Sage Therapeutics®

Fourth Quarter and Full Year 2022 Financial Results

February 16, 2023

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 potential for approval and launch of zuranolone and potential timelines; our belief in the potential benefit and profile of zuranolone and in its potential to be successful and to meet an unmet need in the treatment of MDD and PPD; the potential for commercialization of zuranolone and our commercialization plans, including plans to help enable access; our expectations as to the types of MDD patients who may benefit from zuranolone, if approved; 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 and the potential market for our product candidates, if approved; the goals, opportunity, mission and vision for business; our expectations with respect to cash, expenses and the potential receipt of milestone payments; and our views with respect our financial strength and potential value creation opportunities.
- 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:
  - The FDA may not grant approval of our NDA for zuranolone in MDD and PPD or may grant approval for a narrower indication than we expect or with unexpected limitations or restrictions. The FDA may ask for additional clinical trials, nonclinical studies or other data in order for us to obtain regulatory approval of zuranolone or may find other deficiencies in our development program, data, processes, or manufacturing sites that causes the FDA not to approve our NDA.. Our expectations for timing of review of our NDA and of launch of zuranolone, if approved, may not be accurate.
  - 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; we may encounter different or more severe adverse events at the 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.
  - Even if zuranolone is approved, we may not achieve market acceptance or use of zuranolone in the MDD and PPD patient types we expect and we may not achieve reimbursement of zuranolone at the levels or with the type of access we expect. The benefit and safety profile of zuranolone in clinical practice, if approved, may not meet our expectations. We may not be successful in execution of our planned commercialization activities, including market access activities, or we may change our plans. We may never be successful or achieve our goals with respect to commercialization of zuranolone, if approved.
  - Even if zuranolone or 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 change our plans. Our revenues may be lower than we expect, including if we do not receive approval of our NDA for zuranolone in MDD and PPD or if our launch of zuranolone, if approved, is not as successful as we expect. 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 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.
  - 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.

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Sage Therapeutics call participants

Barry Greene

Chief Executive Officer

Jim Doherty

Chief Development Officer

Chris Benecchi

Chief Business Officer

Kimi Iguchi

Chief Financial Officer

Laura Gault

Chief Medical Officer

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Seeing the brain differently *makes a world of difference*

Sage Therapeutics®

Building a business for the future

Deep Expertise in brain circuitry

Rich Innovative pipeline

- First and only product approved specifically for postpartum depression
- 3 late-stage programs
- 6 NCE development programs across 11+ potential indications
- Strong intellectual property strategy

