Sage Therapeutics®

J.P. Morgan Healthcare Conference

January 2024

Safe Harbor Statement

- The slides presented today and the accompanying oral presentations contain forward-looking statements, which may be identified by the use of words such as “may,” “might,” “will,” “should,” “can,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “opportunity”, “goal”, “mission”, “potential,” “target”, or “continue,” and other similar expressions.
- Forward-looking statements in this presentation include statements regarding: plans, expectations and goals for commercialization of ZURZUVAE as a treatment for women with PPD, including our goal for ZURZUVAE to become first line therapy and standard of care in this indication and our reimbursement/access goals; our belief in the potential benefit and profile of ZURZUVAE in the treatment of PPD; the potential for success of our commercialization of ZURZUVAE for women with PPD; 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 approved products and for our product candidates, if approved; the potential drivers of value in our business; the opportunity, mission, goals and vision for our business; and our expectations with respect to maintaining a strong financial foundation.
- These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risk that:
  - We may not be successful in our commercialization efforts with respect to ZURZUVAE in the treatment of women with PPD; the market size and market acceptance for ZURZUVAE as a treatment for women with PPD may be significantly smaller than we expect; we may encounter reimbursement or market access related issues in the course of our commercialization activities; early positive signs may not be a signal of future success; ZURZUVAE may not achieve the clinical benefit in the treatment of women with PPD that we expect; we may not generate revenue from sales of ZURZUVAE at the levels or on the timing we expect.
  - 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, our planned regulatory pathway, or filing for or obtaining regulatory approval on the timelines we expect or at all and we may be required to conduct additional clinical trials or nonclinical studies which may not be 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, or due to timing and results of consultation with regulatory authorities, and such issues with any trial could cause delay in completion of the trial, availability of results and timing or success of future activities.
  - We may encounter unexpected safety or tolerability issues with respect to any of our product candidates or marketed products; we may encounter different or more severe adverse events at higher doses, different frequency or length of dosing or in new indications.
  - At any stage, regulatory authorities may ask for additional clinical trials, nonclinical studies or other data in order for us to proceed further in development or to file for or obtain regulatory approval. Other decisions or actions of the FDA or other regulatory authorities may affect the initiation, timing, design, size, progress and cost of clinical trials or development efforts and our ability to proceed with further development.
  - 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/reimbursement goals 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 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

OUR VISION: To fearlessly lead the way to create a world with *better brain health*

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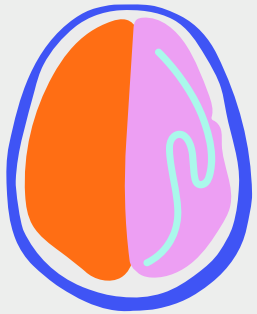
Opportunity to become the leader in brain health

Patient inspired, patient led, *patient first*

ZURZUVAE™
First and only oral product approved by the FDA specifically for postpartum depression *(second approved product)*



Differentiated pipeline driven by patient need, science, and external insights

Scientific and therapeutic leadership within GABA and NMDA opportunities – strong product engine

Strong financial foundation to help create value for sustained growth

Value-driven culture focused on doing what's right for patients

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COMPOUND	TARGET INDICATIONS	PHASE 1	PHASE 2	PHASE 3	STATUS
Postpartum Depression Franchise					
ZURZUVAE™* (zuranolone) CIV	Postpartum Depression				MARKETED
ZULRESSO® (brexanolone) CIV injection	Postpartum Depression				MARKETED
Neuropsychiatry Pipeline					
Zuranolone* (SAGE-217)	Major Depressive Disorder**			IN PHASE 3	
Dalzanemdor (SAGE-718)	Huntington's Disease Cognitive Dysfunction		IN PHASE 2		
	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.

Multiple Expected Catalysts

1. Ongoing commercialization of **ZURZUVAE™** in the treatment of women with postpartum depression

2. Advance **dalzanemdor (SAGE-718)** with 4 topline data readouts expected across HD, PD & AD

3. Advance **SAGE-324** with topline data expected in mid-2024

4. Progress earlier stage **pipeline**

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PPD poses a substantial burden to patients and their families; Significant unmet needs remain and require urgent treatment

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

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

Mothers with perinatal depression often face **significant challenges** with functioning and infant-bonding[5-9]

The **economic burden** associated with perinatal depression is vast and impacts patients, their families, employers, and health care payers[10-12]

The **COVID-19 Pandemic** had a significant effect on perinatal mental health outcomes[13-15]

