Sage Therapeutics®

First Quarter 2023 Financial Results

May 2, 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

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Chief Business Officer

Kimi Iguchi

Chief Financial Officer

Laura Gault

Chief Medical Officer

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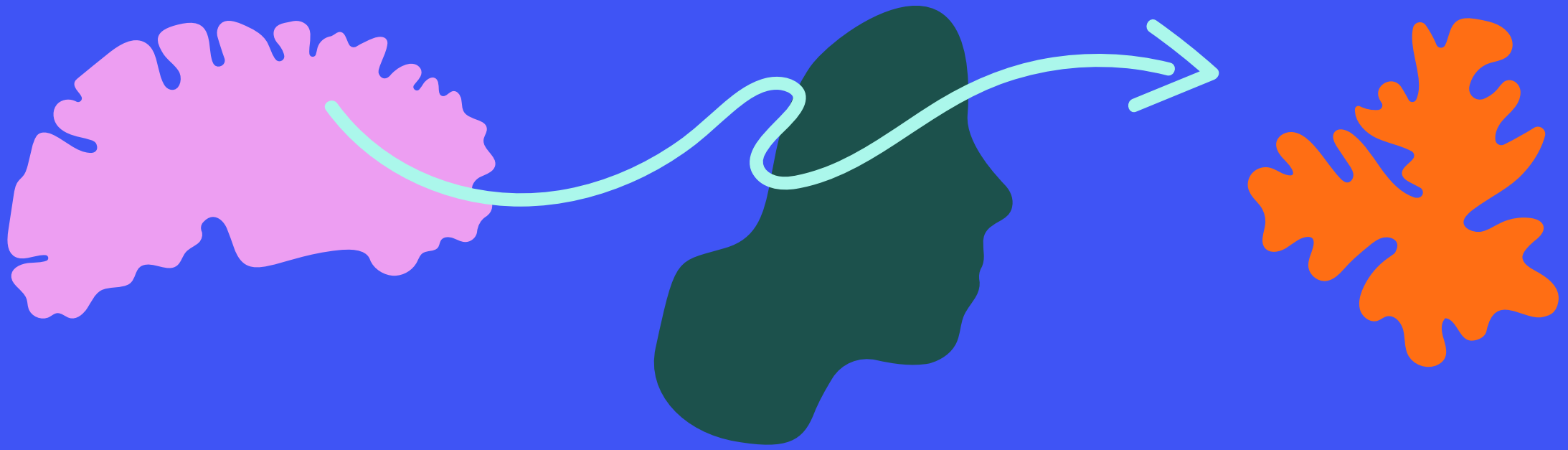
Building impact and scale



Millions of people have been waiting **decades for new treatment options**

Patients, providers, and society can and **must be better served**

Relentless focus on developing **new and effective treatments to address brain health disorders**

