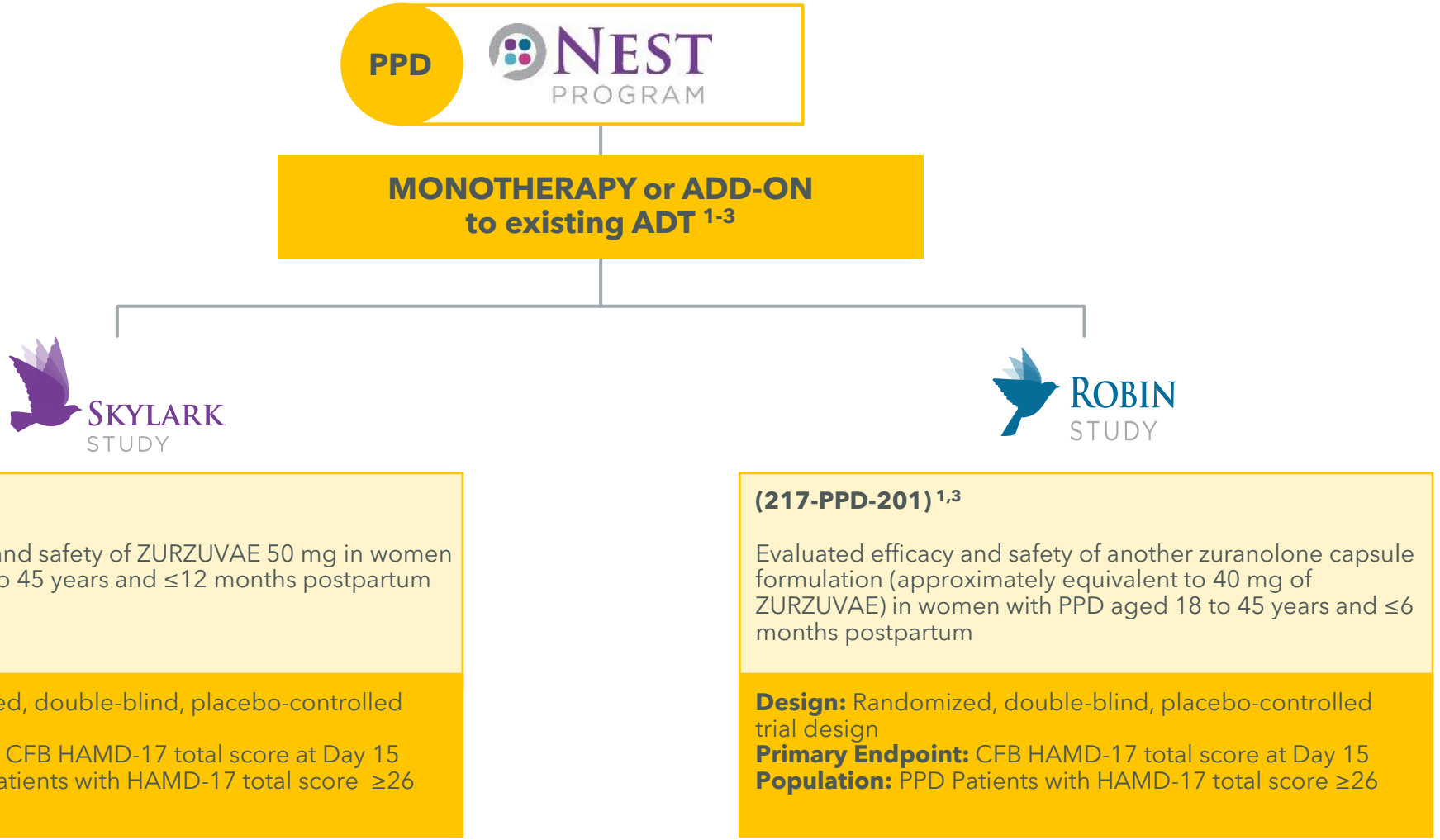
Synaptic and extrasynaptic GABAA receptors regulate the activity of brain regions disrupted in depression[7-9]