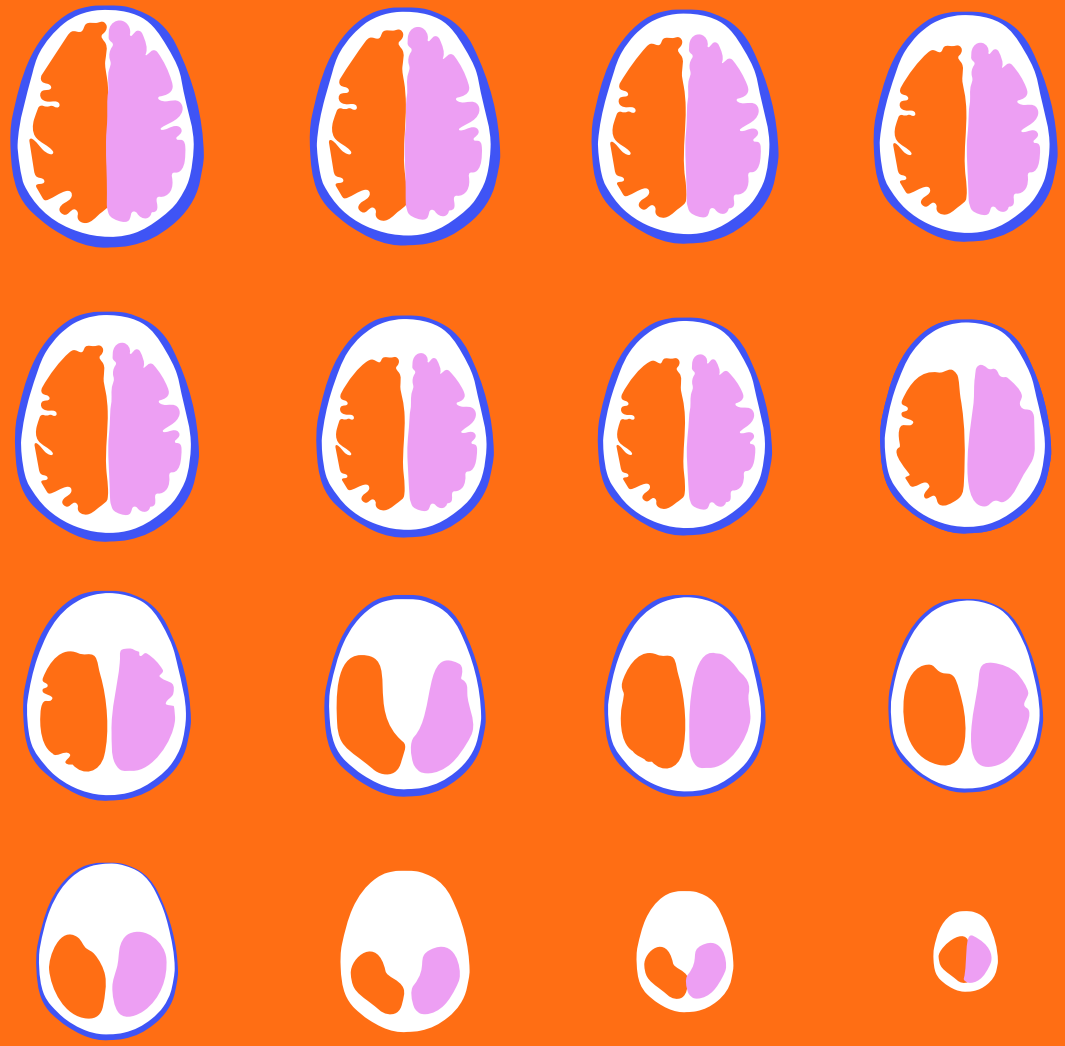
Significant potential patient impact

- Potential to impact an estimated >450M patients globally

Strong cash position to fuel growth

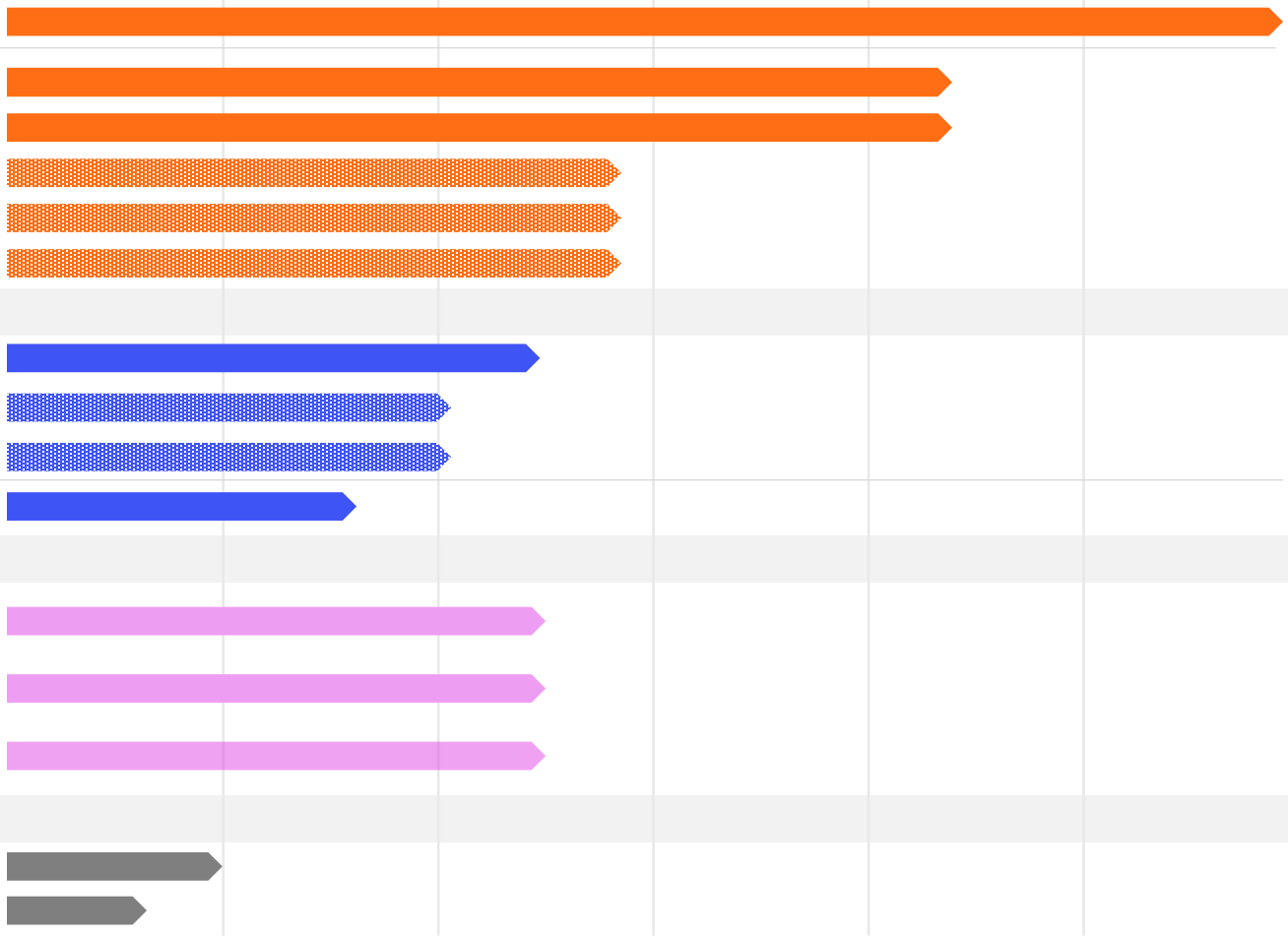
- $1.3B capital (as of 12/31/22) and collaborations to fund efforts to accelerate and advance medicines

