



Third Quarter 2023 Financial Results

November 7, 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: plans and goals for commercialization of ZURZUVAE as a treatment for women with PPD and expected timelines; our belief in the potential benefit and profile of ZURZUVAE in the treatment of PPD; our plans, goals, and expectations regarding access to ZURZUVAE for women with PPD and reimbursement; 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 to 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:
 - We may not be successful in our planned 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 may be significantly smaller than we expect; we may encounter reimbursement or market access related issues in the course of our commercialization activities; ZURZUVAE may not achieve the clinical benefit in the treatment of women with PPD that we expect; we may not generate revenue from sale of ZURZUVAE at the levels or on the timing we expect.
 - 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.
 - At any stage, regulatory authorities may ask for additional clinical trials, nonclinical studies or other data in order for us to proceed further in development or to file for or obtain regulatory approval. Other decisions or actions of the FDA or other regulatory authorities may affect the initiation, timing, design, size, progress and cost of clinical trials or development efforts and our ability to proceed with further development.
 - Even if our other product candidates are successfully developed and approved, the number of patients with the diseases or disorders our products treat or the subset of such patients we believe will use our products, the need for new treatment options, and the actual market for such products may be smaller than our current estimates.
 - The anticipated benefits of our collaborations, including our collaboration with Biogen, may never be achieved. The need to align with our collaborators may hamper or delay our development and commercialization efforts or increase our costs; our business may be adversely affected and our costs may increase if any of our key collaborators fails to perform its obligations or terminates our collaboration.
 - We may not be able to obtain and maintain adequate intellectual property protection or other forms of data and marketing exclusivity for our products, or to defend our patent portfolio against challenges from third parties.
 - We may face competition from others developing products or with approved products for similar uses as those for which our product candidates are being developed.
 - Our operating expenses may be higher than forecasted and we may face unexpected expenses which could cause us to change our plans. 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 goal in this indication, or if our launch for other reasons 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.

Sage Therapeutics call participants



Barry Greene
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Laura Gault
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Kimi Iguchi
Chief Financial Officer



Mike Quirk
Chief Scientific Officer



OUR VISION

To fearlessly lead the way
to create a world with
better brain health




ZURZUVAE™
(zuranolone) capsules **Ⓢ**
20 mg • 25 mg • 30 mg

Is Now Approved

for the treatment of postpartum depression in adults. A full course of ZURZUVAE includes 14 days of treatment.

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.

COMPOUND	POTENTIAL INDICATIONS	PHASE 1	PHASE 2	PHASE 3	STATUS
Postpartum Depression Franchise					
ZULRESSO® (brexanolone) CIV injection	Postpartum Depression	██████████	██████████	██████████	MARKETED
ZURZUVAE™* (zuranolone)	Postpartum Depression	██████████	██████████	██████████	FDA APPROVED
Neuropsychiatry Pipeline					
Zuranolone* (SAGE-217)	Major Depressive Disorder**	██████████	██████████	IN PHASE 3	
	Huntington's Disease Cognitive Dysfunction	██████████	IN PHASE 2		
SAGE-718	Parkinson's Disease Cognitive Dysfunction	██████████	IN PHASE 2		
	Alzheimer's Disease Mild Cognitive Impairment and Mild Dementia	██████████	IN PHASE 2		
SAGE-324*	Essential Tremor	██████████	IN PHASE 2		
Programs In Evaluation					
SAGE-689 Acute GABA Hypofunction		SAGE-421 NMDA Hypofunction		SAGE-319 GABA Hypofunction	



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

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

Please refer to the [U.S. Prescribing Information for ZULRESSO](#) and the [U.S. Prescribing Information for ZURZUVAE](#)

Safety and efficacy for investigational uses or compounds have not been established. There is no guarantee that the outcome of these studies will be positive or result in approval by a Health Authority.

