Sage Therapeutics™

Investor Presentation

August 2021

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: our clinical development plans, including expected timelines for initiation and completion of trials and reporting of results; our belief that we have sufficient data to file an NDA for zuranolone and the potential regulatory pathways for filing and approval of zuranolone and our other product candidates; our belief in the potential benefit and profile for zuranolone and in its potential to be successful and to change the paradigm for treatment of MDD; the potential for success of our other product candidates in various indications, including the potential profile and benefit of our other product candidates; 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 zuranolone and our other product candidates, if approved; our plans and goals with respect to building a commercial engine; the goals, opportunity, mission and vision for our Company and potential for our business; our views with respect to potential value creation opportunities; the potential benefits and results that may be achieved through our collaborations with Biogen and Shionogi; our plans for advancing, accelerating and expanding our development efforts and the output of our product engine; our belief in the potential for upcoming catalysts and milestones to support our mission and goals; our expectations with respect to 2021 year-end cash; and our belief in our ability to become the leading brain health company and top-tier pharmaceutical company with multiple franchises.
- These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risk that:
  - Our 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. Final results of studies where we reported interim results may not be consistent with the interim results. 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.
  - Continued or extended surges of the COVID-19 pandemic may have a more significant impact on our clinical development timelines, data or business than we expect.
  - 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; we may encounter issues with the efficacy or durability of short-term treatment, or co-initiated treatment with zuranolone or safety and efficacy concerns with respect to retreatment that require additional studies be conducted;
  - The FDA and other regulatory authorities may ultimately decide that the design or results of our completed, ongoing or planned clinical trials for zuranolone or any of ourother product candidates, even if positive, are not sufficient to file for or obtain regulatory approval in the indications that are the focus of our development plans despite prior regulatory advice. 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;
  - We may never achieve the rate of new product candidates from our product engine that we expect in the future.
  - Even if our products are successfully developed and approved, the number of patients with the diseases or disorders our products treat, and the actual market for such products may be smaller than our current estimates; or we may not achieve market acceptance or reimbursement at acceptable levels. We may never be successful or achieve our goals with respect to commercialization.
  - 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 its products, or to defend ours patent portfolio against challenges from third parties.
  - We may face competition from others developing 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 also face unexpected expenditures which could cause us to change our plans, and as a result, our expectations as to year-end cash may prove not to be correct.
  - We may not be able to establish and maintain key business relationships with third parties on we may encounter technical and other unexpected hurdles in the manufacture and development 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™

Sage is a leader in brain health – *making medicines that matter*

- Advancing brain health leadership
- Mission to be a top-tier biopharmaceutical company in the next 5 years
- Rich pipeline across 3 franchises
  - First and only product approved specifically for postpartum depression
  - Three late-stage programs; three ongoing phase 3 studies
  - 5 NCE development programs across 12+ indications
  - Strong intellectual property strategy
- Goal of 2 or more IND-enabling programs per year by 2023
- Catalyst rich 2021; topline readouts from four trials to date; multiple additional readouts expected
- $1.9B+ capital to fund efforts to accelerate and advance medicines that have potential to impact an estimated > 450M patients globally

Sage Therapeutics™

A Leading Brain Health Portfolio

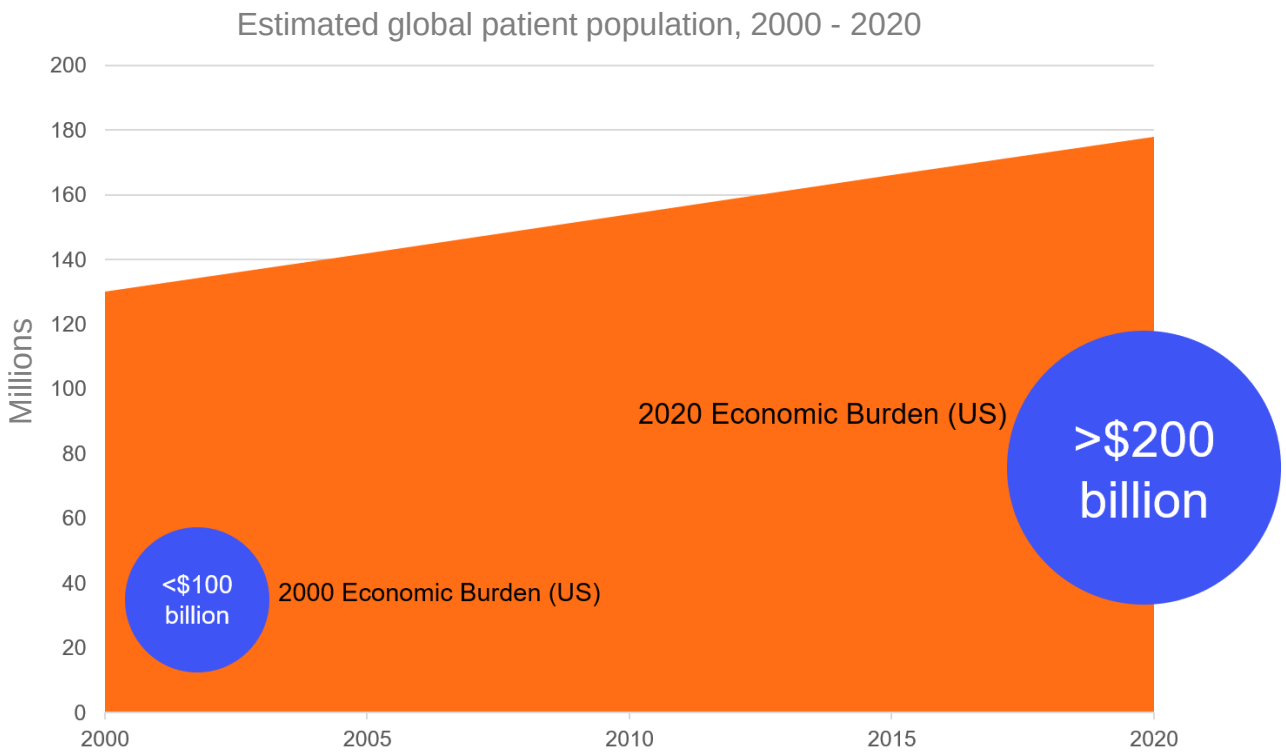
Light shades indicate trials in the planning or evaluation stage

COMPOUND	PARTNER	INDICATIONS	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	MARKETED
DEPRESSION FRANCHISE							
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 FRANCHISE							
SAGE-324	Biogen	Essential Tremor					
		Epileptiform Disorders					
		Parkinson's Disease					
NEUROPSYCHIATRY FRANCHISE							
SAGE-718		Huntington's Disease Cog. Dysfunction					
		Parkinson's Disease Cog. Dysfunction					
		Alzheimer's Disease Mild Cog. Impairment and Mild Dementia					
EARLY DEVELOPMENT							
SAGE-904		NMDA Hypofunction					
SAGE-689		Acute GABA Hypofunction					
SAGE-421		NMDA Hypofunction					
SAGE-319		GABA Hypofunction					
OTHER DEVELOPMENT OPPORTUNITIES							
Brexanolone		Advanced COVID-19 related acute respiratory distress syndrome					

Depression & Mood Disorders

Depression and Mood Disorders

- Despite new classes of medicines developed to treat depression in last 60 years, **prevalence and impact continue to increase globally**
  - > 50% of patients suffer **severe impact on ability to function**
  - Depression shown to **have generational impact** as well as direct impact on caregivers (e.g., caregivers/ partners unable to work full time, increasing economic burden exponentially)
  - Rates continue to increase, particularly in young adults
- Increasing evidence that **depression is episodic in nature** with events that may occur on their own or be triggered by a variety of factors including stressful life events (e.g. personal loss, trauma, postpartum, chronic medical conditions, the COVID-19 pandemic). A family history may increase the risk in some patients
- Sage believes patients can be **treated episodically and/or as needed, reducing burden and impact of chronic management**



BLS CPI (Consumer Price Index) Calculator was used to estimate 2000 and 2020 economic burden using U.S. specific studies in respect to the indications noted.

Abbreviations: PPD = postpartum depression, MDD = major depressive disorder, TRD = treatment resistant depression, GAD = generalized anxiety disorder, BPD = bipolar depression

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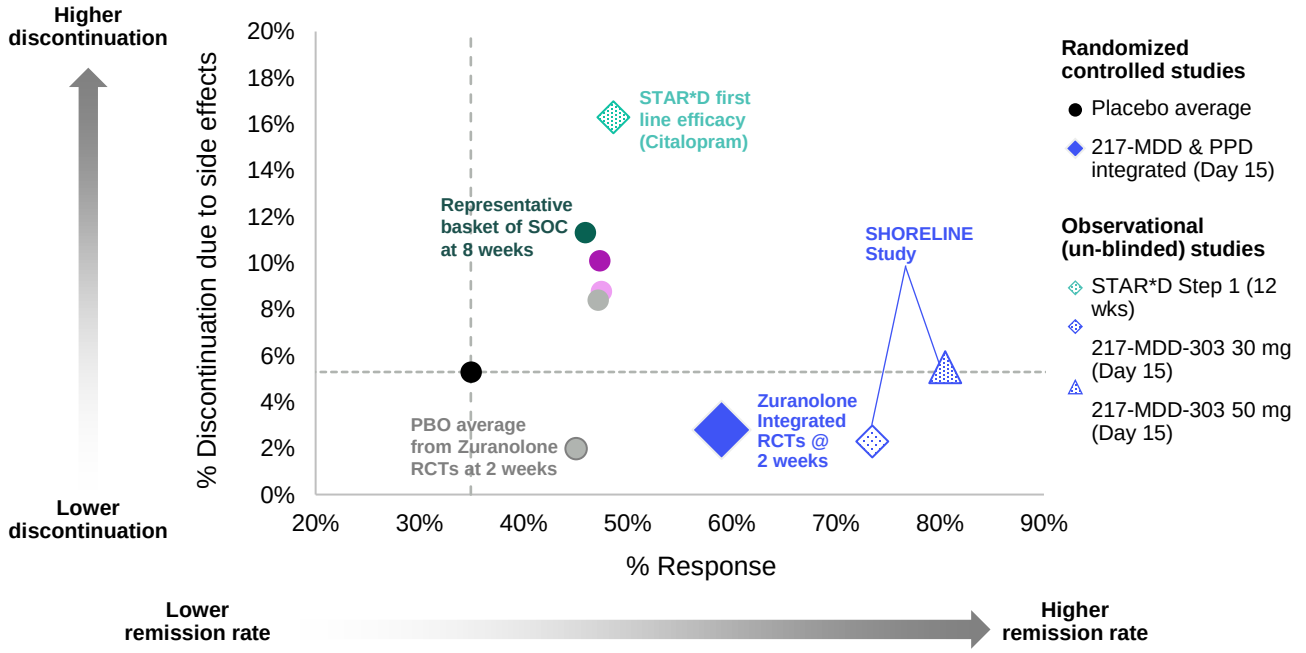
Paucity of innovation plagues patient journey to find effective treatment for depression and other mood disorders

- Benefit/risk profile of treatments for major depressive disorder remains unchanged despite at least 35 approved treatments in last 30 years
- Increasing burden and unmet need support development of more innovative treatments
- In clinical trials to date:
  - Zuranolone demonstrated a reduction of depressive symptoms seen within 72 hours
  - Approximately 70% of participants with positive response to an initial 2-week 30 mg treatment in the SHORELINE Study required at most one additional zuranolone treatment during the 12-month study
  - Zuranolone has been generally well-tolerated in more than 3,000 subjects to date

Benefit Risk Profiles (Response vs. Discontinuation Due to Side Effects)



Side-by-side assessment of ZUR and SOC provides context of the product profiles utilizing metrics with implications for real-world clinical practice

Methods: Average response and discontinuation due to side effects rates for SOC were obtained from Cipriani et al. 2018 (average PBO for SOC trials and representative basket of SOC products), and an integrated analysis of zuranolone clinical data; SHORELINE Study and STAR*D included.