Exciting business momentum into 2023



Sage has a leading brain health portfolio

COMPOUND	PARTNER	INDICATIONS
DEPRESSION		
ZULRESSO® (brexanolone) CIV injection		Postpartum Depression
Zuranolone (SAGE-217)	Biogen, SHIONOGI	Major Depressive Disorder
		Postpartum Depression
		Treatment Resistant Depression
		Generalized Anxiety Disorder
		Bipolar Depression
NEUROLOGY		
SAGE-324	Biogen	Essential Tremor
		Epileptiform Disorders
		Parkinson's Disease
SAGE-689		Acute GABA Hypofunction
NEUROPSYCHIATRY		
SAGE-718		Huntington's Disease Cognitive Dysfunction
		Parkinson's Disease Cognitive Dysfunction
		Alzheimer's Disease Mild Cognitive Impairment and Mild Dementia
EARLY DEVELOPMENT		
SAGE-319		GABA Hypofunction
SAGE-421		NMDA Hypofunction



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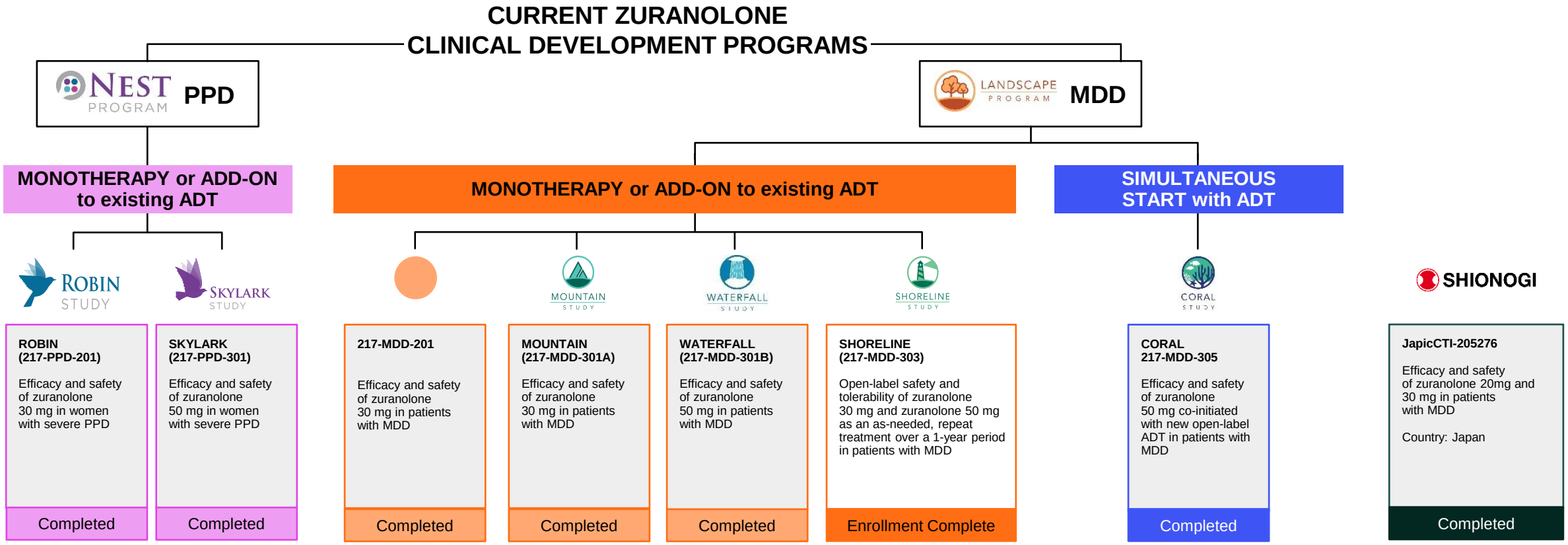
Light shades indicate trials in the planning or evaluation stage

Zuranolone clinical development programs

Potential to reshape the depression landscape



Abbreviations: PPD = postpartum depression, MDD = major depressive disorder, ADT = antidepressant therapy

Sage Therapeutics Biogen SHIONOGI

Zuranolone clinical data supports its potential to fulfill unmet needs for people with MDD and PPD

Rapid & Sustained

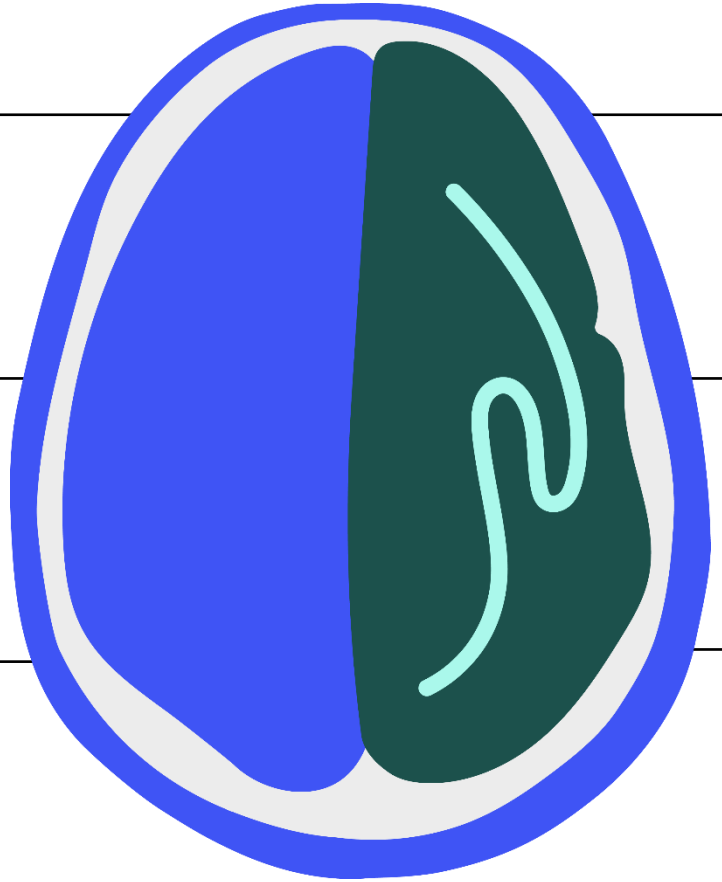
- Rapid symptom reduction observed
- Sustained effects lasted beyond completion of treatment