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



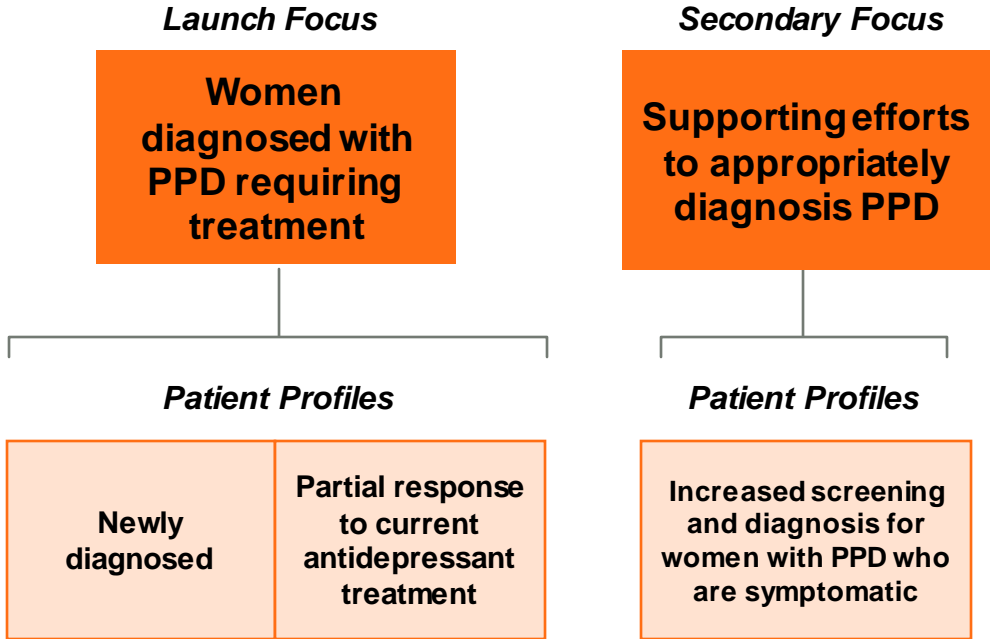
PPD

In the US, an estimated **1 in 8** women experience symptoms of PPD¹

~**477k** women with a live birth experience PPD symptoms annually^{1,2}

~**50%** of PPD cases may go undiagnosed without appropriate screening^{3,4} and less than **25%** of patients screened for PPD receive follow-up care⁵⁻⁷

ZURZUVAE: Potential first-line treatment for women with PPD



Preparing for the successful launch of ZURZUVAE in PPD

Omnichannel Strategy

- ✓ Completed hiring of the Sage field sales teams including seasoned sales professionals with an average of 16 years of experience and established relationships across neuropsychiatry
- ✓ Identified target HCPs who see and treat a high volume of PPD patients
- ✓ Prepared non-personal promotion strategy and "next best actions" to extend customer reach and adoption beyond sales force