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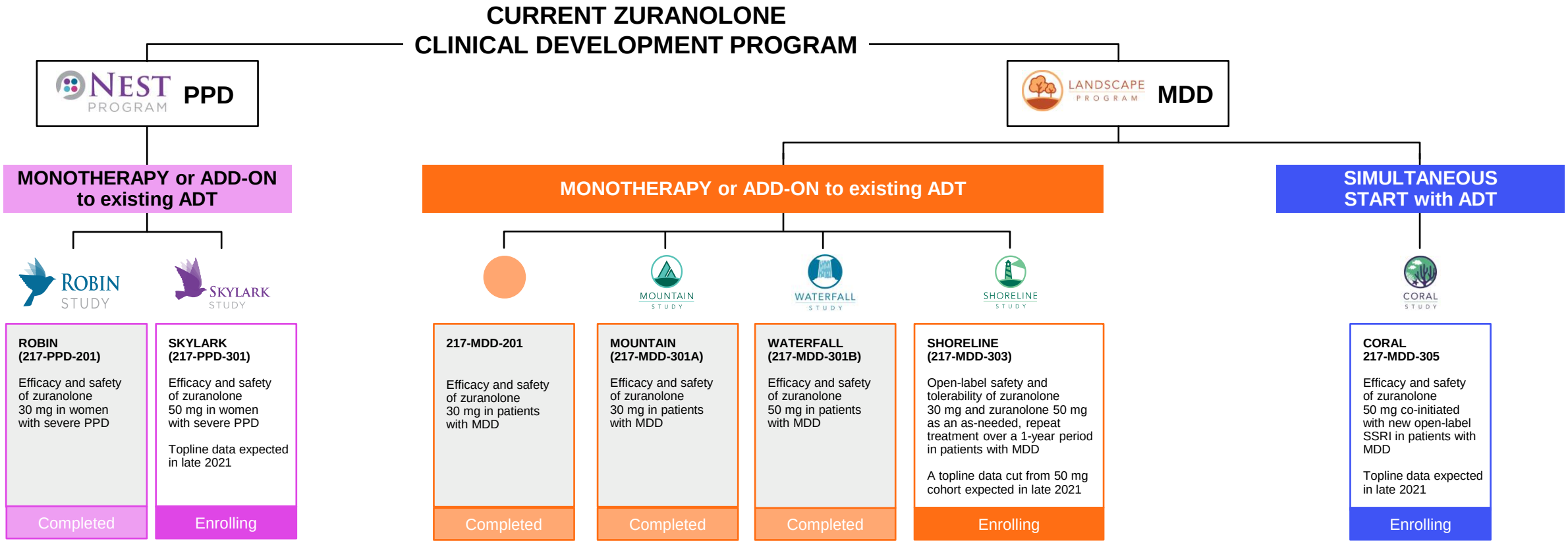
Zuranolone's Landscape and Nest Programs

Potential to reshape the depression landscape



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

Sage Therapeutics™ Biogen SHIONOGI

WATERFALL Study

Primary and select secondary statistical outcomes

Outcome	Day 3	Day 8	Day 12	Day 15
HAMD-17: LS mean TRT diff (p-value)	-3.0 (<0.0001)^	-2.6 (<0.0001)^	-2.5 (0.0003)	-1.7 (0.014)*
CGI-Severity: LS mean TRT diff (p-value)	-0.4 (<0.0001)	-0.4 (0.0001)	-0.3 (0.0014)	-0.2 (0.1193)^
CGI-Improvement Response: Odds ratio (p-value)	1.8 (0.0032)	1.9 (0.0005)	1.6 (0.010)	1.5 (0.0191)
MADRS: LS mean TRT diff (p-value)	Not measured per protocol	-3.4 (0.0003)	Not measured per protocol	-2.4 (0.024)
HAM-A: LS mean TRT diff (p-value)	Not measured per protocol	-1.7 (0.0011)	Not measured per protocol	-1.4 (0.0199)

Except for HAMD-17 at Day 15 (primary) which was statistically significant and CGI-S (first secondary endpoint) which was not significant at Day 15, all p-values in the table are nominal and not adjusted for multiple comparisons
*Pre-specified primary endpoint
^Pre-specified key secondary endpoints
LS = least squares; LS mean difference = difference in LS means of change from baseline between zuranolone and placebo groups

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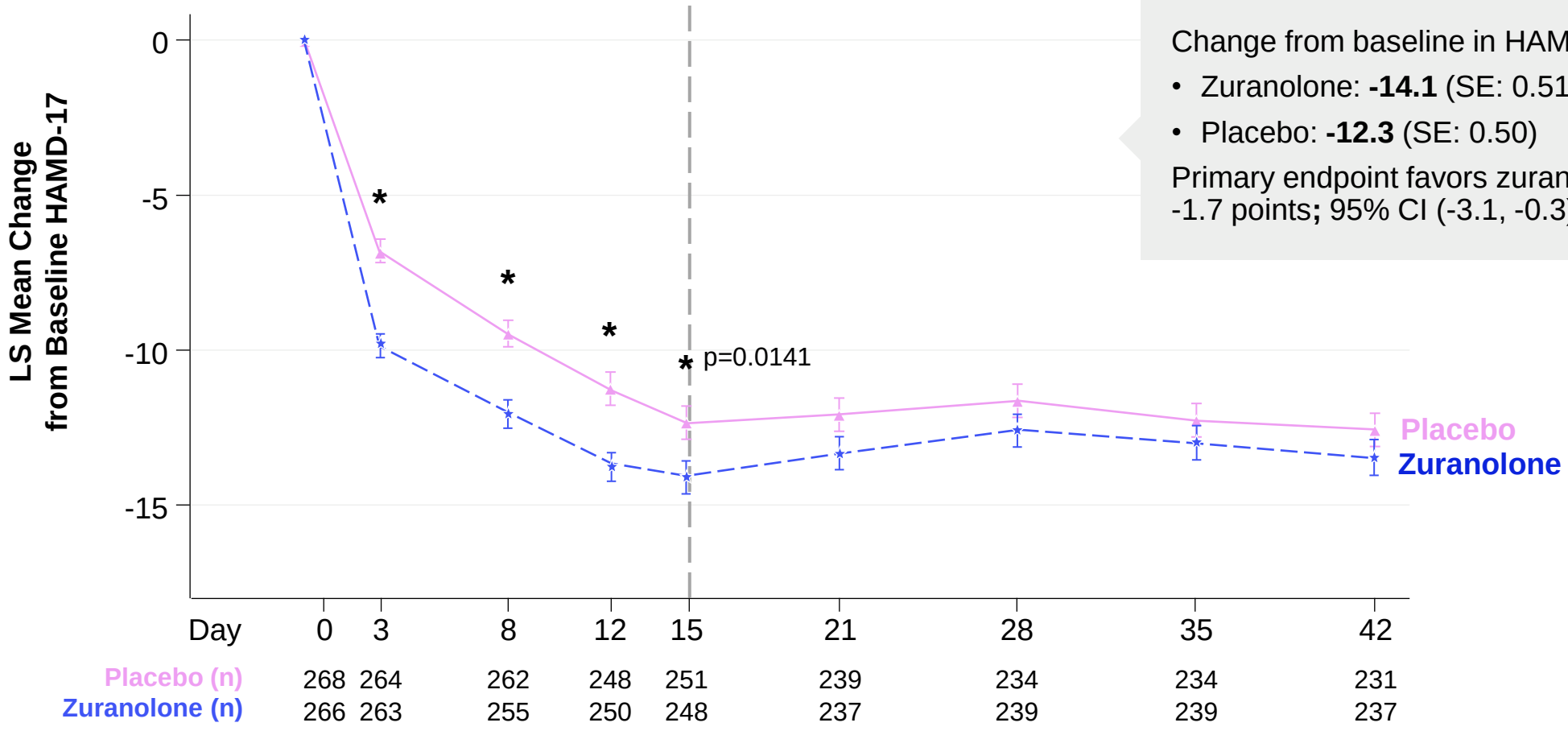
Sage Therapeutics, Inc. Data on file. 217-MDD-301 B topline memo.