Well-Tolerated

- Well-tolerated profile*
- Differentiated side effect profile with no evidence of increased sexual dysfunction or weight gain

Improved Feel/Functioning

- Improvements seen across domains of quality of life
- Measured benefits that patients are looking for from depression treatment



Short Course

- As-needed oral therapy
- 2-week treatment course

Novel MOA

- Selectively modulates $GABA_AR$
- May help neuronal networks rebalance[1]

Flexible Approach

- Improvement seen in depressive symptoms in MDD/PPD patients when used as mono or adjunctive therapy
- Improvements seen in MDD/PPD patients with or without elevated anxiety

*Zuranolone was generally well-tolerated across clinical studies. The most common adverse events associated with zuranolone included headache, somnolence, dizziness and sedation.

Profile based on data demonstrated in clinical studies with zuranolone to date

Note: Success of zuranolone and the product profile depend on the clinical development program and regulatory approval.

[1]Antonoudiou, P. et al. Allopregnanolone mediates affective switching through modulation of oscillatory states in the basolateral amygdala. *Biological Psychiatry*, 2021.2003.2008.434156, doi:10.1016/j.biopsych.2021.07.017 (2021).

MDD = major depressive disorder, PPD = postpartum depression

Zuranolone is being developed in collaboration with Biogen.

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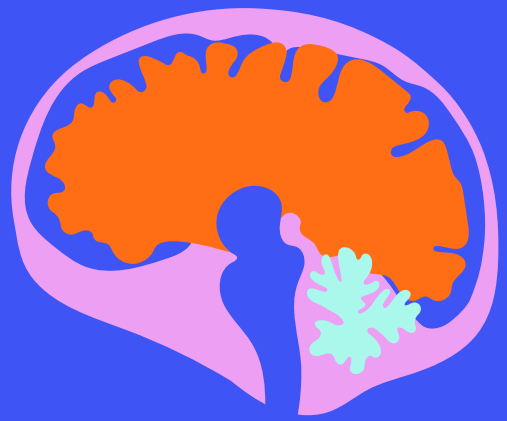
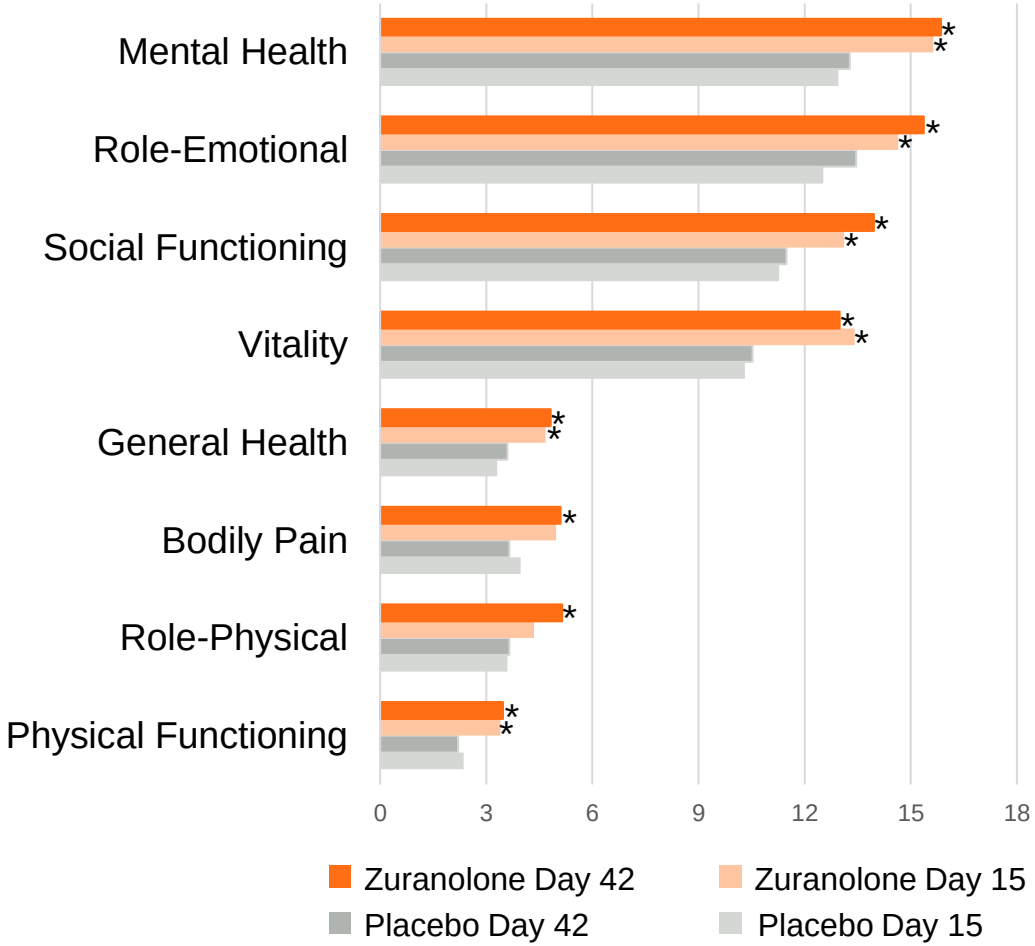
In an integrated analysis of zuranolone data, patients reported overall improvement in functioning and well-being†