1. Bauman BL, Ko JY, Cox S, et al. MMWR Morb Mortal Wkly Rep. 2020;69(19):575-581 2. Ukatu N, et al. Psychosomatics. 2018;59(3):211-219. 3. Wang Z, et al. Transl Psychiatry. 2021;11(1):543. 4. Fonseca A, et al. J Affect Disord. 2020;274:167-173. 5. Beck CT, et al. Am J Nurs. 2006;106(5):40-50. 6. Wouk K, et al. Pediatrics. 2016;137(1). 7. Lilja G, et al. Scand J Caring Sci. 2012;26(2):245-253. 8. Gaglardi L, et al. Arch Dis Child. 2012;97(4):355-357. 9. Kerstis B, et al. Arch Womens Ment Health. 2016;19(1):87-94 10. Epperson CN et al. Curr Med Res & Opinion. 2020;36(10):1707-1716 11. Moore-Simas TA et al. J Med Economics. 2020; 23(2):174-183. 12. Luca DL et al. Math Pol Res. 2019. 13. Farewell CV, Jewell J, Walls J, Leiferman JA. A mixed-methods pilot study of perinatal risk and resilience during COVID-19. J Prim Care Community Health. 2020;11:2150132720944074. 14. Liu CH EC, Mittal L. Risk factors for depression, anxiety, and PTSD symptoms in perinatal women during the COVID-19 pandemic. Psychiatry Res. 2021;295:113552.15. Gustafsson HC, Young AS, Doyle O, et al. Trajectories of perinatal depressive symptoms in the context of the COVID-19 pandemic. Child Dev. Sep 2021;92(5):e749-e763.

Widespread media attention and conversation is driving early demand

"Zuranolone's approval is yet another reminder that when researchers broaden their lens to include women's health needs — and in general, women's biology – the benefits can be profound."

Lisa Jarvis, "New postpartum depression pill is a vital breakthrough"

WSJ
CNN
TODAY
GOOD MORNING AMERICA
CBS NEWS
FAST COMPANY
NIGHTLY NEWS WITH LESTER HOLT
WIRED
People

TIME BEST INVENTIONS 2023

2 billion
people viewed ZURZUVAE social media discussion's online

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Is Now Available

ZURZUVAE (50mg) is approved for the treatment of postpartum depression in adults. A full course of ZURZUVAE includes 14 days of treatment.

Potential Rapid Improvement of PPD Symptoms

In the SKYLARK and ROBIN Studies, an improvement in depressive symptoms vs. placebo was seen with a 14-day course treatment at day 15 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% than placebo) are somnolence, dizziness, diarrhea, fatigue, nasopharyngitis, and urinary tract infection. See boxed warning for additional information.

Important Safety Information

ZURZUVAE may cause serious side effects, including decreased awareness and alertness, which can affect your ability to drive safely or safely do other dangerous activities. Do not drive, operate machinery, or do other dangerous activities until at least 12 hours after taking each dose. You may not be able to tell on your own if you can drive safely or tell how much ZURZUVAE is affecting you. ZURZUVAE may cause central nervous system (CNS) depressant effects including sleepiness, drowsiness, slow thinking, dizziness, confusion, and trouble walking. Taking alcohol, other medicines that cause CNS depressant effects such as benzodiazepines, or opioids while taking ZURZUVAE can make these symptoms worse and may also cause trouble breathing. ZURZUVAE is a federally controlled substance schedule IV because it contains zuranolone, which can be abused or lead to dependence. Tell your healthcare provider right away if you become pregnant or plan to become pregnant during treatment with ZURZUVAE. You should use effective birth control (contraception) during treatment with ZURZUVAE and for 1 week after the final dose. ZURZUVAE and other antidepressant medicines may increase the risk of suicidal thoughts and actions in people 24 years of age and younger. ZURZUVAE is not for use in children. The most common side effects of ZURZUVAE include sleepiness or drowsiness, dizziness, common cold, diarrhea, feeling tired, weak, or having no energy, and urinary tract infection.