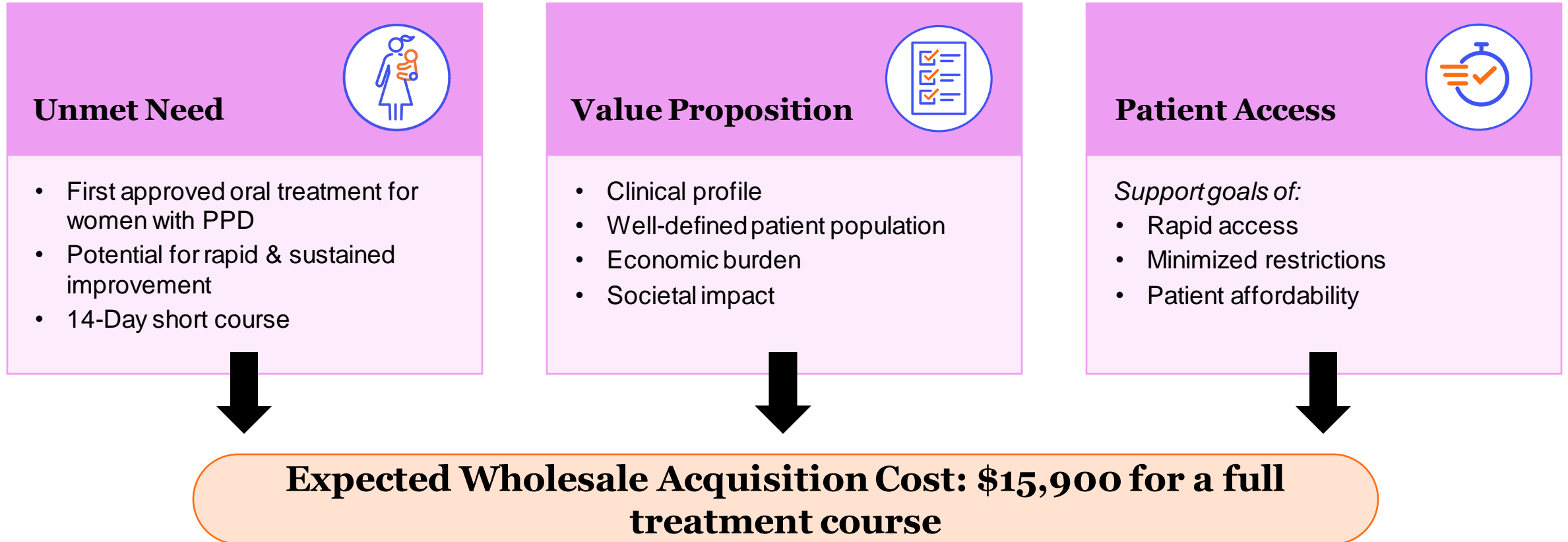
Value & Market Access

- ✓ Discussed ZURZUVAE and PPD with all national payers
- ✓ Completed over 100 engagements with health plan and PBM customers
- ✓ Built a patient support program that provides education and financial support for qualifying patients

Medical Affairs

- ✓ Partnered with key medical societies focused on women's mental health educational initiatives at the local, regional, and national levels
- ✓ Scientific exchange with medical experts to refine our strategy and partner as the field has evolved to prioritize women's mental health

Pricing with cost effectiveness, value and access in mind



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 $\geq 5\%$ and greater than placebo) are somnolence, dizziness, diarrhea, fatigue, nasopharyngitis, and urinary tract infection. See boxed warning and warnings & precautions for additional safety information.

Globally, disorders involving cognitive impairment continue to increase in prevalence

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



~188K

**Huntington's Disease
Global Prevalence¹**

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

~8.8M

**Parkinson's Disease
Global Prevalence²**

Mild cognitive impairment (MCI) is diagnosed in nearly half of people with PD and is associated with poorer treatment outcomes, greater medical costs, and caregiver distress

~134M

**Alzheimer's Disease
Global Prevalence³**

Up to 50% of people with MCI due to AD progress to Alzheimer's dementia within 5-10 years, which may impact a person's ability to remain independent⁴⁻⁷