Clinically meaningful improvements were observed *across mental health, physical and general health domains of SF-36*





*LSM treatment difference p-value <0.05 (nominal); †Integrated analyses combine doses from the ROBIN Study, MDD-201B Study, MOUNTAIN Study (≥24 HAMD-17 subgroup), and WATERFALL Study. ‡For the ROBIN study, data were collected at Day 45.; SF-36 = 36-Item Short Form Health Survey (version 2).

Zuranolone is being developed in collaboration with Biogen.

Selected responder interviews from SHORELINE Study in MDD

Examples of quotes from surveyed patients who responded to initial treatment cycle of 50 mg zuranolone in the open-label SHORELINE Study (n=32)

"It was really impressive that the results happened so quickly, and it was so dramatic. It wasn't just a slight improvement, it was night and day. **It was a 180 degree turn from how I'd been feeling even just the day before**."

Rapid Onset

A substantial majority of interviewed patients noticed improvements within the first week

"...almost like an afterglow of the two week course of treatment, that then it was just working for several months. **I didn't have to think about it constantly. I didn't have to take medication...I wasn't having to think about my depression and try to manage it."**

Durability

Most interviewed patients reported being satisfied with duration of improvements

"I felt better both times… I started feeling better right away…and I wasn't as bad when I took it the second time as I had been before the study."

Retreatment

A significant majority of interviewed patients who received retreatment reported feeling fine, positive, or neutral about needing to be retreated

"Very satisfied because it's helping me. I feel better about myself now than I did when I first started. I know it's good…I'm doing more than I used to. I'm getting up. I'm going to church. Before, I wouldn't be anywhere, I wouldn't go outside, I would just look outside the door. It has helped me."

Satisfaction

All interviewed patients reported being moderately, quite, or very satisfied with zuranolone

Among patients treated in the ongoing open-label Phase 3 SHORELINE Study, the most common TEAEs (>5%) observed in the 30 and 50 mg cohorts were headache, somnolence, dizziness, and sedation.
Patient experiences are provided solely to help illustrate the data collected from the SHORELINE Study interviews. Patient experiences in the SHORELINE Study differed patient-to-patient. Results of the survey are not intended to make claims about zuranolone's potential benefit. Survey information does not represent all patients who took zuranolone.
Interviews conducted with patients who responded to the first 50 mg zuranolone treatment cycle and had been participants in the SHORELINE Study for at least six months. Interviews were conducted at various timepoints for each patient. Based on SHORELINE Study design, patients were allowed to be on background therapy. Sample size of interviewed patients n = 32.
MDD = major depressive disorder
Zuranolone is being developed in collaboration with Biogen.