WATERFALL Study

Primary Endpoint

HAMD-17 Total Score LS Mean Change From Baseline at Day 15 (and other timepoints)



Change from baseline in HAM-D total score on Day 15

- Zuranolone: **-14.1** (SE: 0.51)
- Placebo: **-12.3** (SE: 0.50)

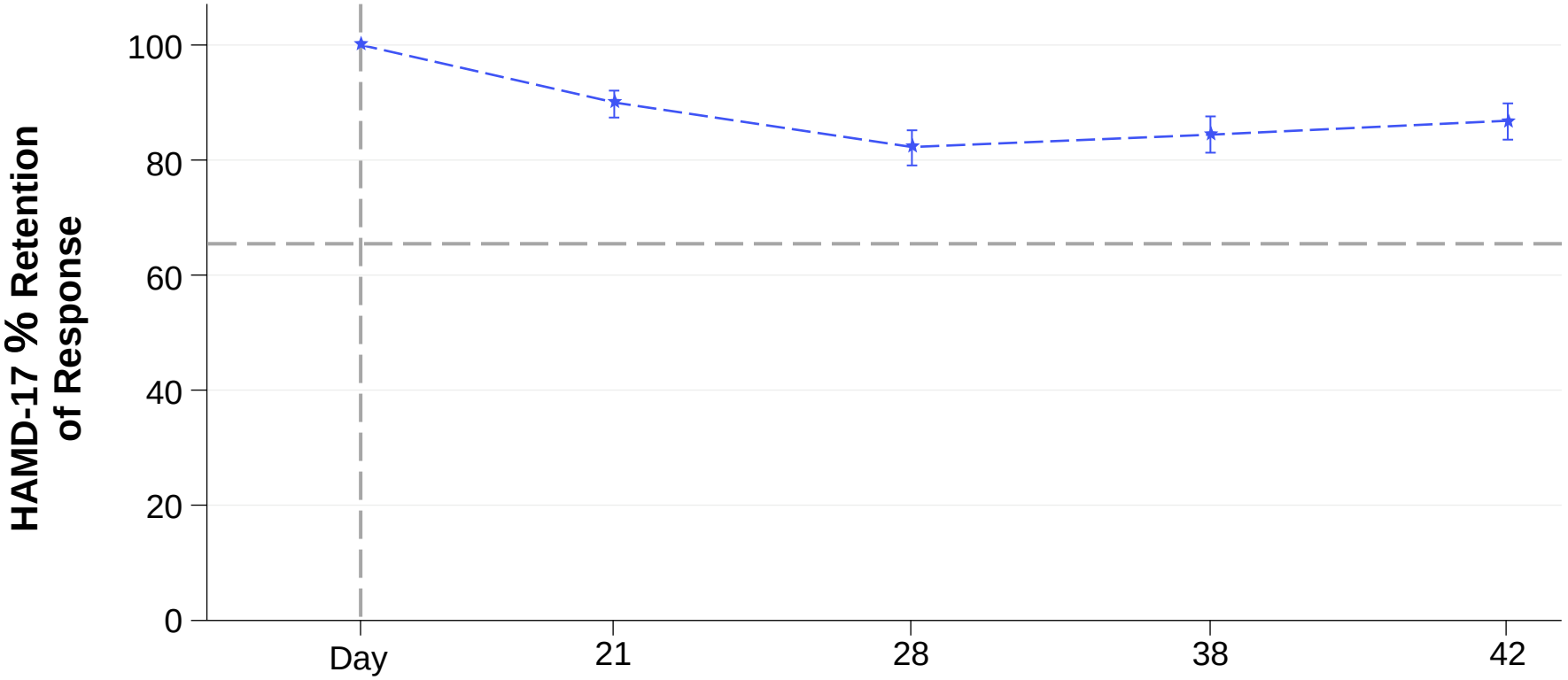
Primary endpoint favors zuranolone over placebo by -1.7 points**;** 95% CI (-3.1, -0.3), *p=0.0141*

LS = least squares.

Sage Therapeutics, Inc. Data on file. 217-MDD-301 B topline memo.

WATERFALL Study

*Mean (SE) of % Day 15 change from baseline retained at subsequent visits (Full Analysis Set; Day 15 zuranolone responders only)**



In the follow-up period (Days 21 through 42), mean percent retention of the D15 gain was over 85%

*Percent retention of Day 15 HAMD-17 total score reduction from baseline is the change from baseline in HAMD-17 total score at post-Day 15 visits as percentage of change from baseline at Day 15 and was evaluated in Day 15 HAMD-17 responders only in the zuranolone treatment group (≥50% change in HAMD-17 total score at Day 15 versus baseline).
Sage Therapeutics, Inc. Data on file. 217-MDD-301 topline memo.

WATERFALL Study
Safety

- TEAEs consistent with known zuranolone profile, with ~60% patients receiving zuranolone 50 mg and ~45% receiving placebo reporting ≥1 TEAE
- Most TEAEs reported by zuranolone 50 mg patients were mild or moderate in severity
- 2 zuranolone 50 mg patients and 2 placebo patients experienced serious adverse events (SAEs); none related to sedation
- No deaths, no loss of consciousness, weight gain, sexual dysfunction, or euphoria reported
- Most common TEAEs leading to study drug (zuranolone) discontinuation were dizziness and sedation

Overview of TEAEs through Day 42

Patients with TEAEs	Zuranolone 50 mg (n = 268)	Placebo (n = 269)
At least 1 TEAE – n (%)	161 (60.1)	120 (44.6)
Mild – n (%)	86 (32.1)	76 (28.3)
Moderate – n (%)	67 (25.0)	41 (15.2)
Severe – n (%)	8 (3.0)	3 (1.1)
SAE – n (%)	2 (0.7)	2 (0.7)
Dose reduction due to TEAE – n (%)	23 (8.6)	1 (0.4)
Discontinuation of treatment due to TEAEs – n (%)	9 (3.4)	4 (1.5)
Discontinuation of study due to TEAEs – n (%)	5 (1.9)	2 (0.7)
Death – n (%)	0	0

Sage Therapeutics, Inc. Data on file. 217-MDD-301B topline memo. .

WATERFALL Study
Safety

- The most common (>5%) events were somnolence, dizziness, headache, and sedation in patients receiving zuranolone 50 mg and diarrhea and headache in patients receiving placebo
- The most common TEAEs observed on zuranolone 50 mg are consistent with the safety profile of zuranolone known to date*

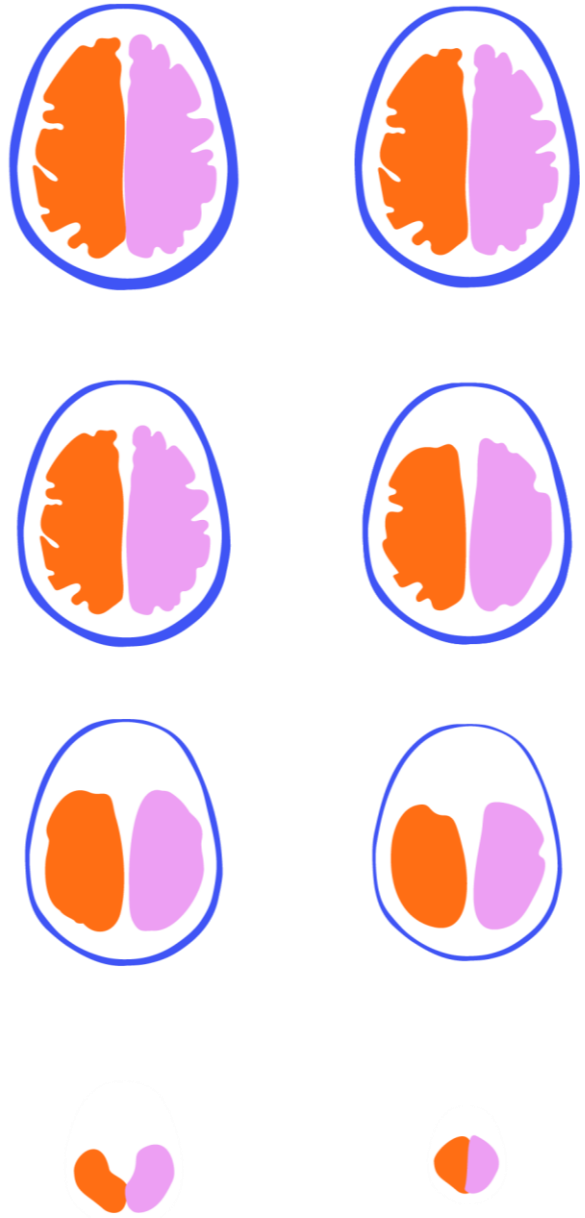
All TEAEs (>5%) incidence through Day 42

Preferred Terms (PTs)	Zuranolone 50 mg (n = 268)	Placebo (n = 269)
Somnolence	41 (15.3%)	8 (3.0%)
Dizziness	37 (13.8%)	6 (2.2%)
Headache	29 (10.8%)	21 (7.8%)
Sedation	20 (7.5%)	1 (0.4%)
Diarrhea	8 (3.0%)	14 (5.2%)

Sage Therapeutics, Inc. Data on file. 217-MDD-301B topline memo. *Gunduz-Bruce H et al. *N Eng J Med*. 2019;381(10):903-911

Upcoming Zuranolone, MDD Data Presentations & Next Steps

- Sage is committed to sharing data from the LANDSCAPE and NEST clinical development programs as well as supportive real-world evidence at premier scientific forums, potentially including:
  - Efficacy and safety data that support the rapid onset and sustained effect of zuranolone 30 and 50 mg from the SHORELINE & WATERFALL Studies
  - Patient reported outcomes that may support clinical understanding of zuranolone in the treatment of depressive symptoms
  - Impact of delayed treatment on the course of MDD
  - Real world evidence on the societal impact of MDD
- Three Phase 3 trials remain ongoing in the LANDSCAPE and NEST clinical development programs
- Sage plans to meet with the U.S. Food and Drug Administration as soon as possible to discuss next steps for zuranolone



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SHORELINE Study Initial Zuranolone Course Response, Remission (30 mg cohort)

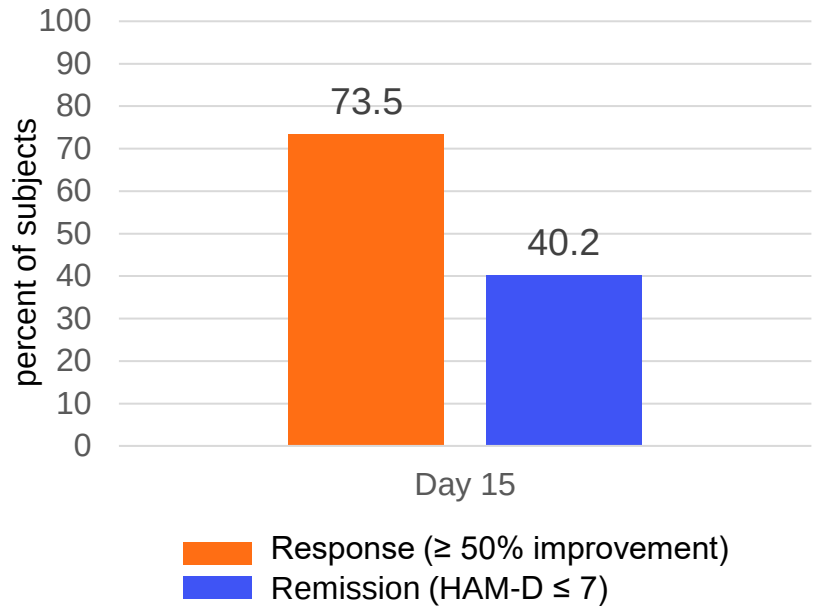
Efficacy:

- The mean baseline HAM-D score (± SD) at entry into the study was 25.3 ± 4.1 (n=725)
  - 173 (23.9%) exited the study with the primary reason of not achieving response in the first course of treatment
- At Day 15, the mean change from baseline was -15.2 ± 7.1 (n=687)
- 304 (42%) patients were on pre-existing antidepressant therapy (ADT) which was continued, while 421 (58%) were on no ADT; there were no meaningful differences in efficacy outcomes between the two groups