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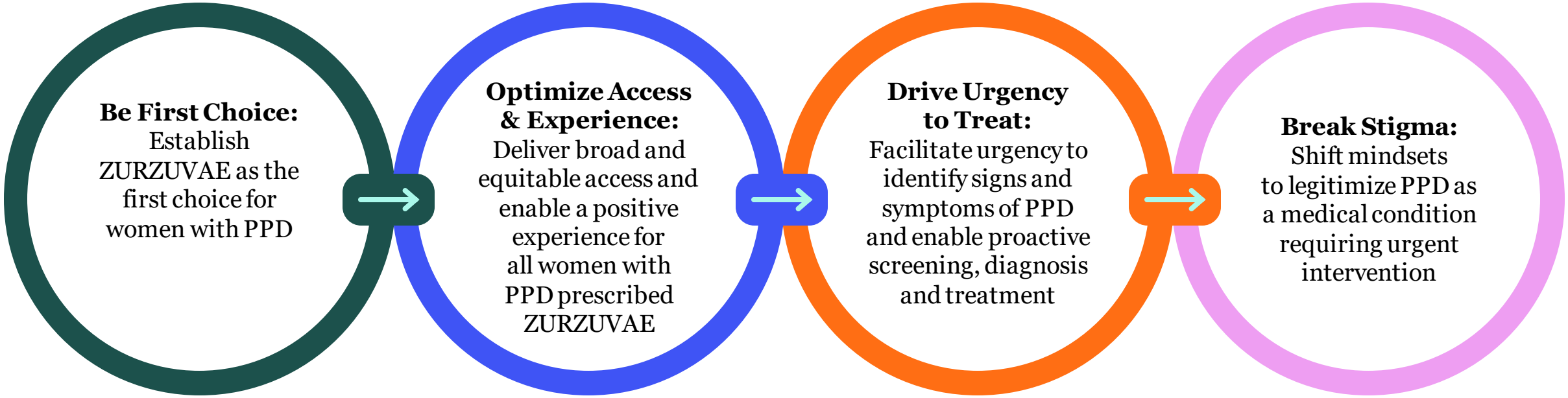
Note: image does not represent actual size of blister pack

Focused on establishing ZURZUVAE as the first line therapy for women with PPD

ZURZUVAE KEY LAUNCH GOALS



ZURZUVAE™ FOR YOU (zuranolone) capsules CV 20 mg • 25 mg • 30 mg

Specialty Distribution Model

JAMA and other publications

ACOG treatment guidelines

POLICY CENTER FOR Maternal Mental Health™

WSJ

CBS NEWS

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Multiple Expected Catalysts

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2. Advance **dalzanemdor (SAGE-718)** with 4 topline data readouts expected across HD, PD & AD

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Katie – Caregiver,
Huntington's Disease

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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 Prevalence[1]

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

~8.8M

Parkinson's Disease Global Prevalence[2]

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 Prevalence[3]

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 independent[4-7]

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 Raymund 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. Silvaggi, 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.

Cognitive impairment affects the ability to function every day and for many, the ability to stay independent

Executive Function

Individuals in early stages of HD[1]

"**There's zero multitasking** in my life. And what it causes is extreme anxiety"

"I wrote for websites and blogs, it used to take me maybe 20 or 30 minutes. **And now, it tends to take me a couple hours**"

Concentration & Planning

Individuals with PD-MCI[3]

"If I have a call where I have to focus, I'm done. All the energy I had was focusing on this one call and trying to be an active participant."

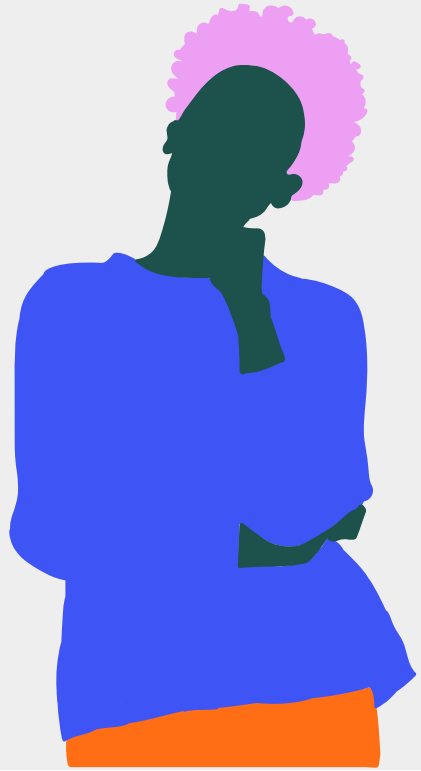
"**I can do only one thing at time.** Otherwise I get stressed and it affects my speaking"

Memory & Learning

Caregiver and Individual with AD-MCI[2]

"She started making a sandwich, then walked away, sat down and spaced out. She left the water on stove boiling. **She forgets what she started**"

"He'll give me a task and I'll scratch my head. What was I supposed to do? **Not on drugs, not drinking, just a mental fog"**