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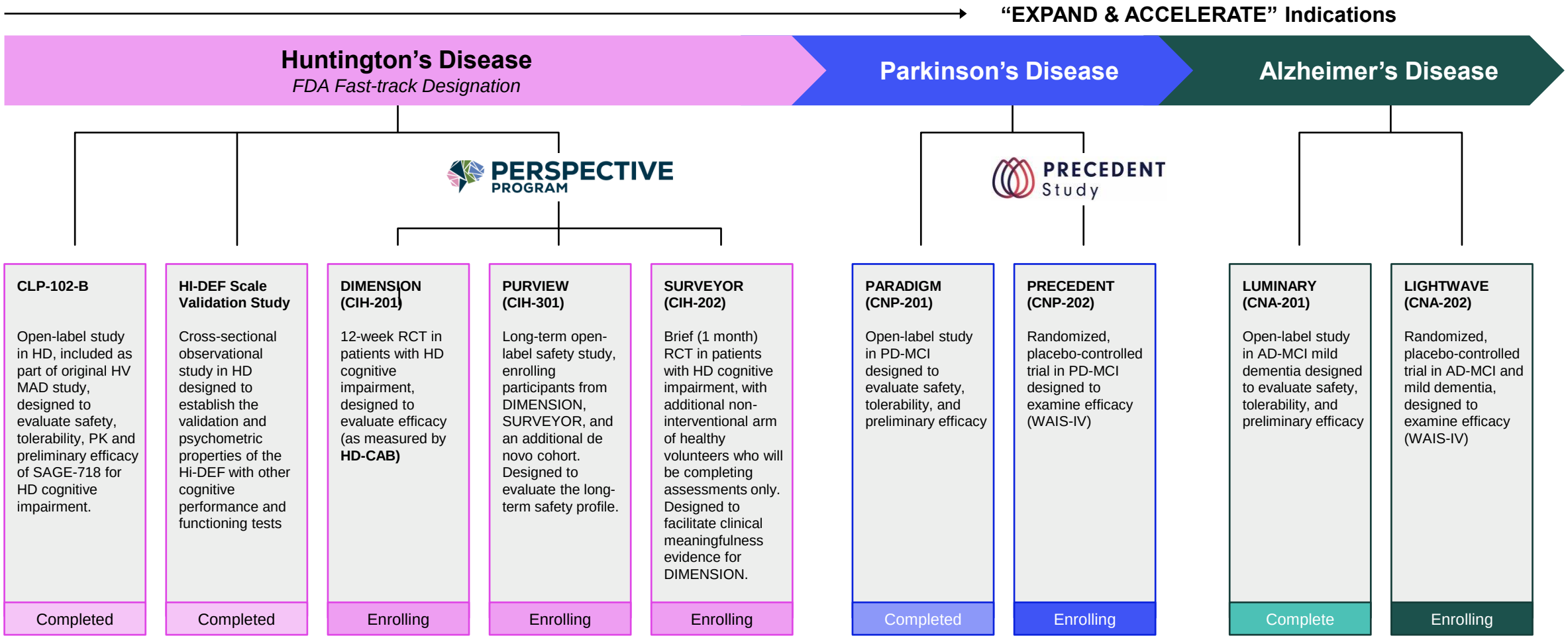
The SAGE-718 clinical development programs

Potential to reshape the treatment of patients with cognitive decline



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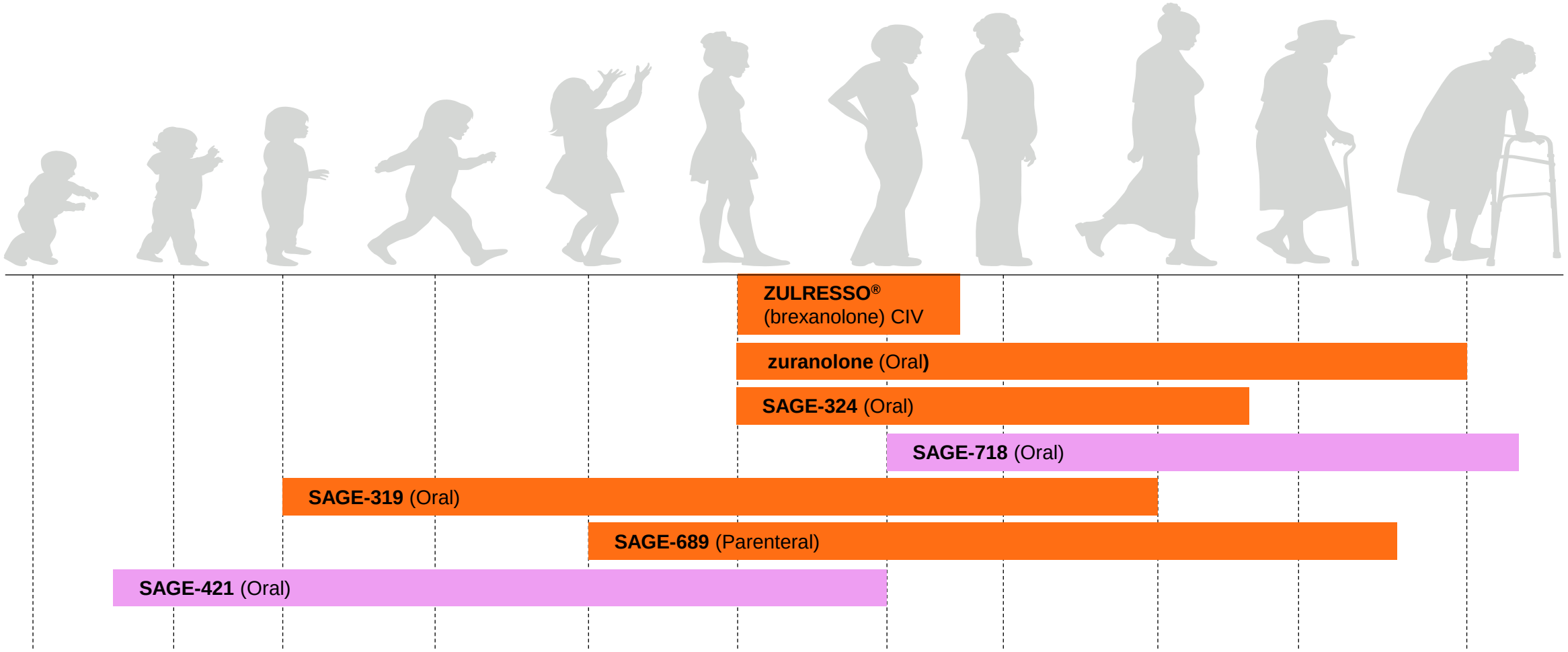
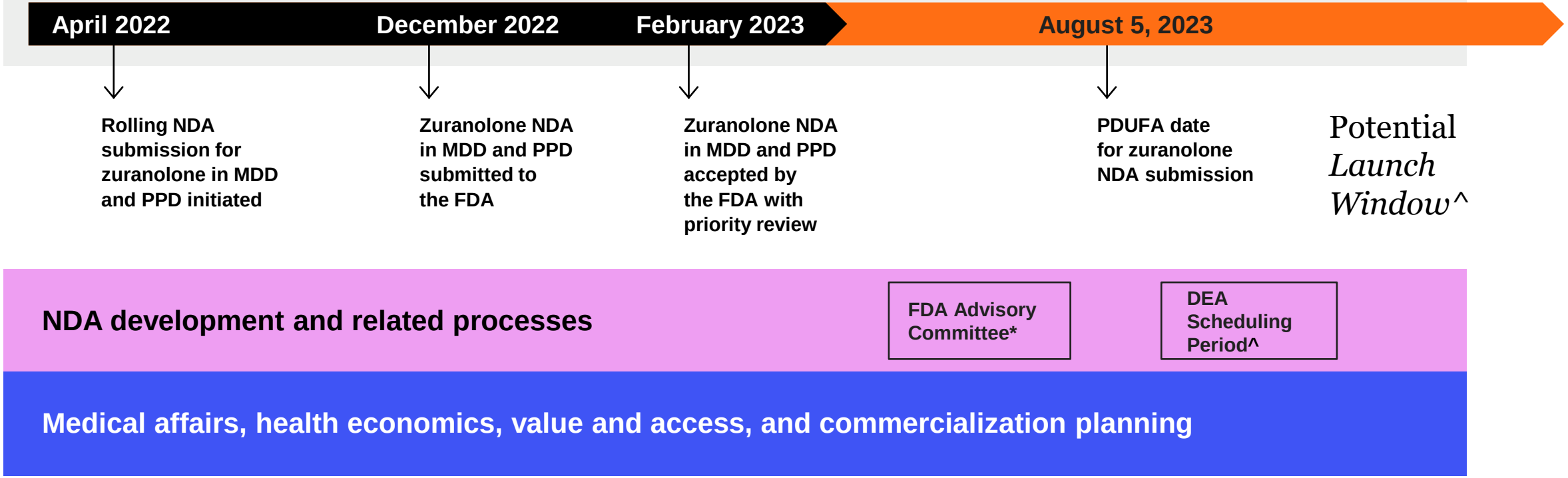
Sage's robust portfolio features NCEs with differentiated target profiles that may be suited for study across the lifespan