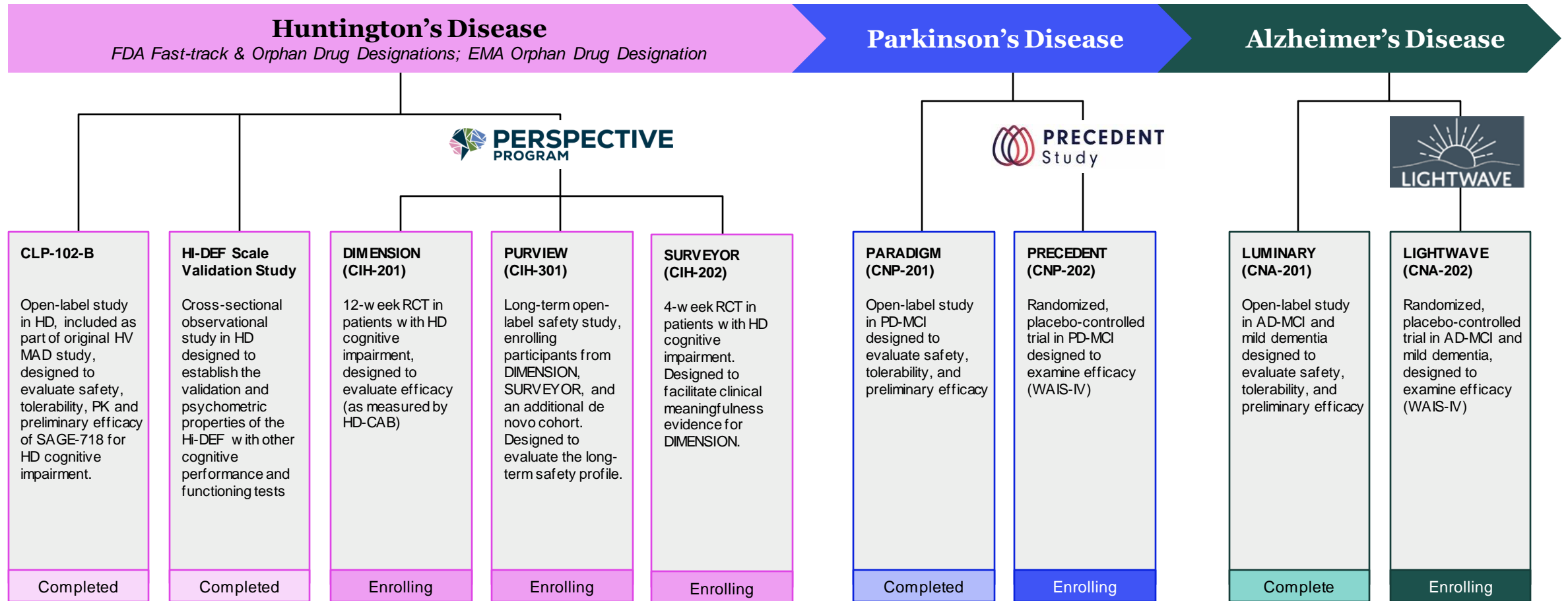
HD = Huntington's disease, PD = Parkinson's disease, AD = Alzheimer's disease

1. Pringsheim T, Wiltshire K, Day L, Dykeman J, Steeves T, Jette N. The incidence and prevalence of Huntington's disease: a systematic review and meta-analysis. *Mov Disord.* 2012 Aug;27(9):1083-91. doi: 10.1002/mds.25075. Epub 2012 Jun 12. PMID: 22692795. 2. Sage Therapeutics, Inc. Data on file. 3. Sage Therapeutics, Inc. Data on file. 4. Beglinger, Leigh J., et al. "Earliest functional declines in Huntington disease." *Psychiatry research* 178.2 (2010): 414-418. 5. Jacobs, Milou, Ellen P. Hart, and Raymond AC Roos. "Cognitive performance and apathy predict unemployment in Huntington's disease mutation carriers." *The Journal of Neuropsychiatry and Clinical Neurosciences* 30.3 (2018): 188-193. 6. Koerts, Janneke, et al. "Working capacity of patients with Parkinson's disease—A systematic review." *Parkinsonism & related disorders* 27 (2016): 9-24. 7. Silvaghi, Fabiola, et al. "Keeping people with dementia or mild cognitive impairment in employment: a literature review on its determinants." *International journal of environmental research and public health* 17.3 (2020): 842.