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

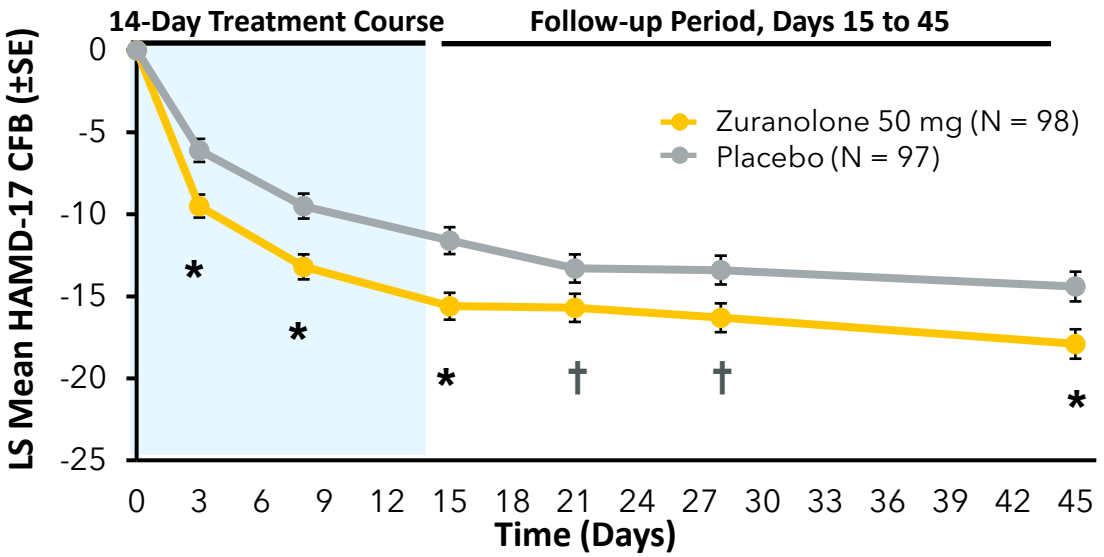


ADT = antidepressant therapy; CFB = change from baseline; HAMD-17 = 17-item Hamilton Rating Scale for Depression; PPD = postpartum depression

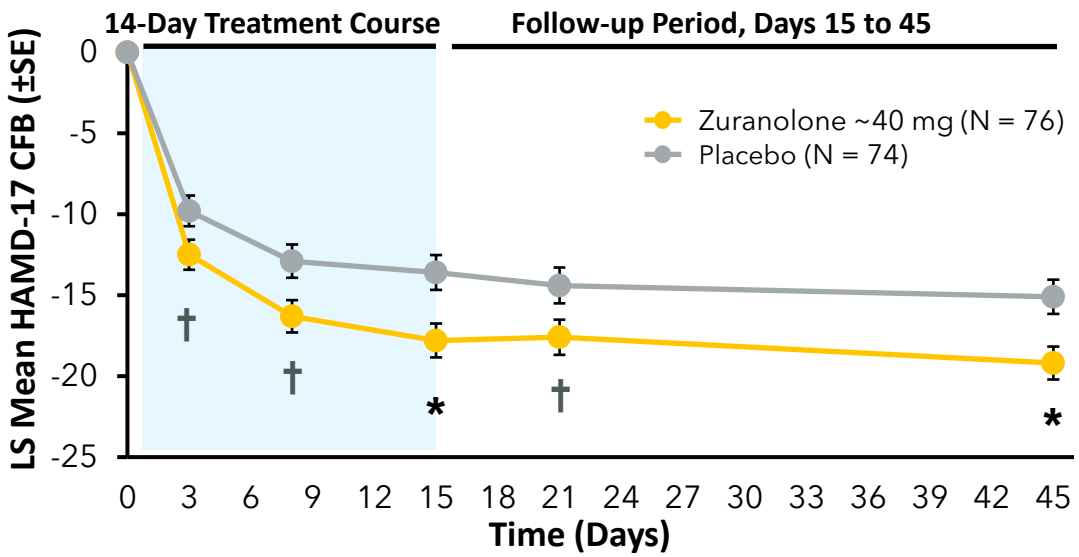
1. ZURZUVAE (zuranolone) [package insert]. Cambridge, MA: Sage Therapeutics, Inc and Biogen; 2023. 2. Deligiannidis KM et al. *Am J Psychiatry*; 2023. 3. Deligiannidis KM, et al. *JAMA Psychiatry;* 2021.