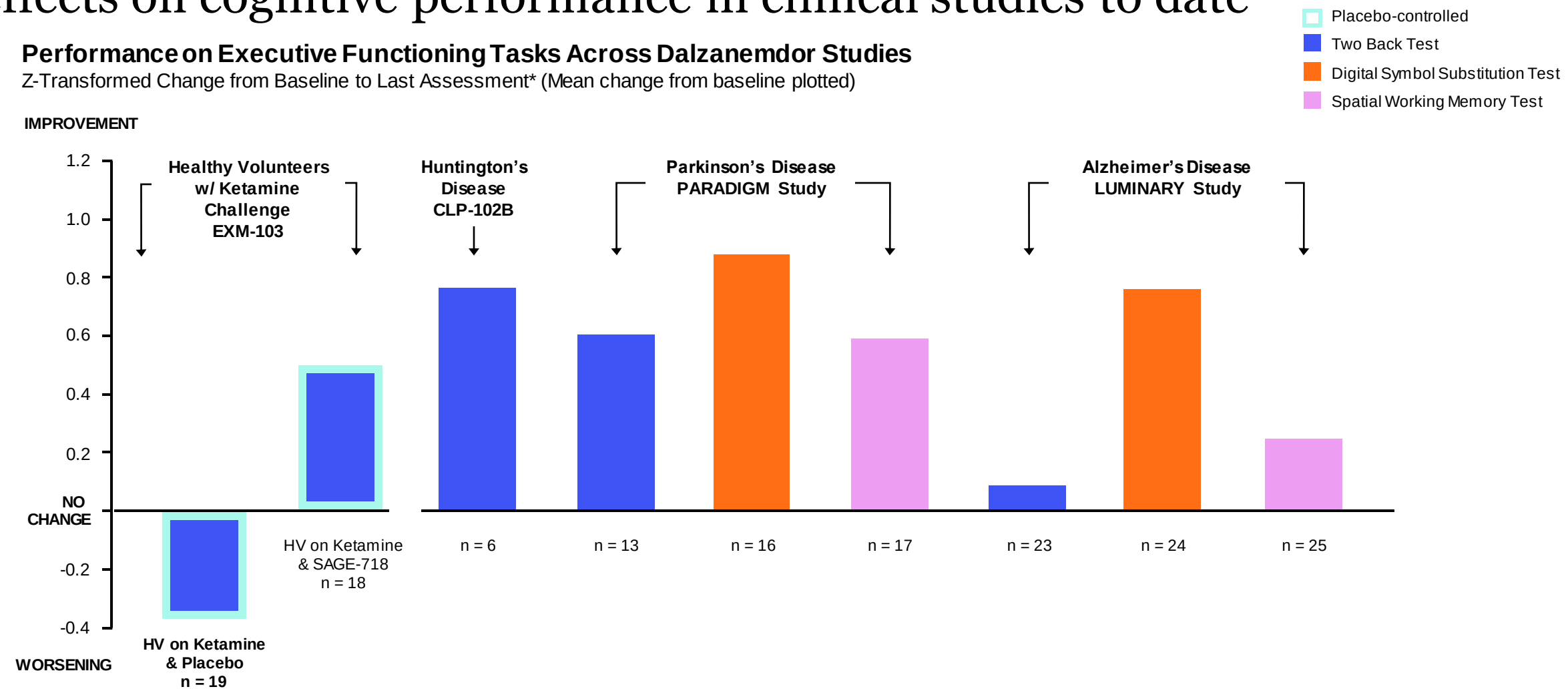
AD: Alzheimer's disease; PD: Parkinson's disease; HD: Huntington's disease; MCI: Mild cognitive impairment;

1. Petrillo J. et. al. Patient Experiences in Early Huntington's Disease. Poster presented at American Academy of Neurology Annual Meeting. Seattle, WA. April 2-7, 2022 2. Sage Data on File; 3. Petrillo J et. al. The Impact of Mild Cognitive Impairment on Functioning in People With Parkinson's Disease. Poster presented at the International Parkinson and Movement Disorder Society, Copenhagen, Denmark. August 27-31, 2023;

Dalzanemdor (SAGE-718) has demonstrated consistent beneficial effects on cognitive performance in clinical studies to date