Safety:

- In the first course of treatment (14-day treatment + 14-day follow up) the adverse events (AEs) reported were similar in nature and frequency to those previously reported for completed zuranolone studies, with 368 (51%) patients reporting at least one AE
  - The most common AE within the 14-day first course of treatment (reported >5%) were somnolence (70/348-20.1%), headache (59/348=17.0%) and dizziness (42/348=12.1%). Most adverse events were mild or moderate
- Causes of adverse event-related discontinuations during the 14-day course of treatment were varied
  - The overall rate of study drug discontinuation due to treatment emergent adverse events was 2.6%
- Similar adverse events were reported regardless of the presence or absence of ADT at baseline
- No events of loss of consciousness were reported at any time during the study

30 mg Cohort Initial Treatment Course Response, Remission



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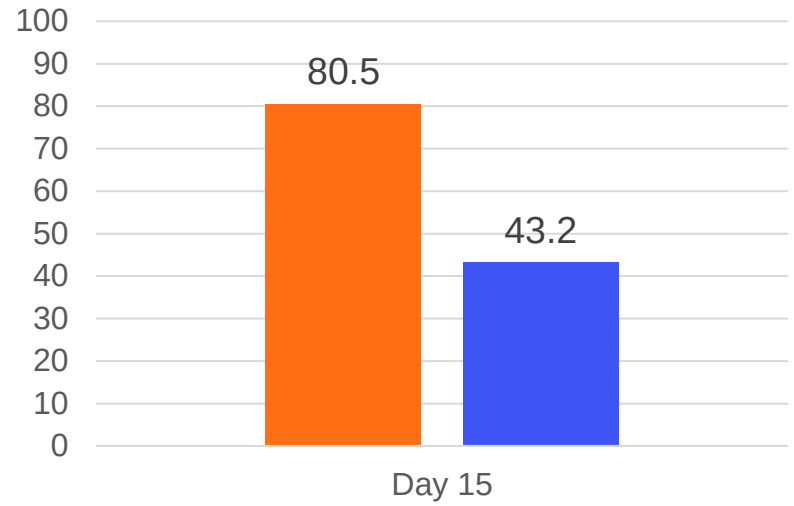
SHORELINE Study Interim 50 mg Data
Initial treatment with zuranolone

- In the 199 patients who received zuranolone 50 mg only, approximately 80% achieved response and 43.2% achieved remission after the initial 2-week treatment period.

- In this cohort the adverse event profile was similar to that seen in patients who received 30 mg zuranolone, with 58.8% (117/199) subjects reporting at least one AE during the first course of treatment (14-day treatment + 14-day follow up). Events >5% of somnolence, dizziness, and sedation were observed to be more frequent in the 50 mg cohort, but were similar in severity to the events seen with 30 mg. Most adverse events were mild or moderate.

50 mg Cohort Initial Treatment Course Response, Remission (Interim Data)



Retreatment in the SHORELINE Study (30 mg Cohort)

In the completed 30 mg zuranolone cohort, approximately 70% of participants with positive response to an initial 2-week treatment required at most one additional zuranolone treatment during the 12-month study

Number of zuranolone courses

	30 mg (n=489)
1 course (no re-treatment)	210 (42.9%)
2 courses	125 (25.6%)
3 courses	58 (11.9%)
4 courses	53 (10.8%)
5 courses	43 (8.8%)

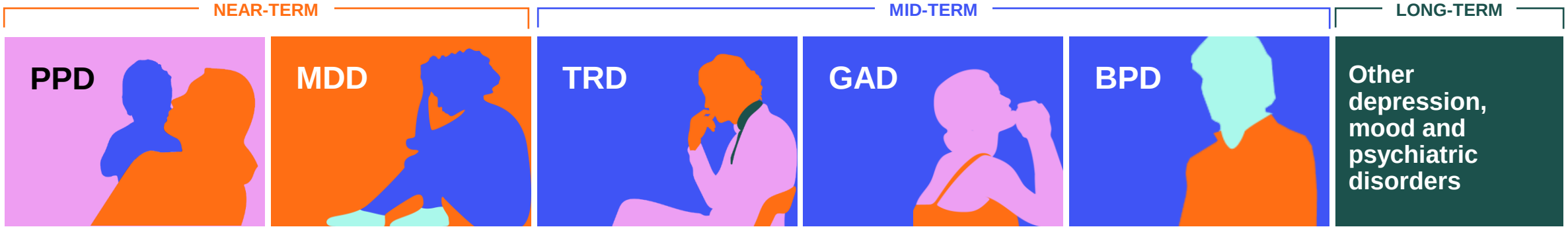
- 489 patients were responders to initial 30 mg treatment and continued in the study beyond the first treatment course
- The number of zuranolone retreatments used were similar regardless of the presence or absence of antidepressant therapy
- The overall incidence rates of treatment emergent adverse events (TEAEs) during the first, second, third, fourth, and fifth treatment courses were, 51% (368/725), 42% (120/286), 29% (45/157), 29% (28/96), and 28% (12/43), respectively
  - The TEAEs were observed to decrease in frequency through the first three courses and remained stable over the next two courses
- Safety profile on treatment, off-treatment, and in between treatments has shown a consistent pattern to date, in AE presentation across treatment courses
- No signal on suicidality was identified during or in between treatment courses
- Outcomes on efficacy measures and safety events were similar to those observed in the initial treatment course; and the presence or absence of ADT did not change the results

Subjects were required by protocol to achieve response to continue into the naturalistic follow-up period

Sage Therapeutics™

Zuranolone is a Sage-created innovation with potential to impact millions globally

Development plan has potential to be accelerated by strategic collaboration with Biogen



	2021 Early	2021 Mid	2021 Late	*Early:Q1-Q2; Mid:Q2-Q3; Late: Q3-Q4
DEPRESSION FRANCHISE				**Expected milestones:**
Zuranolone (Sage-217)		✓		Report topline data from WATERFALL Study in major depressive disorder **(1H21)**
		✓		Report full data from SHORELINE Study 30 mg cohort in major depressive disorder
			●	Report topline data from CORAL Study in major depressive disorder for rapid response treatment when co-initiated with new antidepressant therapy
			●	Report topline data cut from SHORELINE Study 50 mg cohort in major depressive disorder

Composition of Matter Patent through 2034, subject to potential extensions

Sage Therapeutics™ Biogen SHIONOGI

Abbreviations: PPD = postpartum depression, MDD = major depressive disorder, TRD = treatment resistant depression, GAD = generalized anxiety disorder, BPD = bipolar depression

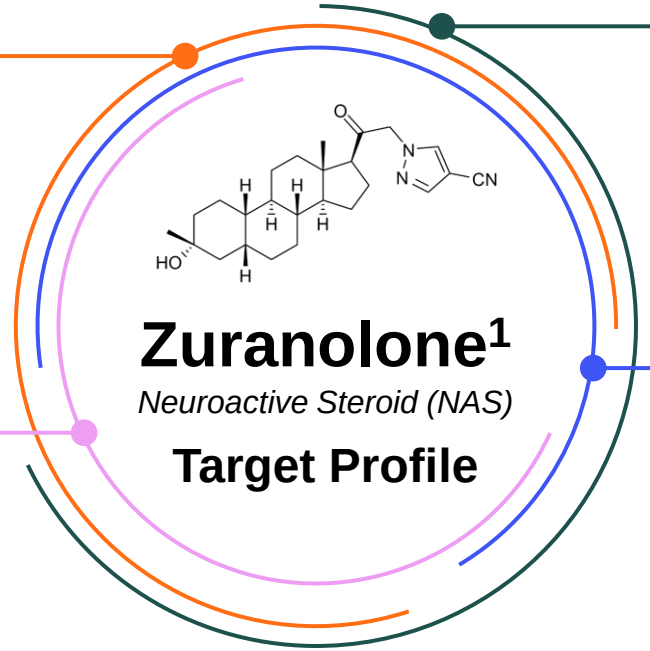
Zuranolone's Unique Target Profile Has the Potential to Revolutionize the Care of Depression

Rapid Onset & As-Needed

- Rapid response – within days
- As-needed therapy

Well-Tolerated

- Favorable tolerability profile
- Differentiated side effect profile



Short Course

- Oral
- 2-week treatment, with sustained effect

Novel MOA

- Selectively modulates $GABA_A$ receptors
- May help neuronal networks rebalance

We believe zuranolone, if successful, has the potential to address significant unmet need for patients with depression

Sage Therapeutics™

Zuranolone is being developed in collaboration with Biogen
Note: Success of zuranolone and the product profile depend on the clinical development program and regulatory approval.
1. Martinez Botella GM et al. *J Med Chem*. 2017;60:78109-7819.

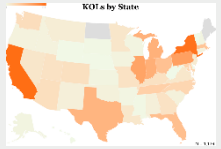
Our Commercialization Plan Will Focus on Shifting the Treatment Paradigm & Capitalizing on Substantial Market Opportunity

POTENTIAL KEY DRIVERS TO SHIFT PARADIGM:

1. Recognize **depression** as a priority medical illness
2. Elevate a **new scientific approach** to treating depression
3. Educate on **zuranolone's unique profile** to shift the paradigm of depression
4. Optimize the **customer & patient** experience in depression

Sage is developing a **best-in-class commercialization program** to modernize the care of depression