The time is now…

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

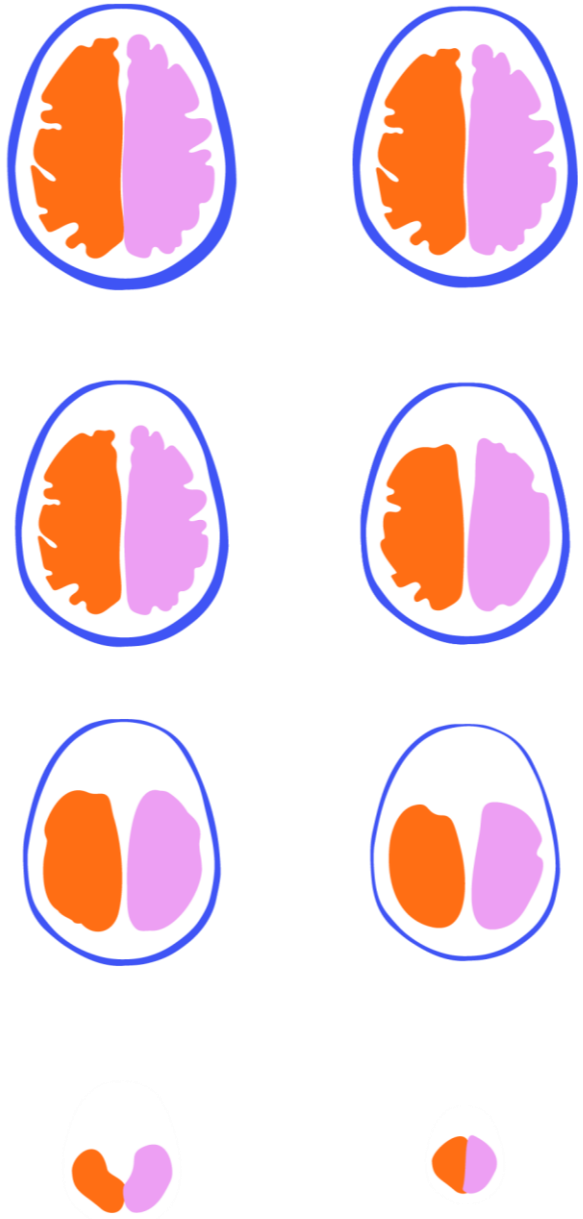
Significant potential patient impact

- Potential to impact an estimated >450M patients globally

Strong cash position to fuel growth

- $1.1B (as of 3/31/23) and collaborations to fund efforts to accelerate and advance medicines

Exciting business momentum into 2023



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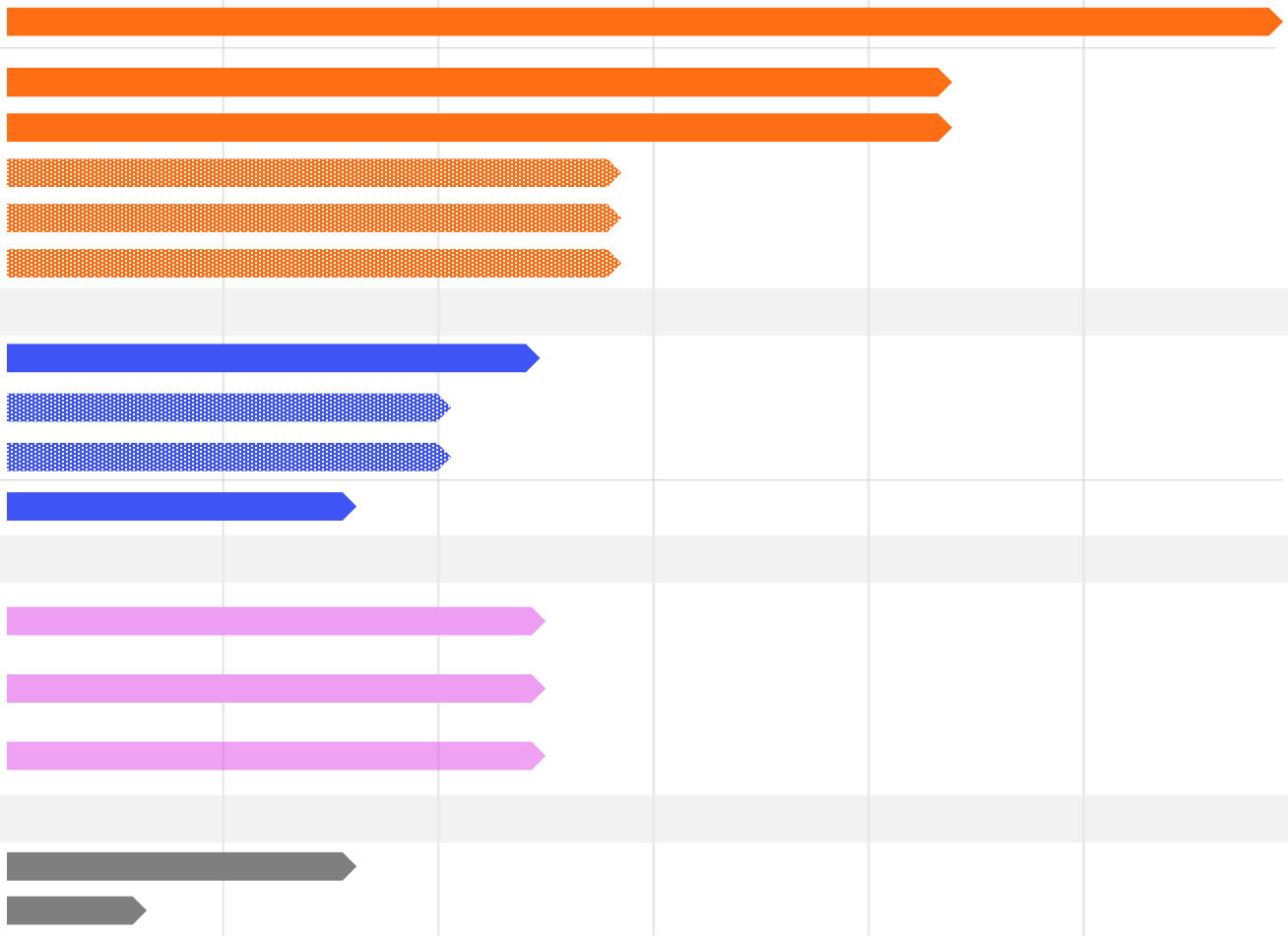
Sage has a leading brain health portfolio