Performance on Executive Functioning Tasks Across Dalzanemdor Studies

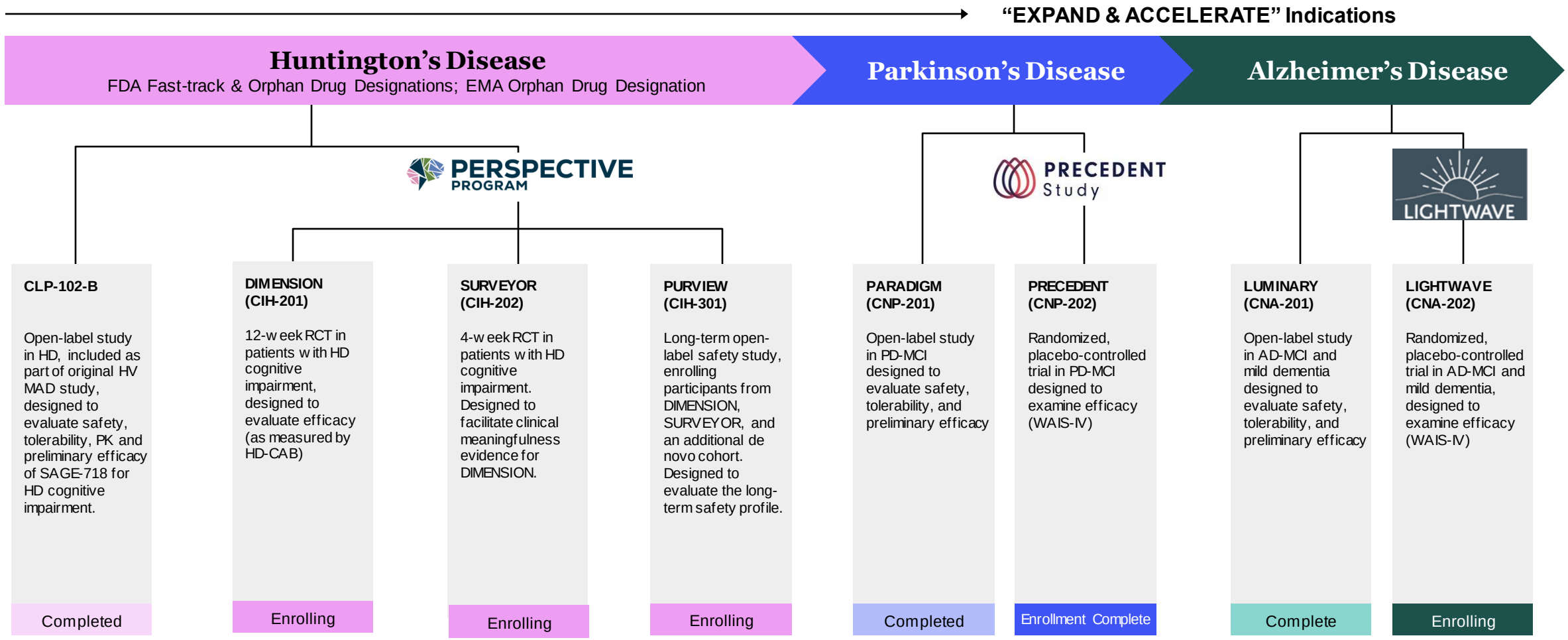
Z-Transformed Change from Baseline to Last Assessment* (Mean change from baseline plotted)



HV = healthy volunteers

The dalzanemdor (SAGE-718) clinical development program

Potential to reshape the treatment of patients with cognitive decline



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Data expected across all 3 indications over the course of 2024

EARLY 2024 (Q1/Q2)

- Topline data from the **PRECEDENT Study in PD**

MID 2024 (Q2/Q3)

- Topline data from the **SURVEYOR Study in HD**

LATE 2024 (Q3/Q4)

- Topline data from the **LIGHTWAVE Study in AD**
- Topline data from the **DIMENSION Study in HD**

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Diann – Patient/Advocate
Essential Tremor

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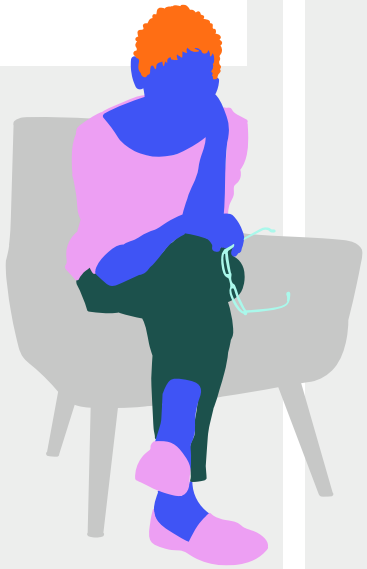
Gaps remain in bringing effective treatments to people suffering from Essential Tremor