Clinical studies in PPD

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

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.

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

WARNING: IMPAIRED ABILITY TO DRIVE OR ENGAGE IN OTHER POTENTIALLY HAZARDOUS ACTIVITIES

ZURZUVAE causes driving impairment due to central nervous system (CNS) depressant effects. Advise patients not to drive or engage in other potentially hazardous activities until at least 12 hours after ZURZUVAE administration. Patients that they may not be able to assess their own driving competence, or the degree of driving impairment caused by ZURZUVAE.

Warnings and Precautions

- CNS depressant effects
- Suicidal thoughts and behaviors
- Embryo-fetal toxicity

Most Common Adverse Reaction (≥5% and greater than placebo)

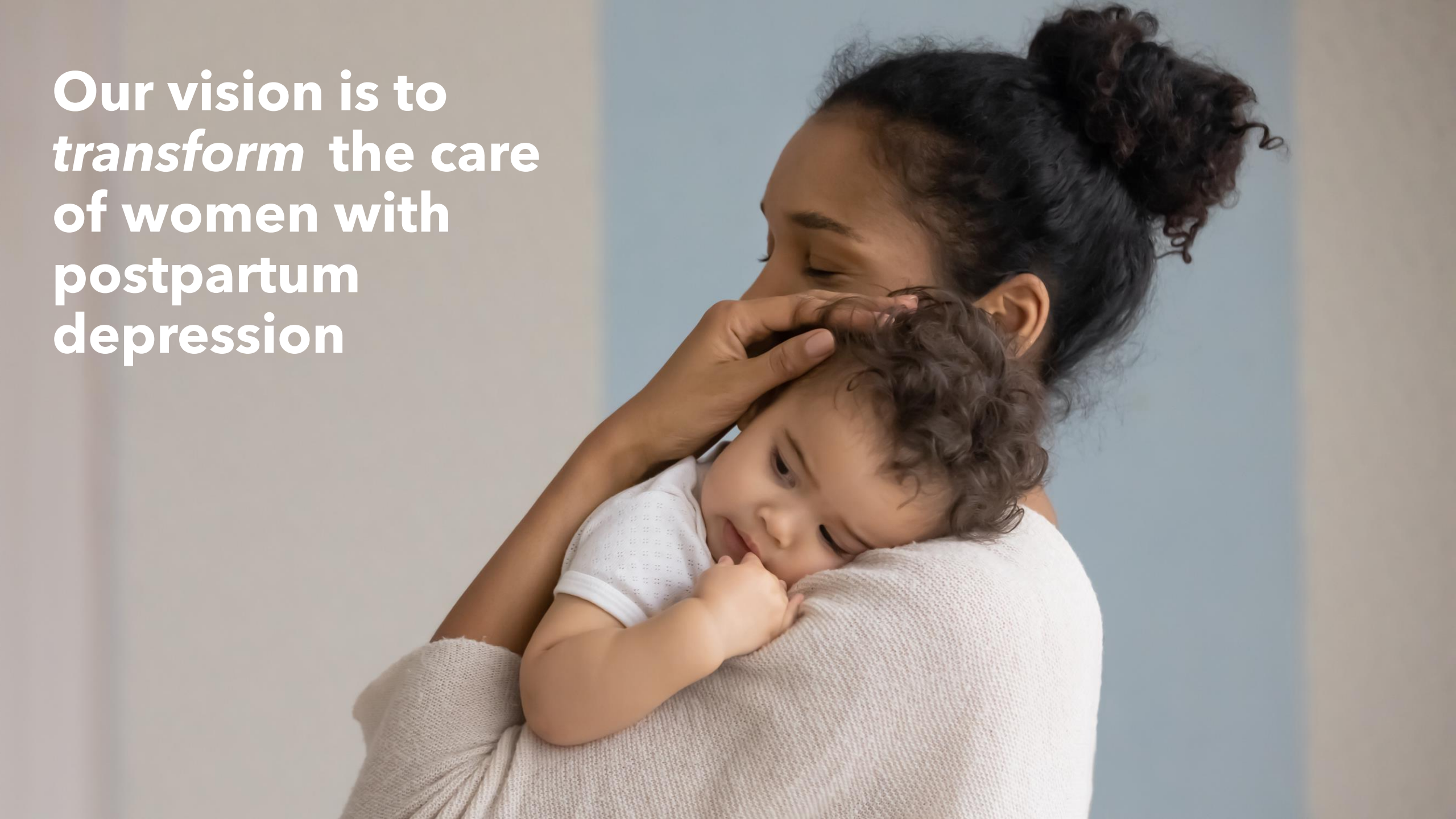
- Somnolence, dizziness, diarrhea, fatigue, nasopharyngitis, and urinary tract infection