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

Rapid & Sustained

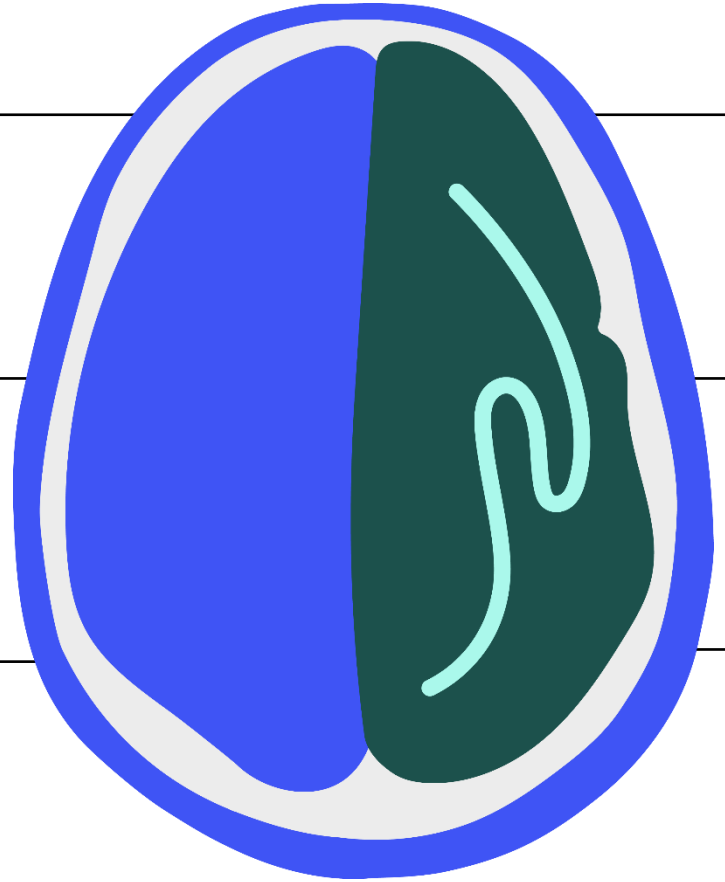
- Rapid symptom reduction observed
- Sustained effects lasted beyond completion of treatment

Well-Tolerated

- Well-tolerated profile*
- Differentiated side effect profile with no evidence of 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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Data presented at AMCP reinforce the significant burden associated with MDD

In the WATERFALL Study, faster reductions in HAMD-17 scores lead to improvements in HRQoL

- Study analyzed health state values (utility scores) reported by patients in the WATERFALL study
- Scores at baseline further highlight the poor HRQoL that exists amongst people living with moderate or severe MDD
- Rapid HAMD-17 response or remission was associated with a substantial and clinically meaningful gain in utility scores highlighting patient preference for rapid response or remission

Total healthcare costs were high following treatment with a standard of care ADT

- Analysis aimed to evaluate the total healthcare costs among employed adults with MDD who were treated with ADTs
- A high-cost burden in both all-cause and MDD-related costs was consistently observed during the 90-day period following treatment across 3 consecutive years driven by outpatient costs and comorbidity burden

MDD creates burden for all adults in a household, even those without MDD themselves

- Assessed the impact of adults with MDD on other adults without MDD in the same household
- Adults without MDD living with another adult who has MDD experienced an excess burden related to reduced yearly income and employment, more workdays missed per year, lower quality of life and increased mental health visits.