"I can't write. That's the worst thing in the world… I send my son to the bank for things. It's getting to the point where I'm going to have to let him do all the financial work, because I just can't do it… **My mind is okay, but my body is falling apart."**



An estimated 6.8M adults in the US have ET[1], **approximately 10-15% are diagnosed**[2]

ET impacts individuals' ability to perform a **wide range of activities of daily living** and their social-emotional well-being

In an interview study of ET patients and care partners with ET ranging **from mild to very severe** [3] :

100% had difficulty writing and pouring liquids

≥80% had difficulty drinking, performing grooming and hygiene activities, dressing, eating, and holding reading material

90% had at least one emotional impact of ET

ADL and social-emotional impacts **were greater** as severity of ET increased

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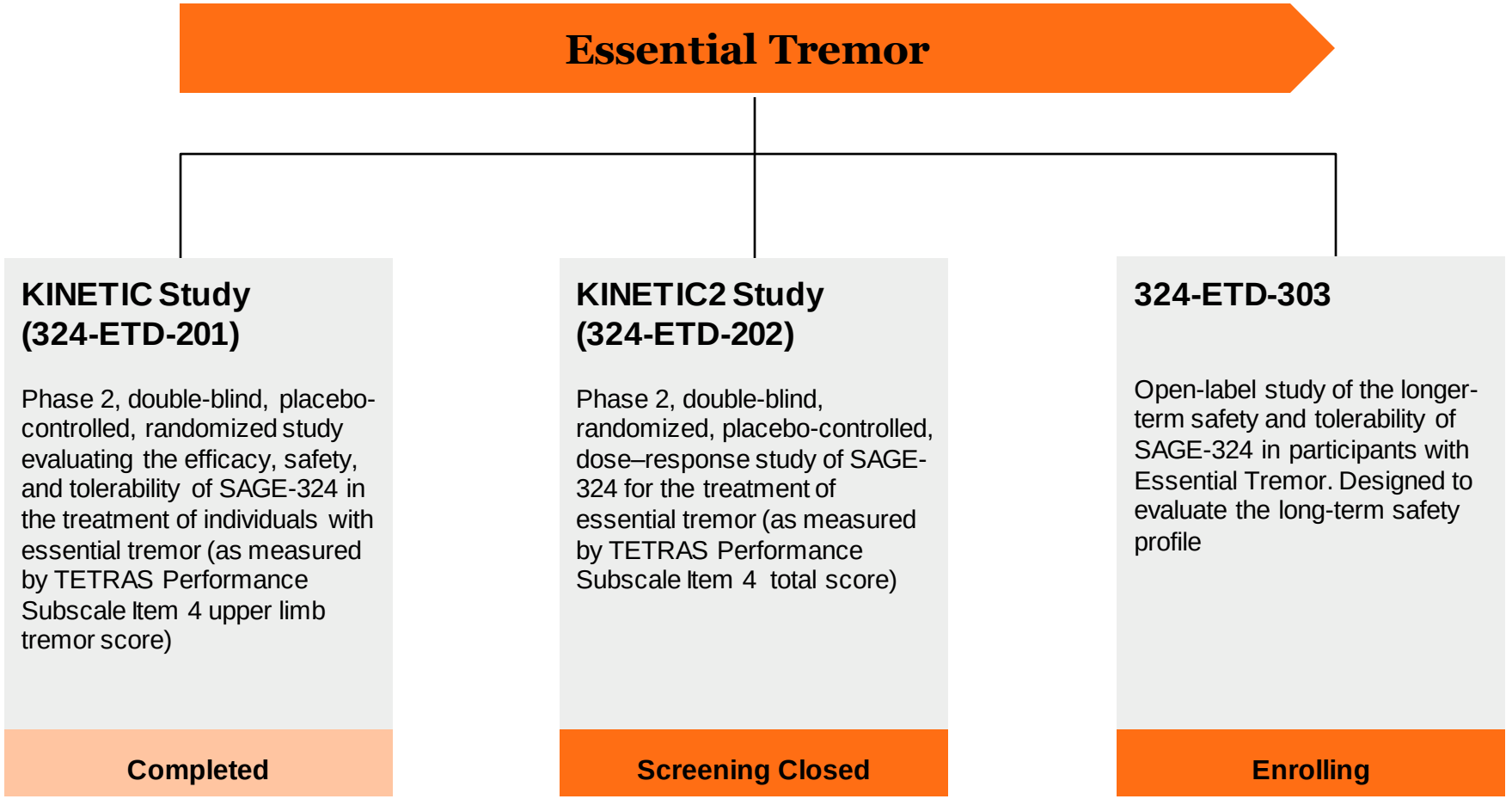
1. Furtado et al. Estimation of global age-specific prevalence of essential tremor by literature review of population-based studies. ICPE, 2023. 2. Saad et al. Diagnosed and drug-treated prevalence of essential tremor in adult patients: retrospective analyses of two US healthcare claims databases. MDS 2022. 3. Gerbasi et al. Patient experiences in essential tremor: Mapping functional impacts to existing measures using qualitative research. MDS 2023.