NDA for zuranolone accepted, with multiple key milestones expected over next 18 months

Planned activities and anticipated timelines



*Potential timing. Advisory committee not confirmed; it is an FDA decision whether to hold an advisory committee

^Potential launch window and DEA scheduling period assume no review extensions

FDA = U.S. Food and Drug Administration; DEA = Drug Enforcement Administration; MDD = major depressive disorder; PPD = postpartum depression; NDA = new drug application

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The MDD landscape presents significant opportunity for a new therapy to help patients who are not satisfied with current treatment

MDD Patient Opportunity

Adults with a Major Depressive Episode **~21 M[1]**

▼ 66%

Diagnosed & Treated MDD Patients **~14 M[1]**

▼ 75%

Rx-Treated MDD Patients **~10.5 M[1]**

▼ 62%

MDD Patients Making a Treatment Change **~6.5 M[2]**

Planned launch focus on subset of these patients

Figure not to scale. All patient numbers are estimates based on data we have obtained from published literature which references market research, claims research or other sources in some cases applying our own assumptions and analyses. As is generally the case with prevalence/population calculations, there are other data, studies or analyses that reach different conclusions as to estimates or ranges. If the data and assumptions we use turn out to have been inaccurate, the actual number of patients in each segment may differ from our estimates.

1. SAMHSA: 2020 NSDUH Detailed Tables 2. Zhu L, et al. J Manag Care Spec Pharm. 2022 Nov.

There is a clear unmet need for patients experiencing PPD symptoms

Despite being a common mental health disorder,
Postpartum Depression (PPD) *may often go undiagnosed or untreated*

In the US, about **1 in 8** mothers experiences symptoms of PPD [1]

This equates to **~477K** women with a live birth experiencing PPD symptoms [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]

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.

Zuranolone has the potential to address a range of treatment needs in MDD and PPD, if approved

MDD CORE LAUNCH FOCUS

Current or Prior ADT Treatment^	Treatment Naïve	Treatment Resistant*

Zuranolone MDD: First Add or First Switch

MDD Patient With:
- Unresolved symptoms of depression
- Elevated anxiety
- Adherence or tolerability issues

Estimated Patient Burden:
- $4.7k household income lost per year[2]
- 53% reduction in quality of life for patients with severe MDD[3]
- 2.7x more likely for children to develop MDD[4]

PPD CORE LAUNCH FOCUS

Current or Prior ADT Treatment	Treatment Naïve	Treatment Resistant*

Zuranolone PPD: First Line Therapy

PPD Patients Who Often Experience:
- Unresolved symptoms of depression
- Difficulty bonding with baby
- Anxiety
- Sleep disturbances

Estimated Patient Burden:
- Delayed or impaired long-term developmental, psychological, cognitive, and physical outcomes in children[6-16]
- $31.8k average cost per child and mother affected[5]
- 24% to 50% of partners experience depression when mom has PPD[1]

^While physicians may prescribe across a wider MDD treatment range (e.g., treatment naïve, breakthrough episode, etc.), our launch focus will be on these specific MDD patient types. *MDD patients with treatment resistant depression were not included in zuranolone clinical trials and are outside the scope of planned marketing/promotional efforts.