KOL Engagement



Congress & HCP Education

Patient & Customer Experience

SAGE CENTRAL® PATIENT SUPPORT

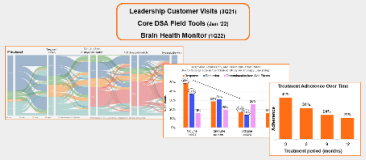
Patient Education & Advocacy

NAMI National Alliance on Mental Illness

Differentiated Product/Profile

Customer Engagement Model

Value, Access, Proactive VBAs



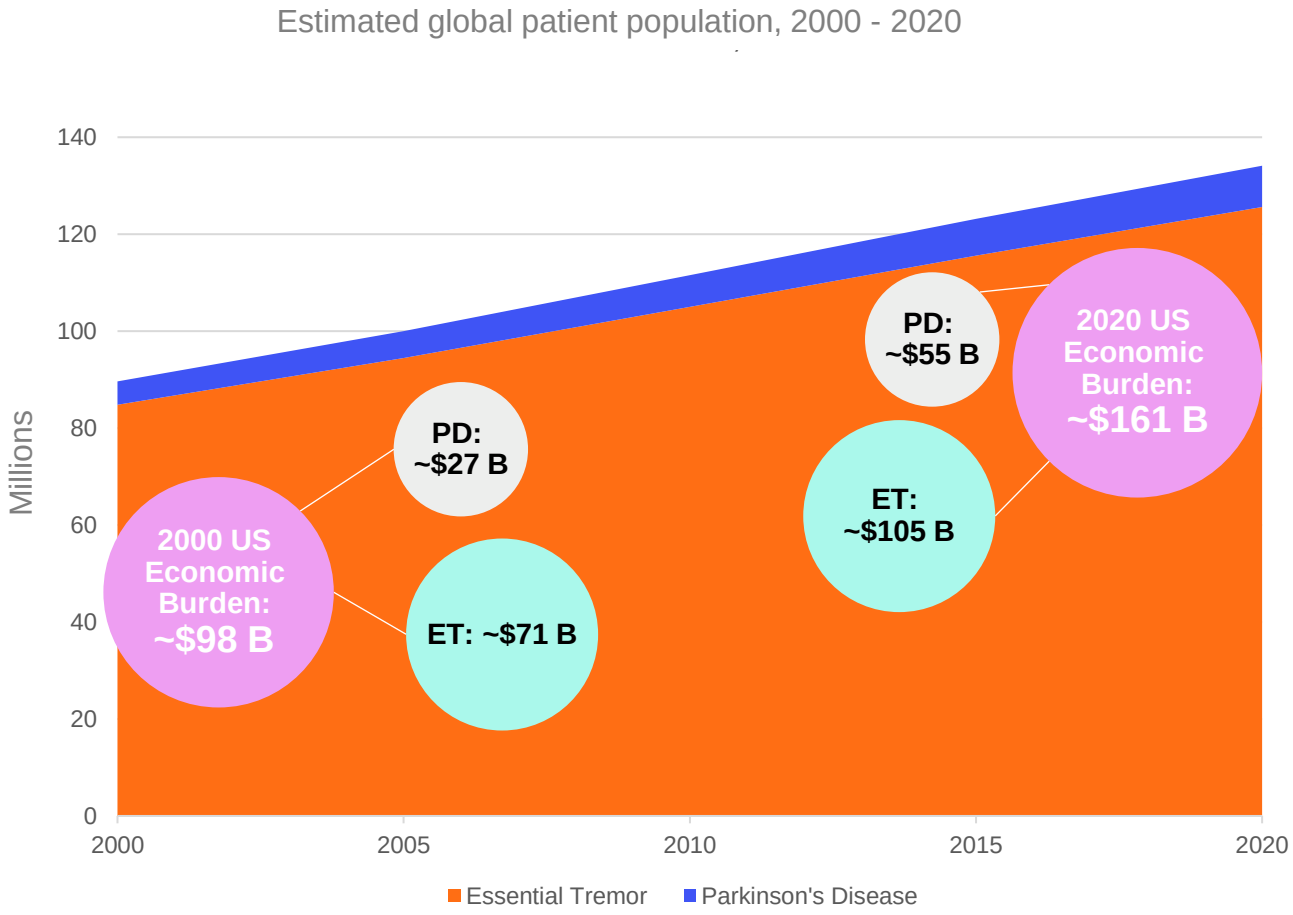
Zuranolone is being developed in collaboration with Biogen
Note: Success of zuranolone and the product profile depend on the clinical development program and regulatory approval. All function-specific strategies and tactics will be consistent with Sage policies and appropriate based on remit, intended audience and status of the zuranolone program

Neurology Franchise

Movement and neurological disorders

Gaps remain in bringing effective treatments to people with movement disorders

- Standards of care are inadequate for many people suffering from debilitating movement disorders
  - It's estimated that nearly 135 million people globally suffer from essential tremor (ET) or Parkinson's disease (PD)
- Movement disorders can make the simplest activities of daily life difficult, if not impossible
  - Chewing, eating, standing, walking, self-care
- Substantial mental health impact and caregiver burden
  - Depression/low mood, anxiety, poor sleep
- Sage has demonstrated that the GABA positive allosteric modulation mechanism is important in movement disorders



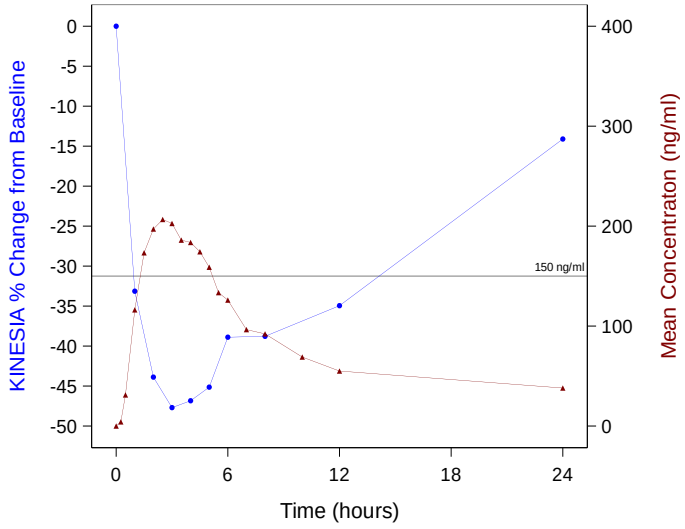
BLS CPI (Consumer Price Index) Calculator was used to estimate 2000 and 2020 economic burden using U.S. specific studies in respect to the indications noted.

SAGE-324: Novel potential treatment for movement disorders

Predictable PD effects and PK profile with long half-life

- SAGE-324 is well-suited for development in essential tremor (ET):
  - Most prevalent movement disorder in the US (est. 6M+)
  - Last pharmacological treatment for ET was approved in 1967
  - High unmet need; 50% of treated patients do not respond or have sub-optimal response to standard of care
- In an open-label, phase 1 study, a single dose of SAGE-324 resulted in nearly 50% tremor reduction in ET patients, demonstrated on measure most closely associated with disability
- Good oral bioavailability and long half-life provides flexibility in dosing paradigms for potential development in additional disorders including Parkinson's disease and epilepsies

Total upper limb combined score after single dose in 6 people with ET as measured by accelerometer



PK over time in 6 people with ET dosed with SAGE-324

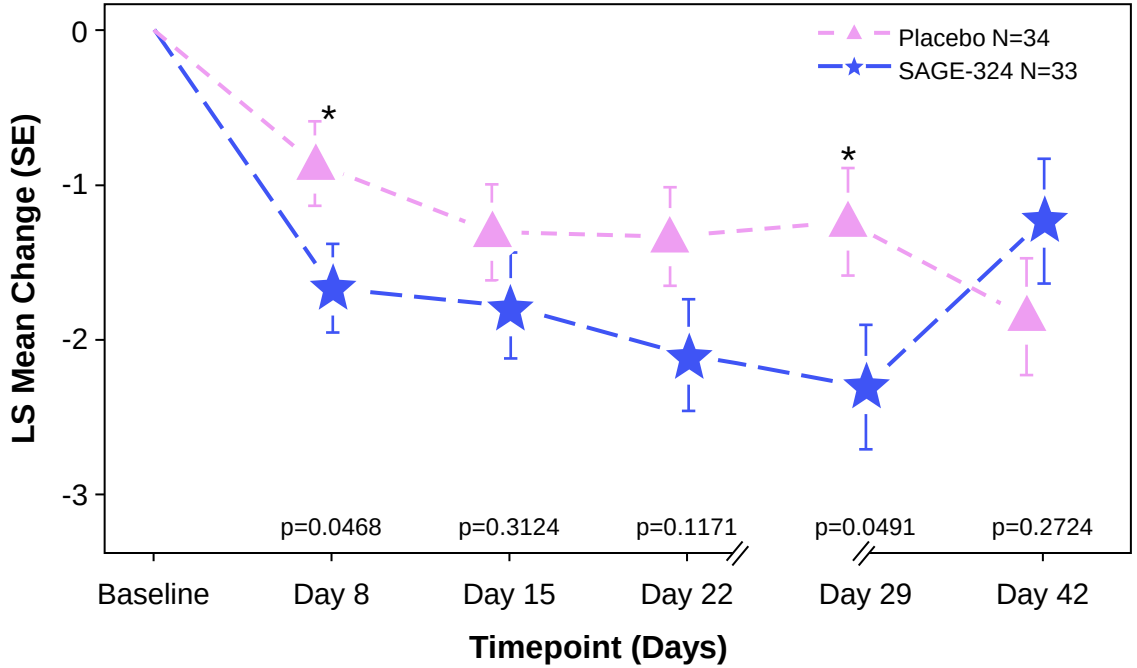
- Clear PK/PD relationship
- Promising signals of tremor reduction, consistent with those observed previously for brexanolone and SAGE-217
- Most common AEs (≥5%) included somnolence, dizziness, and feeling of relaxation

Sage Therapeutics™ Biogen

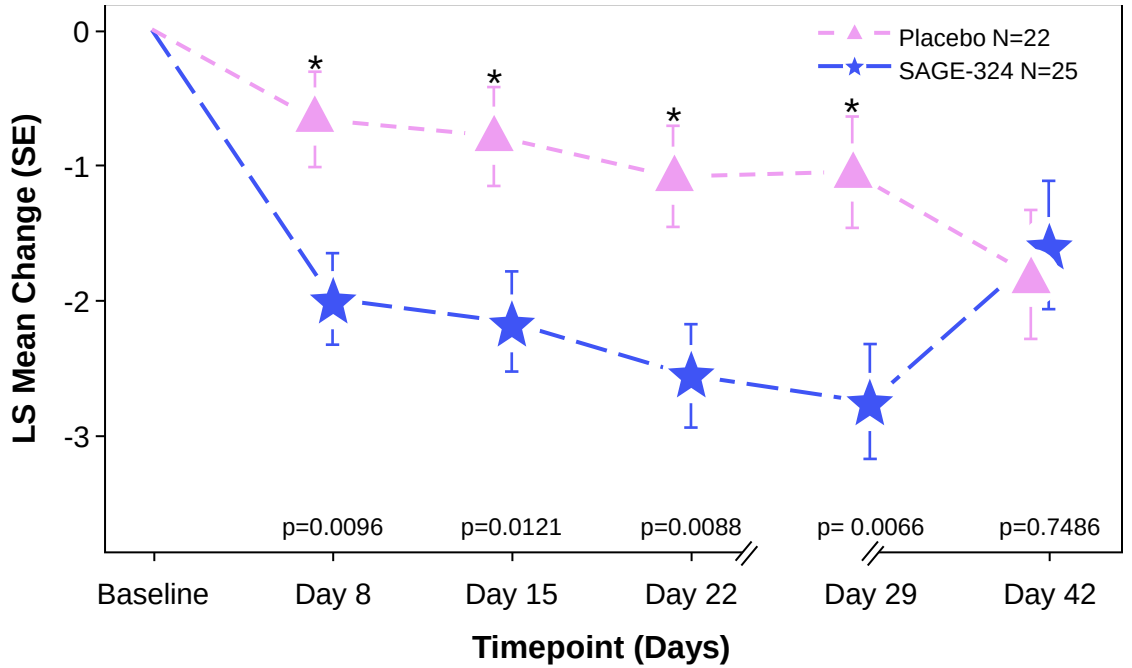
Kinetic Study: Positive Phase 2 Study in Essential Tremor

Primary Endpoint: Change from baseline in TETRAS Performance Subscale Item 4 (Upper Limb Tremor) at Day 29 compared to Placebo

SAGE-324 showed a statistically significant reduction from baseline in Upper Limb Tremor Score at Day 29 (Full Analysis Set)



Greater and statistically significant reductions in those with moderate to severe upper limb tremor at baseline (TETRAS Upper Limb Score ≥ 12) during treatment period



The most common treatment emergent adverse events that occurred in ≥10% of patients in the SAGE-324 treatment group and at a rate at least twice as high as that of patients in the placebo group were: somnolence 68%; dizziness 38%; balance disorder 15%; diplopia 12%; dysarthria 12%; and gait disturbance 12%.