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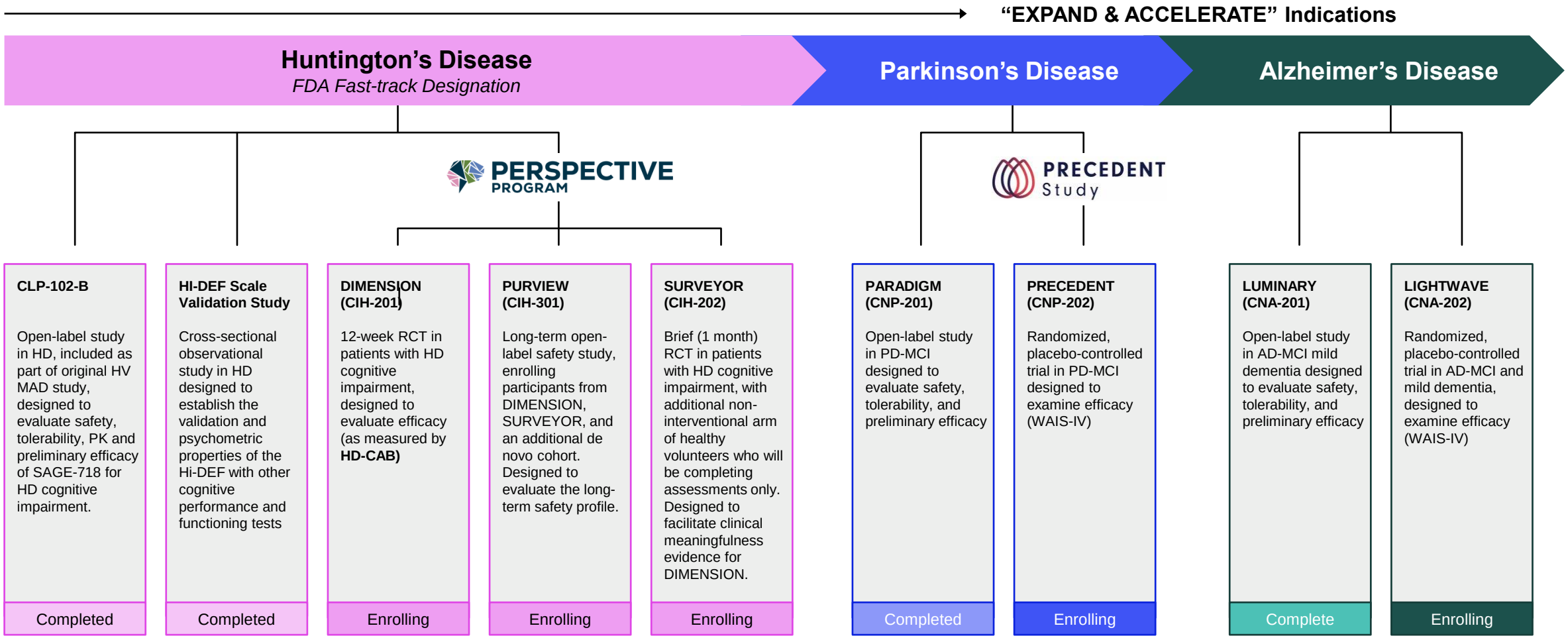
HRQoL = health-related quality of life; ADT = antidepressant therapy; AMCP = Academy of Managed Care Pharmacy Annual Meeting

1. Estimating SF-6D Utility Values for Health States in Major Depressive Disorder. Presented at AMCP Annual Meeting 2023. 2. Total Cost of Care During a 90-Day Period Post Antidepressant Treatment Initiation Following a Recent Insurance Coverage Gap Among US Employees with Major Depressive Disorder. Presented at AMCP Annual Meeting 2023. 3. Impact of Living with an Adult with Major Depressive Disorder Among Households in the United States. Presented at AMCP Annual Meeting 2023.