1. Goodman JH. J Adv Nurs. 2004;45(1):26-35. 2. Population estimates were computed from the Vintage 2020 Monthly Postcensal Civilian Population census data. Source: United States Census Bureau. (2020). Monthly Postcensal Civilian Noninstitutionalized Population, July 2019 and July 2020. Retrieved January 18, 2022, from https://www.census.gov/programs-surveys/popest/technical-documentation/research/evaluation-estimates/2020-evaluation-estimates/2010s-national-detail.html. 3. Gao, K., Su, M., Sweet, J., & Calabrese, J. R. (2019). Correlation between depression/anxiety symptom severity and quality of life in patients with major depressive disorder or bipolar disorder. Journal of Affective Disorders, 244, 9–15. https://doi.org/10.1016/j.jad.2018.09.063 4. Aazh, Danesh, A. A., & Moore, B. C. J. (2019). Parental Mental Health in Childhood as a Risk Factor for Anxiety and Depression among People Seeking Help for Tinnitus and Hyperacusis. Journal of the American Academy of Audiology, 30(9), 772–780. https://doi.org/10.3766/jaaa.18001. 5. Luca DL, et al. Am J Public Health. 2020;110(6):888-896. 6. Eastwood JG et al. BMC Pregnancy Childbirth. 2012;12:148. 7. Yamaoka Y et al. Matern Child Health J. 2016;20(2):326-336. 8. Kerstis B et al. Arch Womens Ment Health. 2016;19(1):87-94. 9. Valla L et al. Infant Behav Dev. 2016;45(Pt A):83-90. 10. Koutra K et al. Soc Psychiatry Psychiatr Epidemiol. 2013;48(8):1335-1345. 11. Woolhouse H et al. Arch Womens Ment Health. 2016;19(1):141-151. 12. Netsi E et al. JAMA Psychiatry. 2018;75(3):247-253. 13. Hanington L et al. Child Care Health Dev. 2012;38(4):520-529. 14. Surkan PJ et al. BMC Pediatr 2014;14:185. 15. Verkuijl NE et al. Lancet Psychiatry. 2014;1(6):454-460. 16. Pearson RM et al. JAMA Psychiatry. 2013;70(12):1312-1319.

Fourth quarter and full year 2022 and 2021 financial results

Strong financial position with $1.3B in cash at the end of 2022

Item	Q4 ‘22	Q4 ’21	Full Year ‘22	Full Year ‘21
Revenue	*$2.9M*	*$1.6M*	*$7.7M*	*$6.3M*
R&D Expense	$89.3M	$75.4M	$326.2M	$283.2M
SG&A Expense	$67.3M	$51.6M	$227.7M	$183.5M
Cost of Goods Sold	$0.1M	$0.1M	$0.8M	$0.6M
Total Operating Costs and Expenses	$156.8M	$127.1M	$554.7M	$467.2M
Net Income (Loss)	($147.1M)	($124.7M)	($532.8M)	($457.9M)
Cash, Cash Equivalents and Marketable Securities	$1.3B	$1.7B	$1.3B	$1.7B

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Anticipated 2023 milestones

**Early:Q1-Q2; Mid:Q2-Q3; Late: Q3-Q4*

	Early	Mid	Late	
DEPRESSION				
Zuranolone (SAGE-217)	✓			FDA acceptance of rolling NDA submission for zuranolone in MDD and PPD
		●		Present additional data from SHORELINE Study
			●	PDUFA date for zuranolone in MDD and PPD (August 5th)
			●	Commercial availability of zuranolone in MDD and PPD, if zuranolone is approved with no review extensions
			●	Initiate a lifecycle innovation study with zuranolone
	●	●	●	Present additional analyses of data from LANDSCAPE and NEST clinical programs, including health economics and patient reported outcomes
NEUROLOGY				
SAGE-324			●	Complete enrollment in Phase 2b KINETIC 2 Study
	●	●	●	Present additional analyses of data from clinical development program as well as disease state and burden of disease research in ET
NEUROPSYCHIATRY				
SAGE-718	●	●	●	Progress recruitment in the ongoing DIMENSION, SURVEYOR, PURVIEW, PRECEDENT, and LIGHTWAVE Studies
	●	●	●	Present additional analyses of data from clinical development program as well as disease state and burden of disease research in HD, PD and AD
ADDITIONAL CLINICAL PROGRAMS & MILESTONES				
Additional Pipeline Programs			●	Provide update on next steps for pipeline programs (e.g., SAGE-319)
Cash Balance	●	●	●	Maintain strong balance sheet

MDD = major depressive disorder, PPD = postpartum depression, ET = essential tremor, HD = Huntington's disease, PD = Parkinson's disease, AD = Alzheimer's disease

Q&A

Sage Therapeutics