KINETIC Study treatment period Day 1 – Day 28

Sage-created innovation with potential to impact millions globally

Development plan has potential to be accelerated by strategic collaboration with Biogen

MID-TERM

LONG-TERM

Essential Tremor

Parkinson's Disease

Epilepsies

Other movement and neurological disorders

2021

	Early	Mid	Late	*Early:Q1-Q2; Mid:Q2-Q3; Late: Q3-Q4
NEUROLOGY FRANCHISE				**Expected milestones:**
SAGE-324	✓			Report topline data from KINETIC Study in essential tremor
			●	Initiate placebo-controlled Phase 2 study in essential tremor to explore dose and frequency
SAGE-689			●	Complete Phase 1 SAD study

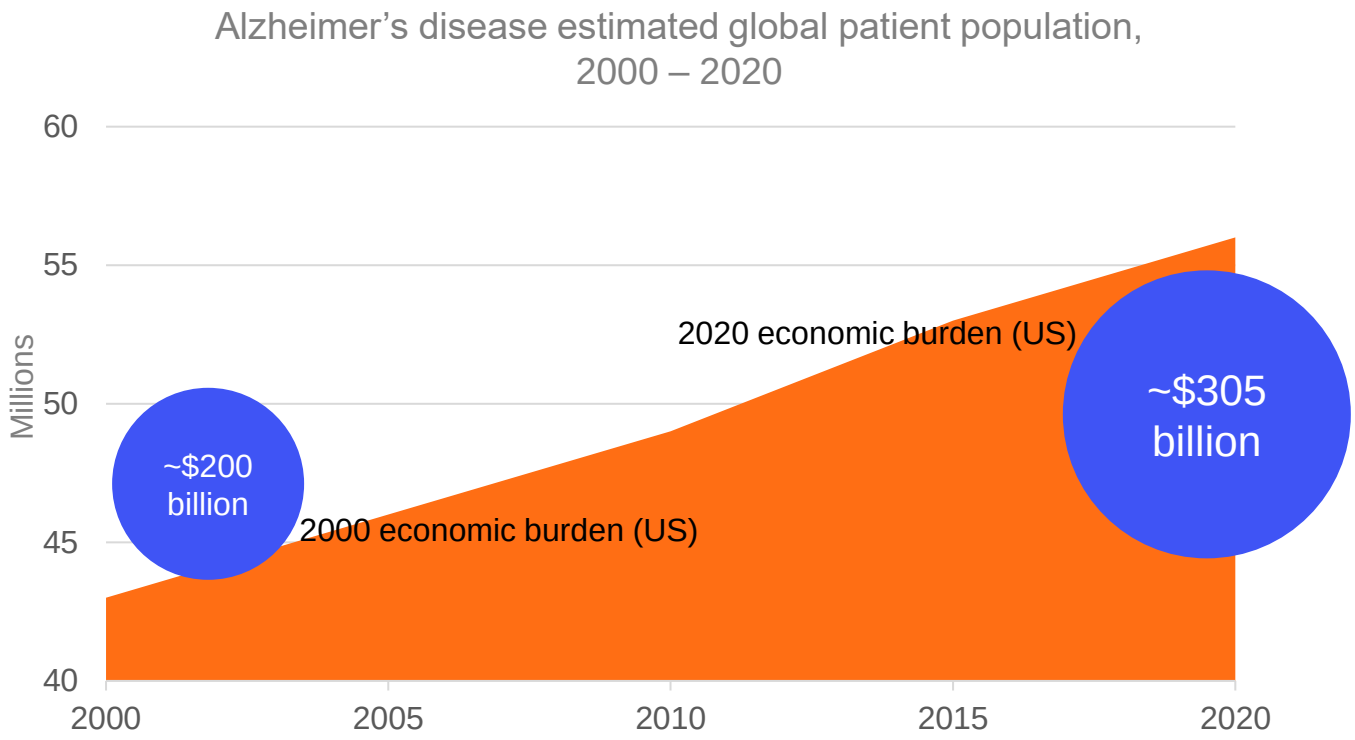
Sage Therapeutics™ Biogen

Neuropsychiatry Franchise

Neuropsychiatric Disorders

Dearth of innovative treatments approved for disorders of cognition

- Globally, disorders involving cognitive dysfunction continue to increase and are one of the greatest areas of unmet need
  - Currently available treatments are limited in efficacy
- People with cognitive impairment report:
  - Executive deficits: multi-tasking, organization, planning, working memory
  - Difficulty concentrating
  - Memory loss
- Significant impact on patient ability to work, live independently, adhere to medical care, and interact with family



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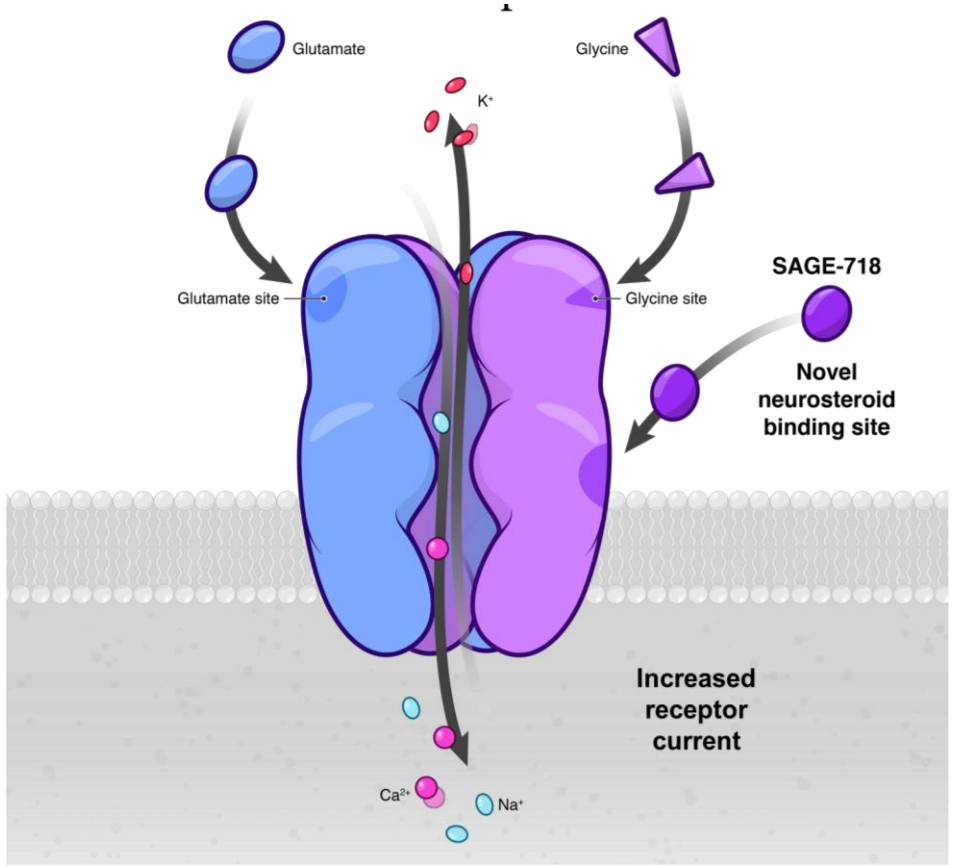
BLS CPI (Consumer Price Index) Calculator was used to estimate 2000 and 2020 economic burden using U.S. specific studies in respect to the indications noted.

Re-thinking Treatment of Neuropsychiatric Disorders

Sage has developed a robust library of NMDA receptor modulators

- NMDA receptors play a critical role in the process of neuroplasticity and are important in a host of cognitive, learning and behavioral processes
  - NMDA receptor function can be reduced by disease and declines during aging
- NMDA positive allosteric modulators (PAMs) may have potential to address disorders of cognition & behavior across the lifespan:
  - Neurodegenerative disorders
  - Neurodevelopmental disorders
  - Disorders requiring recovery or rehabilitation of cognitive function
- Sage has developed a library of novel, wholly-owned, NMDA modulators with unique profiles, including SAGE-718
- Biomarkers identified by Sage may inform development

Endogenous & Exogenous Ligands at the NMDA Receptor



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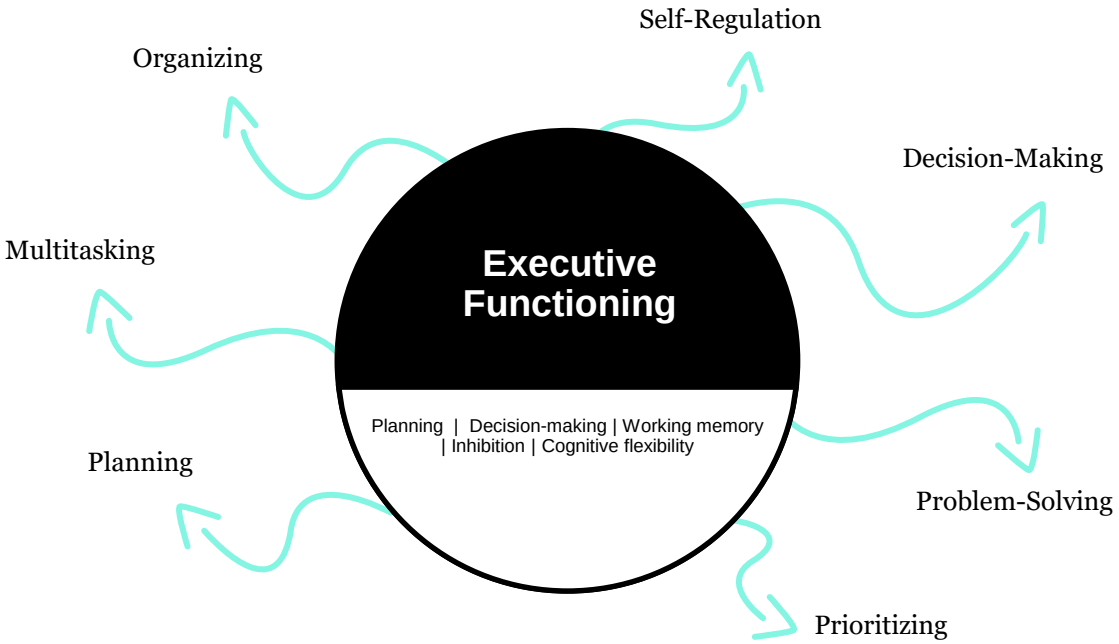
SAGE-718: Improving cognitive and executive function