The SAGE-718 clinical development programs

Potential to reshape the treatment of patients with cognitive decline



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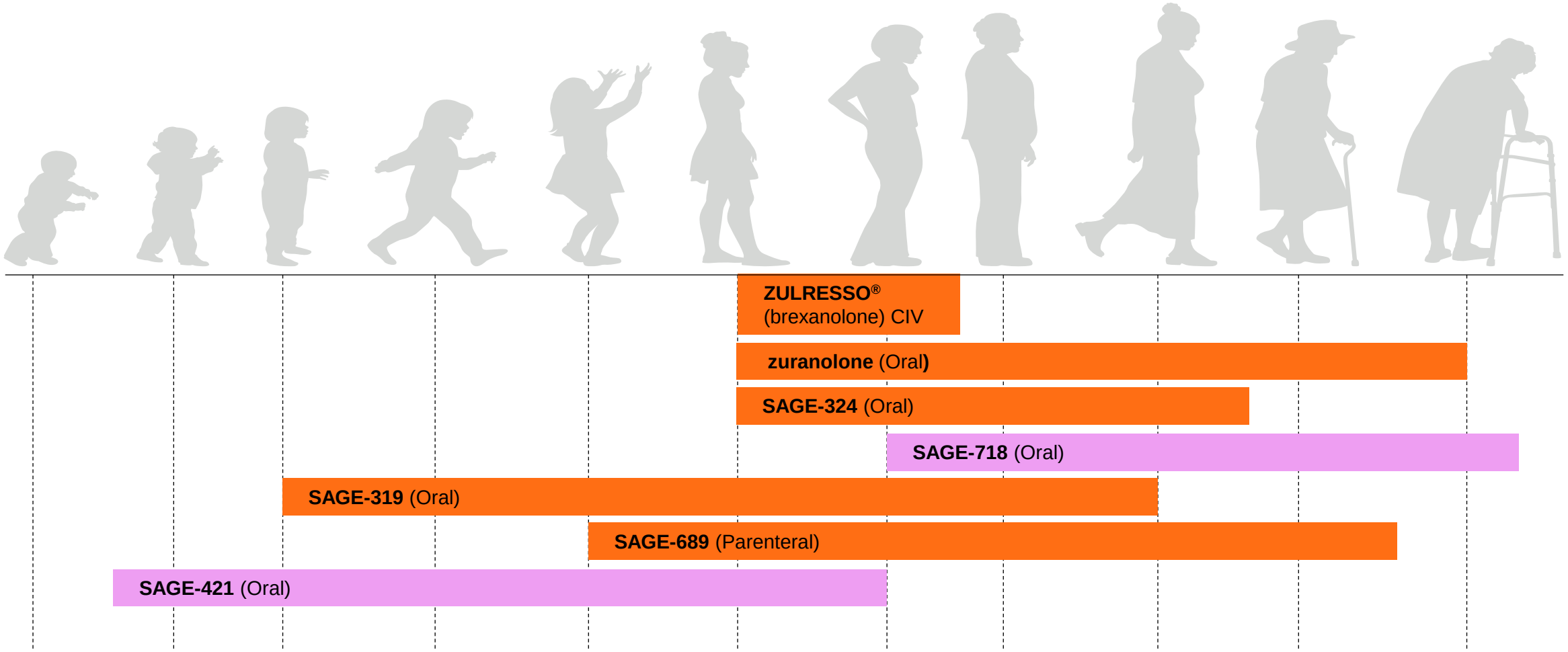
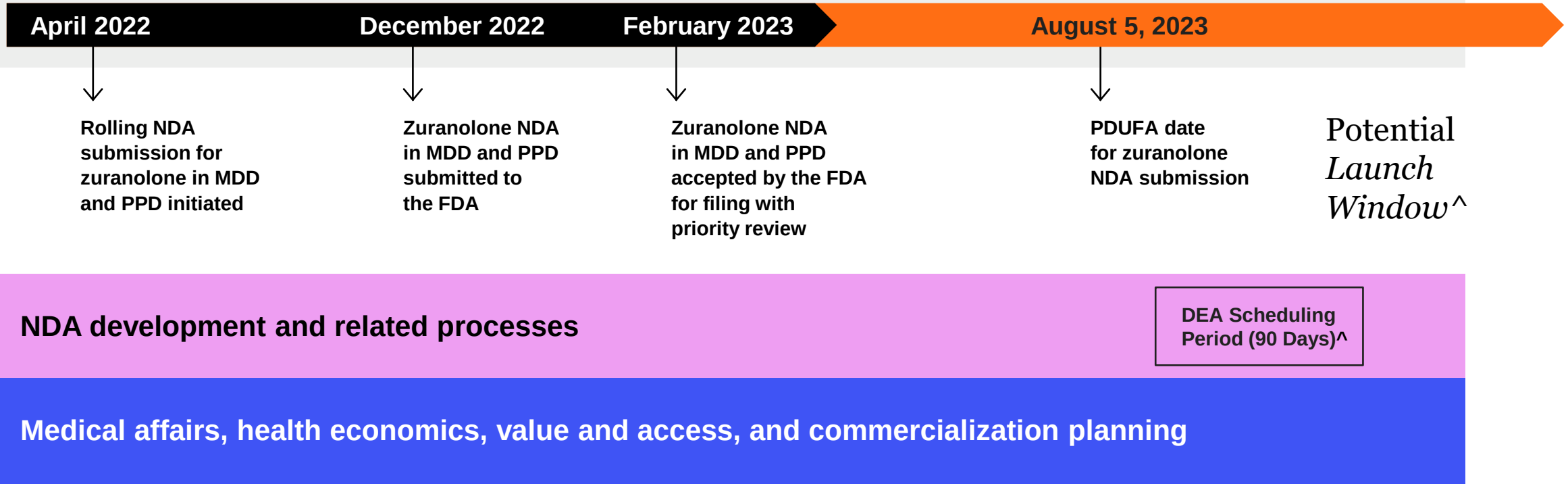
Sage's robust portfolio features NCEs with differentiated target profiles that may be suited for study across the lifespan