The SAGE-718 clinical development programs

Potential to reshape the treatment of patients with cognitive decline

“EXPAND & ACCELERATE” Indications



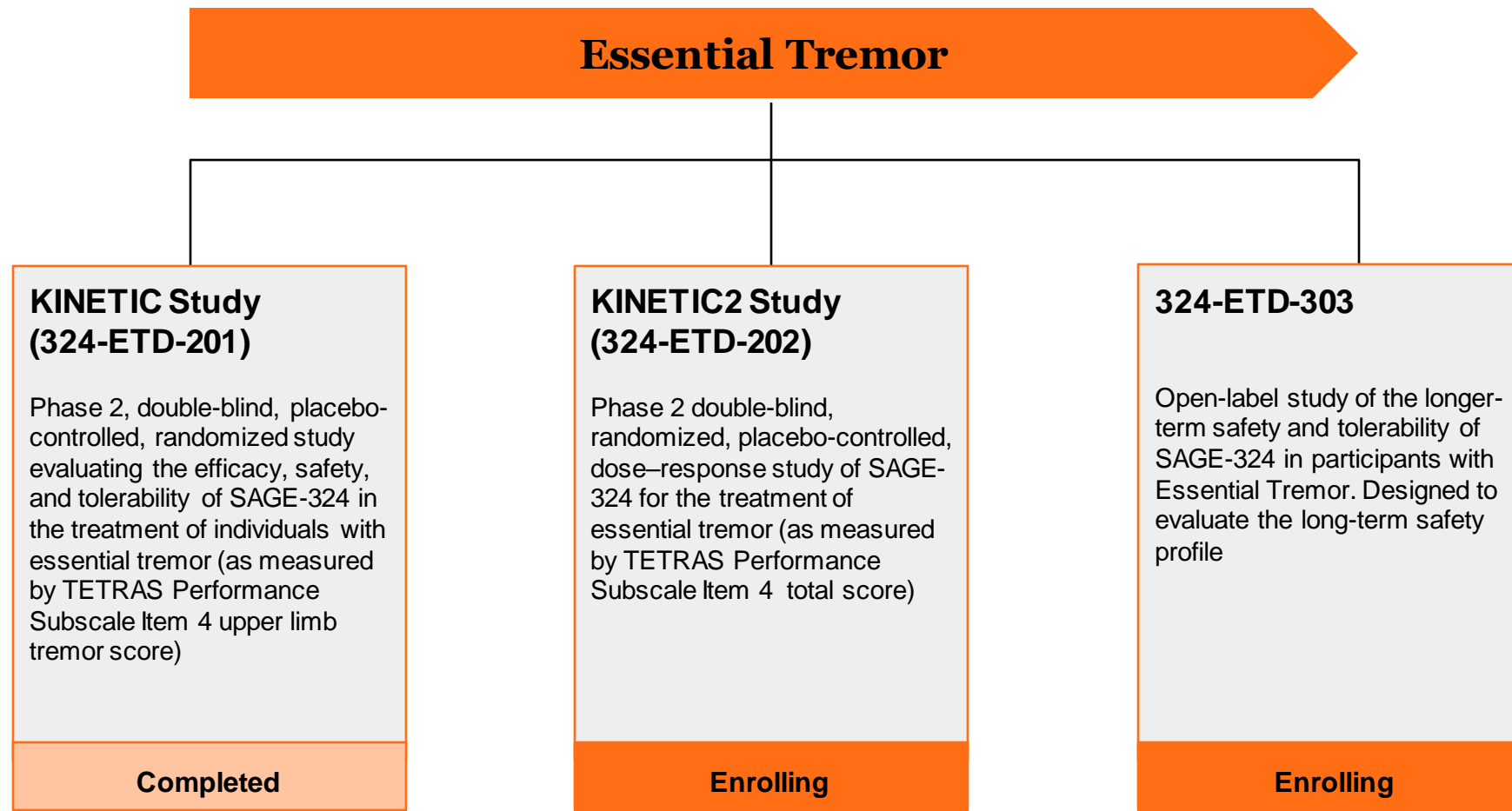
Gaps remain in bringing effective treatments to people with movement disorders

An estimated 6.8M adults in the US have ET¹, approximately 10-15% are diagnosed²

- ET impacts individuals' ability to perform a wide range of activities of daily living (ADL) as well as their social-emotional well-being. In an interview study of ET patients and care partners with ET ranging from mild to very severe³:
 - **100%** had difficulty writing and pouring liquids
 - **≥80%** had difficult drinking, performing grooming and hygiene activities, dressing, eating, and holding reading material
 - **90%** had at least one emotional impact of ET
 - **75%** experienced worry/anxiety related to tremor
 - **70%** reported feelings of stigma
- ADL and social-emotional impacts **were greater** as the severity of ET increased



The SAGE-324 clinical development program



Third Quarter 2023 Financial Results

Item	Q3 '23	Q3 '22
Revenue	\$2.7M	\$1.7M
R&D Expense	\$101.9M	\$81.6M
SG&A Expense	\$78.1M	\$61.5M
Restructuring	\$33.6M	-
Cost of Goods Sold	\$0.9M	\$0.2M
Total Operating Costs and Expenses	\$214.6M	\$143.2M
Net Loss	(\$201.6M)	(\$137.3M)
Cash and Marketable Securities	\$0.9B	\$1.4B

Q&A