Potential to provide unique cognitive benefits for patients with neurodegenerative disorders

- SAGE-718 profile well-suited for study of potential to benefit executive function in patients with neurodegenerative disorders:
  - Clinical findings from Phase 1 studies suggest potential to improve executive function, a key component of brain health across life-span
- Ongoing exploration in areas of cognitive dysfunction in diseases with high unmet need, including Alzheimer's, Parkinson's, and Huntington's disease
- Five Phase 1 studies to date and one Phase 2 open-label study – generally well-tolerated and with meaningful activity suggesting potential in brain health disorders



SAGE-718 Data Suggest Potentially Transformational Activity in the Brain

- A suite of three experimental medicine studies was designed to investigate CNS-target engagement using a low-dose ketamine challenge paradigm

- Results from an integrated data analysis from all three studies demonstrate that SAGE-718:
  - Had effects on electrophysiological, functional imaging and cognitive endpoints in healthy volunteers consistent with CNS activity
  - Modulated the effects of ketamine on regional and global measures of resting brain activity indicating functional interaction with NMDA receptors

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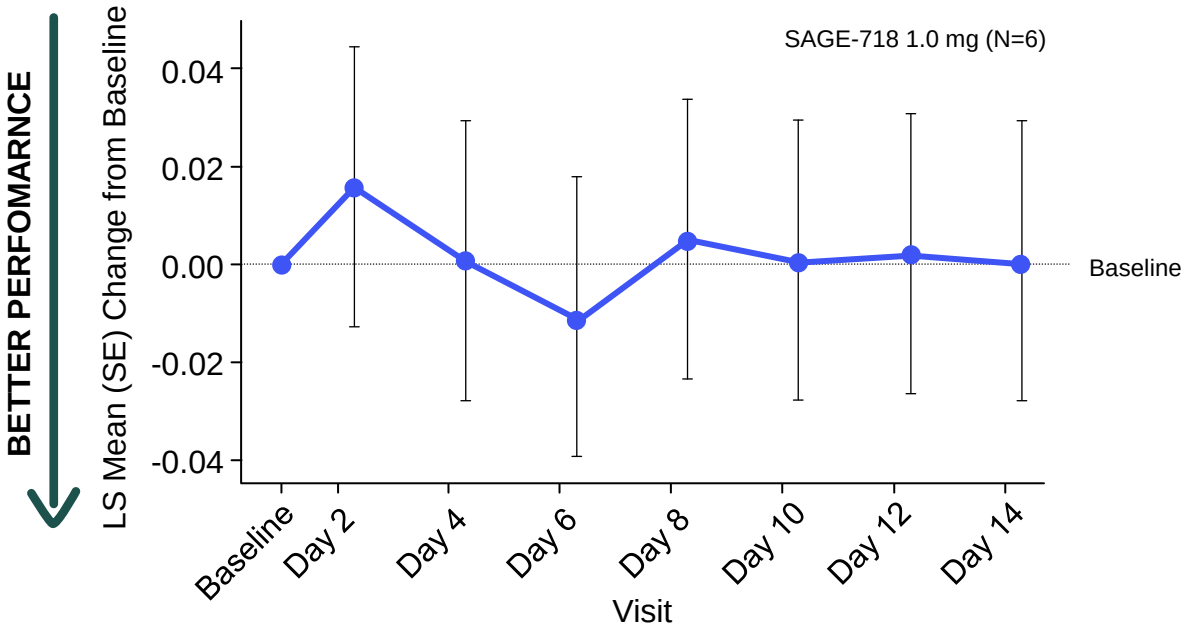
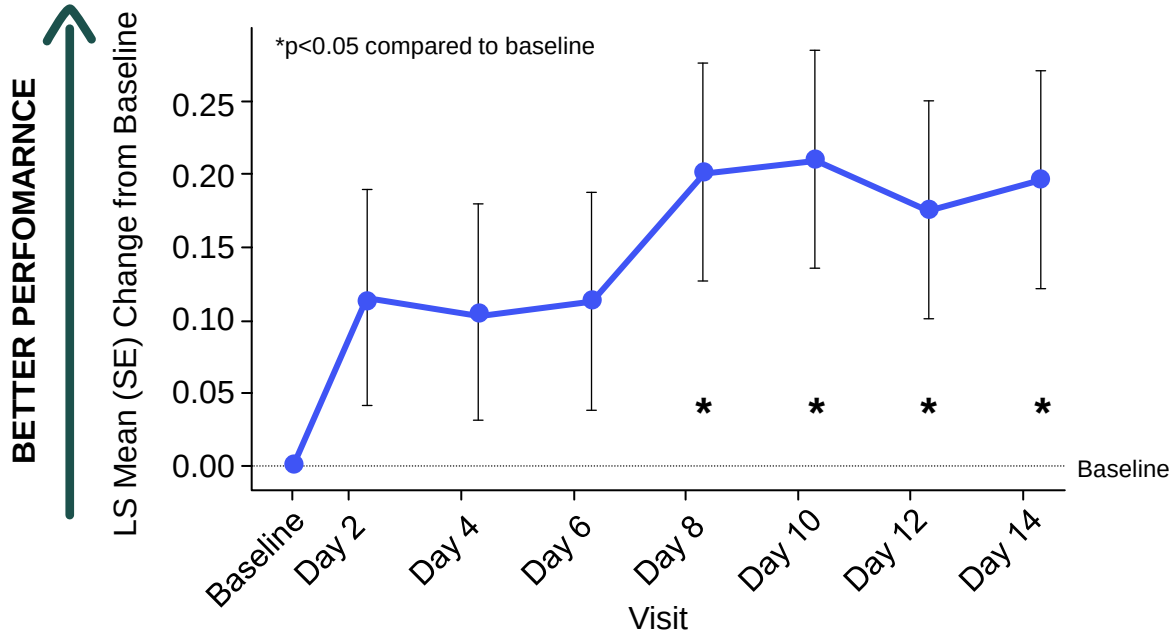
Cognitive Performance in Patients w/ Early HD Treated with Open-Label Sage-718 Over 2 Weeks

Detection Task



Two-Back Test



VARIABLE	MEAN (SD)	RANGE
Total Functional Capacity	11.3 (2.87)	(7, 13)
Baseline MoCA	23.3 (4.99)	(16, 27)
UHDRS Motor Score	7.5 (5.26)	(0,12)

Subjects had mild to moderate disease (HD1 or HD2, defined by TFC) and cognitive impairment at baseline

In Phase 1 studies of SAGE-718 no serious adverse events or deaths have occurred, and most treatment-emergent adverse events have been mild in severity.

PARADIGM Study Results
SAGE-718 Demonstrated Improvement on Multiple Tests of Executive Function and Learning and Memory

- In the Phase 2a open-label PARADIGM Study, eight patients aged 50 to 75 years old with mild cognitive impairment due to Parkinson's disease received SAGE-718 3 mg daily for 2-weeks.
- Patients showed performance improvements from baseline on multiple tests in the cognitive domain of executive function during the 14 days of treatment.
- Emerging signals on several measures also suggested improved performance from baseline on additional cognitive tests in the domains of learning and memory over a similar timeframe.
- SAGE-718 was generally well tolerated; there were no serious adverse events, and no treatment emergent adverse events were determined to be related to SAGE-718.
- As expected, and due to its unique profile, in certain tests of attention and psychomotor speed SAGE-718 demonstrated neutral results. Other classes of medicines, including amphetamines, have been shown to alter simple attention or reaction time but not improve cognitive attributes.
- Sage has dosed the first patient in a new 4-week dosing cohort in the PARADIGM study to gather additional data in the PD patient population.

Sage Therapeutics™

NMDA PAM

Sage-created innovation with potential to impact millions globally

Cash position provides resources for acceleration of plans for internal pipeline, including SAGE-718

MID-TERM

LONG-TERM

Parkinson's Disease Cognitive Dysfunction

Alzheimer's Disease Cognitive Dysfunction

Huntington's Disease Cognitive Dysfunction

Other conditions with impaired cognitive/executive dysfunction

2021

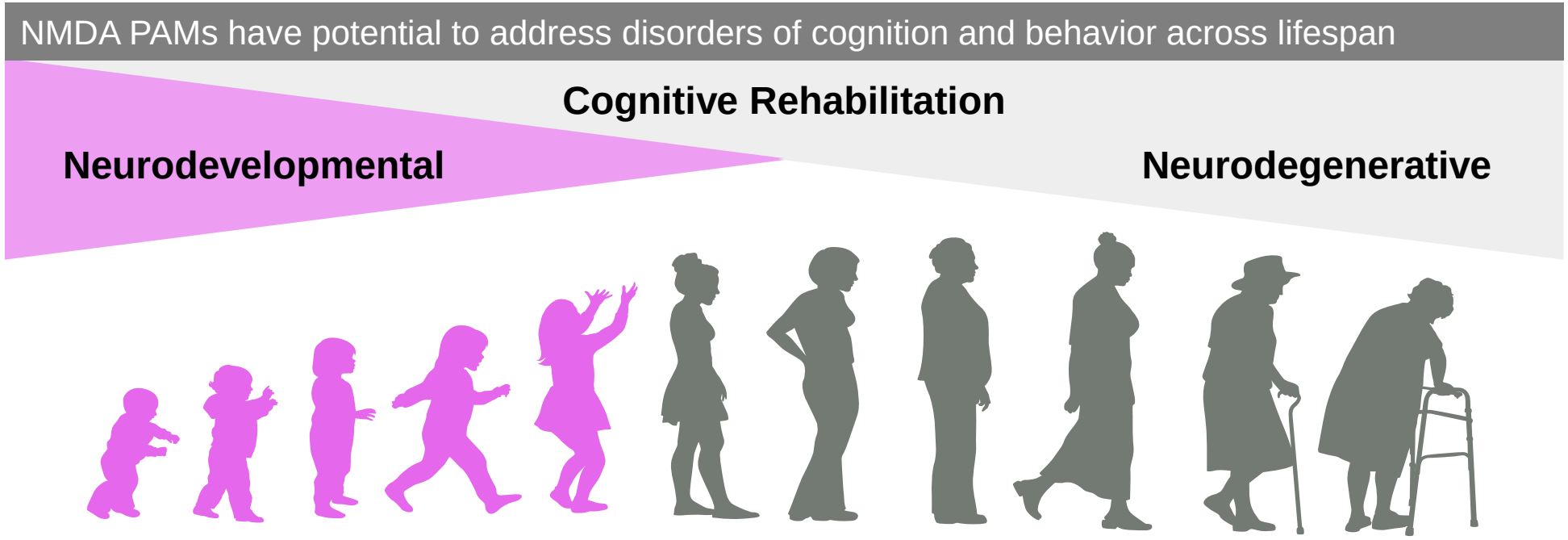
	Early	Mid	Late	*Early:Q1-Q2; Mid:Q2-Q3; Late: Q3-Q4
NEUROSPYCHIATRY FRANCHISE				**Expected milestones:**
SAGE-718	✓			Report topline data from PARADIGM Study in Parkinson's disease cognitive dysfunction
			●	Report topline data from LUMINARY Study in Alzheimer's disease mild cognitive impairment and mild dementia
			●	Initiate placebo-controlled Phase 2 study in early to moderate HD
SAGE-904			●	Complete Phase 1 SAD/MAD studies