See slide 22 for Important Safety Information

ZURZUVAE
Planned Commercial Strategy in the Treatment of Women with PPD

Chris Benecchi – Chief Business Officer

Our vision is to *transform* the care of women with postpartum depression



ZURZUVAE is the first and only oral treatment specifically approved for women with postpartum depression

PPD

In the US, an estimated **1 in 8** women experience symptoms of PPD[1,2]

~477k women with a live birth experiencing PPD symptoms[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 increase diagnosis of PPD

Patient Profiles

Increased screening and diagnosis for women 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.

Omnichannel intended to drive broad engagement and advance HCPs through the ZURZUVAE adoption journey in the treatment of women with PPD

ZURZUVAE Omnichannel Strategy

Prescriber reach: Focus promotion on prescribing PSYCHs, OBGYNs, and PCPs who treat women with PPD through personal and non-personal promotion

Focused messaging: Deliver customized messages with effective cadence based upon HCP specialty and experience treating women with PPD

Preferred delivery: Provide content through the customer's preferred channels to deliver a relevant and engaging experience

Personal Promotion

Non-Personal, Digital Promotion

Optimize: Continuously learn about customers and leverage analytics (human and AI) to refine engagements across personal and non-personal channels to deliver a truly orchestrated experience for HCPs who treat women with PPD

HCP clinical experience and rapid and easy access for women with PPD are critical to building confidence and accelerating adoption of ZURZUVAE in this indication

Planned efforts

1

Full Course Therapy Sample Program

Distribute 14-day course of therapy to appropriate HCPs to trial ZURZUVAE in the treatment of women with PPD

2

Patient Access Programs for women with PPD

Support our goal that every woman with PPD who is prescribed ZURZUVAE can access it, regardless of financial circumstances

3

Patient Support

Deliver exceptional patient support for women with PPD

The planned ZURZUVAE market access strategy is expected to leverage the clinical profile and unmet need with the goal of maximizing access for women with PPD

Unmet Need

- First approved oral treatment for women with PPD
- Potential for rapid & sustained improvement
- 14-Day short course

Value Proposition

- Clinical Profile
- Economic Burden

Patient Access

Support Goals of:

- Rapid Access
- Minimized Restrictions
- Patient Affordability

Our goal is to maximize impact by aligning with our stakeholders

1.	**Inspire Patients**	Inspire women with PPD to ask their HCPs about ZURZUVAE
2.	**Drive Early HCP Experience**	Drive positive early experience with ZURZUVAE as a treatment for women with PPD with targeted HCPs through omnichannel efforts
3.	**Enable Access**	Lead with value with the goal of enabling rapid access for women with PPD and limit onerous restrictions
4.	**Optimize Patient Experience**	Provide best-in-class patient support for women with PPD

Financial Update

Q&A

Important Safety Information

What is ZURZUVAE (zur-ZOO-vay)?

ZURZUVAE is a prescription medicine used to treat adults with postpartum depression (PPD). It is not known if ZURZUVAE is safe and effective in children.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ZURZUVAE?