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

Planned activities and anticipated timelines



FDA indicated that it does not currently plan to hold an advisory committee for zuranolone

^Potential launch window and DEA scheduling period assumes approval and 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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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: Start, 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 a mother 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. *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.

Planned launch approach designed to educate and engage stakeholders

Stakeholder Needs		Strategic Imperatives
Patients	Rapid, durable therapy without stigmatizing side effects often associated with chronic treatments (e.g., sexual dysfunction/weight gain)	**Inspire** people with MDD and PPD to talk to their HCP about zuranolone
HCPs	Rapid, durable, well-tolerated therapy for a range of patients with MDD and PPD with limited access hurdles	**Mobilize** targeted HCPs to identify and treat appropriate patient types in MDD and PPD early in the course of treatment
Payors	Achieve budget predictability and cost containment for new MDD and PPD therapies	**Align** with payers to increase budget predictability through innovative proactive Value Based Agreements with the goal of enabling those with MDD and PPD to access zuranolone quickly and affordably
Patient Advocacy and **Policy Makers**	Education to advocate for and advance the standard of care for those who need more from MDD and PPD treatment	**Raise** treatment expectations in MDD and PPD through grassroots efforts, leveraging policy interventions that have been proven effective in addressing access to treatment

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Zuranolone is being developed in collaboration with Biogen.

First Quarter 2023 Financial Results

Strong financial position with $1.1B in cash

Item	Q1 ‘23	Q1 ’22
Revenue	*$3.3M*	*$1.6M*
R&D Expense	$92.8M	$78.0M
SG&A Expense	$65.7M	$46.5M
Cost of Goods Sold	$0.2M	$0.3M
Total Operating Costs and Expenses	$158.8M	$124.8M
Net Loss	($146.8M)	($122.1M)
Cash and Marketable Securities	$1.1B	$1.6B

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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

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