The SAGE-324 clinical development program



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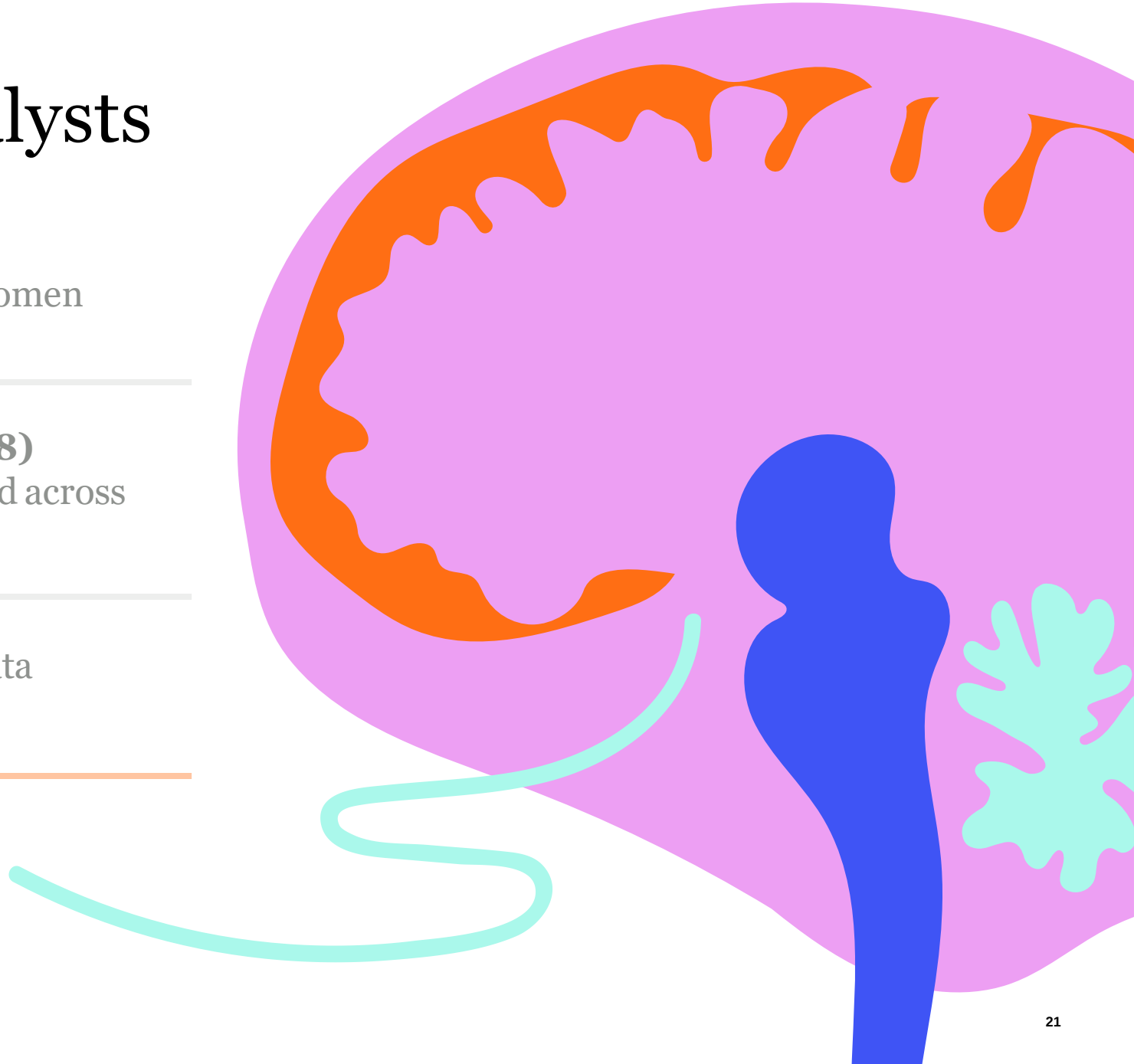