ZURZUVAE may cause serious side effects, including:

- **Decreased ability to drive or do other dangerous activities.** ZURZUVAE may decrease your 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** during your 14-day treatment course of ZURZUVAE.
  - You may not be able to tell on your own if you can drive safely or tell how much ZURZUVAE is affecting you.
- **Decreased awareness and alertness [central nervous system (CNS) depressant effects].** ZURZUVAE may cause sleepiness, drowsiness, slow thinking, dizziness, confusion, and trouble walking.
  - Because of these symptoms, you may be at a higher risk for falls during treatment with ZURZUVAE.
  - Taking alcohol, other medicines that cause CNS depressant effects, or opioids while taking ZURZUVAE can make these symptoms worse and may also cause trouble breathing.
  - Tell your healthcare provider if you develop any of these symptoms, or if they get worse during treatment with ZURZUVAE. Your healthcare provider may decrease your dose or stop ZURZUVAE treatment if you develop these symptoms.

ZURZUVAE is a federally controlled substance (C-XX) because it contains zuranolone that can be abused or lead to dependence. Keep ZURZUVAE in a safe place to protect it from theft. Do not sell or give away ZURZUVAE because it may harm others and is against the law.

Before taking ZURZUVAE, tell your healthcare provider about all of your medical conditions, including if you:

- drink alcohol
- have abused or been dependent on prescription medicines, street drugs, or alcohol
- have liver or kidney problems
- are pregnant or plan to become pregnant. ZURZUVAE may harm your unborn baby.
- are breastfeeding or plan to breastfeed. ZURZUVAE passes into breast milk, and it is not known if it can harm your baby. Talk to your healthcare provider about the risks and benefits of breastfeeding and about the best way to feed your baby during treatment with ZURZUVAE.

Females who are able to become pregnant:

- Tell your healthcare provider right away if you 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.
- There is a pregnancy registry for females who are exposed to ZURZUVAE during pregnancy. The purpose of the registry is to collect information about the health of females exposed to ZURZUVAE and their baby. If you become pregnant during treatment with ZURZUVAE, talk to your healthcare provider about registering with the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or visit online at https://womensmentalhealth.org/research/pregnancyregistry/antidepressants/.

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

Especially tell your healthcare provider if you take antidepressants, opioids, or CNS depressants such as benzodiazepines.

What should I avoid while taking ZURZUVAE?

- **Do not** drive a car, operate machinery, or do other dangerous activities **until at least 12 hours after taking each dose of ZURZUVAE** because ZURZUVAE may make you feel sleepy, confused, or dizzy.
- **Do not** drink alcohol or take other medicines that make you sleepy or dizzy while taking ZURZUVAE without talking to your healthcare provider.

See "**What is the most important information I should know about ZURZUVAE?"**

- **ZURZUVAE may cause serious side effects, including:**
- See **"What is the most important information I should know about ZURZUVAE?"**
- **Increased risk of suicidal thoughts or actions.** 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.**
- **How can I watch for and try to prevent suicidal thoughts and actions?**
- Pay close attention to any changes, especially sudden changes in mood, behavior, thoughts, or feelings, or if you develop suicidal thoughts or actions. This is very important when an antidepressant medicine is started or when the dose is changed.
- Tell your healthcare provider right away if you have any new or sudden changes in mood, behavior, thoughts, or feelings.
- Keep all follow-up visits with your healthcare provider as scheduled. Call your healthcare provider between visits as needed, especially if you have concerns about symptoms.

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
- feeling very agitated or restless
- trouble sleeping (insomnia)
- new or worse anxiety
- panic attacks
- new or worse irritability
- acting aggressive, being angry, or violent
- an extreme increase in activity and talking (mania)
- acting on dangerous impulses
- other unusual changes in behavior or mood

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

These are not all of the possible side effects of ZURZUVAE. Call your doctor for medical advice about side effects. You can report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see the Full Prescribing Information, including Boxed WARNING, and Medication Guide for ZURZUVAE.