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Other potential areas of growth within the GABA and NMDA platforms

Profile of SAGE-319

GABA Receptor PAM

- Extra-synaptic GABAA receptor preferring positive allosteric modulator
- Profile supporting daily, oral, chronic dosing
- Differentiated clinical EEG signature compared to zuranolone and SAGE-324

Potential indications:

NEURODEVELOPMENTAL / MOTOR DISORDERS

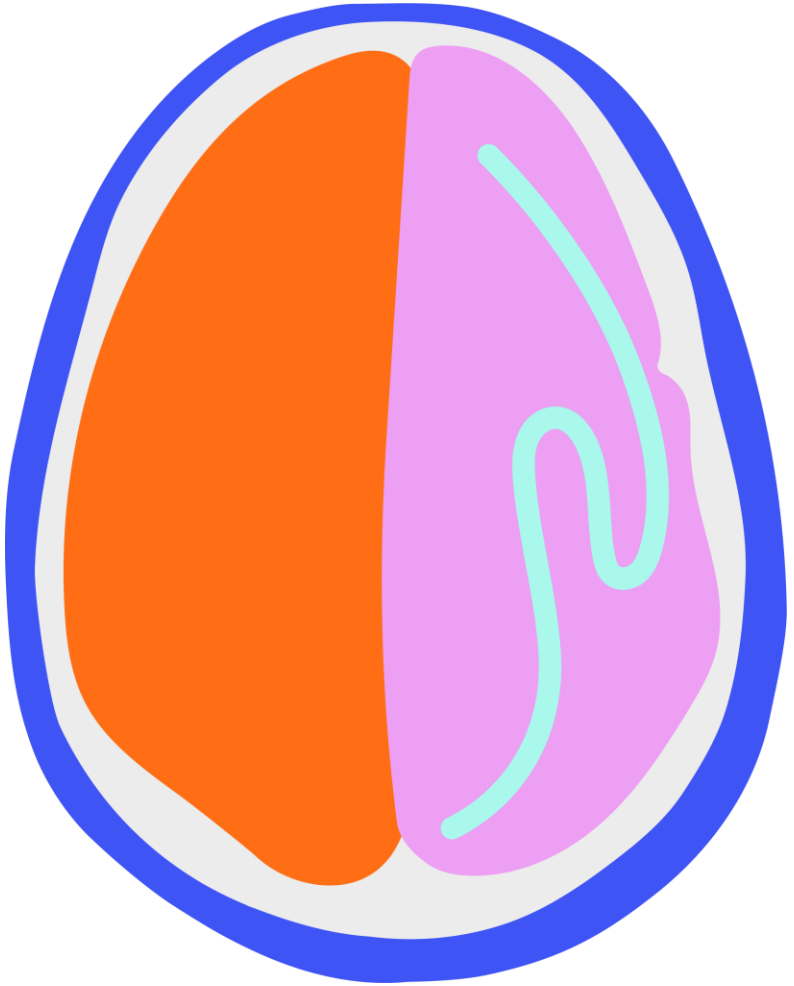
Preclinical profile of SAGE-421

NMDA Receptor PAM

- NMDA receptor positive allosteric modulator
- Profile supporting daily, oral, chronic dosing

Potential indications:

COGNITIVE IMPAIRMENT, SCHIZOPHRENIA



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Potential Value Creating Catalysts

Neuropsychiatry – Anticipated Events		
ZURZUVAE*	Broader complement of commercial capabilities	EARLY 2024
	Present additional analyses of data from NEST clinical program, including health economics and patient reported outcomes	2024
Dalzanemdor (SAGE-718)	Topline data from the PRECEDENT Study in PD	EARLY 2024
	Topline data from the SURVEYOR Study in HD	MID 2024
	Topline data from the LIGHTWAVE Study in AD	LATE 2024
	Topline data from the DIMENSION Study in HD	LATE 2024
	Present additional analyses of data from clinical development program as well as disease state and burden of disease research in HD, PD and/or AD	2024
SAGE-324*	Topline data from Phase 2 KINETIC 2 Study in ET	MID 2024
	Present additional analyses of data from clinical development program as well as disease state and burden of disease research in ET	2024
Additional Expected Milestones		
Cash Balance[1]	Maintain strong financial foundation	2024

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

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

[1] In December we achieved the milestone from Biogen related to first commercial sale of ZURZUVAE for PPD. We expect to receive the $75M payment in the first quarter of 2024.

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

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