Sage Therapeutics™

Sage proprietary product engine

SAGE-904: Differentiated NMDA PAM profile

Pharmacological profile suited for study in neurodevelopmental therapeutics



- SAGE-904 designed for potential use as ***neurodevelopmental*** therapy
- Druglike profile supporting once-daily, oral, chronic dosing
- Phase 1 studies to inform selection of development path

SAGE-689: Rapid acting, intramuscular GABA PAM

Multiple opportunities in diseases with high unmet need

- Potent preclinical anxiolytic and anticonvulsant activity
- Rapid absorption and good bioavailability following *intramuscular* administration
- Planned Phase 1 translational studies designed to accelerate specific indication selection
- Formulation flexibility and high intrinsic solubility enables multiple potential pathways based on patient needs
  - Acute use with faster onset may provide opportunities in areas like agitation or social anxiety

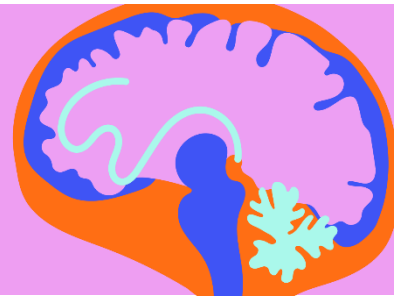
Continuing Innovation with the GABA and NMDA platforms

Preclinical profile of SAGE-319
GABA PAM

- Extra-synaptic $GABA_A$ receptor preferring positive allosteric modulator
- Profile supporting daily, oral, chronic dosing
- Differentiated preclinical EEG signature compared to SAGE-217 and SAGE-324

Potential indications:
DISORDERS OF SOCIAL INTERACTION

Preclinical profile of SAGE-421
NMDA PAM



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

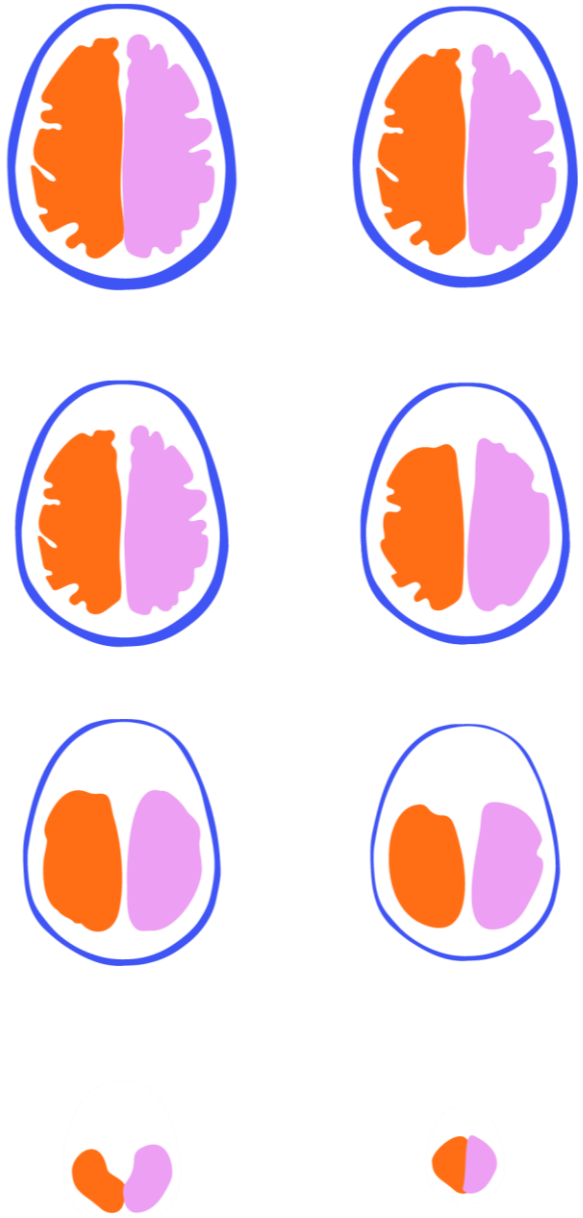
Potential indications:
NEURODEVELOPMENTAL DISORDER

Sage Therapeutics™

Proactive, predictive and productive drug development approach:

Enables product engine and potential portfolio expansion into diseases with high unmet needs

- Sage is a leader in NAS and oxysterol chemistry with >8K compound library and >800 issued patents and patent applications globally
- Focus on understanding how to modify circuitry that impacts brain function at the network level
- Robust engine for turning early ideas into clinical proof-of-concept rapidly



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Second Quarter 2021 Financial Results

Strong financial position with over $1.9B in cash

Item	Q2 '21	Q2 '20
Revenue - *Zulresso*	*$1.6M*	*$1.1M*
R&D Expense	$66.2M	$73.3M
SG&A Expense	$43.3M	$38.2M
Cost of Goods Sold	$0.1M	$0.1M
Restructuring	-	$28.4M
Total Operating Costs and Expenses	$109.7M	$140.1M
Net Loss	($107.2M)	($136.3M)
Cash and Marketable Securities	$1.9B	$0.8B

- Sage anticipates a cash balance of more than $1.7 billion at end of 2021
- The Company does not anticipate milestone payments from collaborations in 2021

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Anticipated 2021 Milestones

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

	Early	Mid	Late	
DEPRESSION FRANCHISE				
Zuranolone (Sage-217)		✓		Report topline data from WATERFALL Study in major depressive disorder (1H21)
		✓		Report full data from SHORELINE Study 30 mg cohort in major depressive disorder
			●	Report topline data from CORAL Study for rapid response treatment
			●	Report topline data cut from SHORELINE Study 50 mg cohort in major depressive disorder
NEUROLOGY FRANCHISE				
SAGE-324	✓			Report topline data from KINETIC Study in essential tremor
			●	Initiate placebo-controlled Phase 2 study in essential tremor to explore dose and frequency
NEUROSPYCHIATRY FRANCHISE				
SAGE-718	✓			Report topline data from PARADIGM Study in Parkinson's disease cognitive dysfunction
			●	Report topline data from LUMINARY Study in Alzheimer's disease mild cognitive impairment and mild dementia
			●	Initiate placebo-controlled Phase 2 study in early to moderate HD
EARLY DEVELOPMENT				
SAGE-689			●	Complete Phase 1 SAD study
SAGE-904			●	Complete Phase 1 SAD/MAD studies
OTHER DEVELOPMENT OPPORTUNITIES				
Brexanolone			●	Report data from study in COVID-19 related acute respiratory distress syndrome
Product Engine		**By 2023**		Capable of delivering 2+ IND-enabling compounds per year

Sage is a leader in brain health – *making medicines that matter*

Disciplined execution in 2020 created strong foundation for near, mid, and long-term value-creation potential for patients and shareholders

Leading brain health pipeline spanning three core franchises, each with differentiated assets with goal of delivering two or more IND-enabling compounds per year, starting in 2023

Catalyst rich 2021 includes meaningful data flow across all franchises

Expertise in place to focus on successful patient access and global commercial execution if product candidates are approved

Financial flexibility enables continued investment in innovation, with mission of creating top-tier biopharma in 5 years

Sage Therapeutics™

Appendix

Brain Health Disorders — Global Healthcare Challenge

In 10 years, Sage has expanded the potential for solutions and through collaborations expects to further accelerate and expand estimated patient reach

18M
Sage

22M
Sage + Shionogi

>450M
Sage + Shionogi + Biogen
+ potential acceleration of Sage proprietary programs

- Huntington's Disease
- Alzheimer's Disease and other Dementias
- Epilepsy
- Treatment Resistant Depression
- Bipolar Depression
- General Anxiety Disorder
- Parkinson's Disease
- Essential Tremor
- Postpartum Depression
- Major Depressive Disorder

Shionogi Collaboration

2020 Biogen Collaboration

Sage Therapeutics™

Strategic Zuranolone Collaboration with Shionogi

- **Expansion of Global Footprint**
  - Goal of collaboration to accelerate development of a potentially groundbreaking medicine to patients in key Asian markets
  - Sage maintains exclusive rights to develop and commercialize zuranolone outside of those geographies
- **Expert Partner in Key Asian Markets**
  - Shionogi is responsible for clinical development and commercialization of zuranolone in Japan, Taiwan, and South Korea
  - Shionogi has strong presence in Asia in developing & commercializing therapeutics for CNS disorders
- **Attractive Terms**
  - Sage to receive tiered royalties on sales averaging in the greater than 20% range, if commercialized
  - Shionogi has also granted Sage certain rights to co-promote zuranolone in Japan across all indications

Sage Therapeutics™ + SHIONOGI

$90M

Upfront payment

$485M

Potential development & commercial milestones

Strategic Zuranolone and SAGE-324 Collaboration with Biogen

- **50:50 joint development and commercialization of zuranolone and SAGE-324 in the United States**
  - Opportunity to expand the number of indications, patient impact and thereby the commercial value of zuranolone and SAGE-324, assuming successful development
- **Enables expansion and acceleration of pipeline**
  - Financial and operational flexibility from collaboration allows Sage to fully evaluate the potential of existing programs and fuels product engine enabling continued identification and development of product candidates
- **Attractive terms, with potential total deal value of more than $3.1 billion**
  - Sage to receive tiered royalties on sales outside of the United States in the high teens to low twenties percentage if commercialized
  - 50:50 cost and profit sharing within the United States

Sage Therapeutics™ + Biogen®

$1.5B

Upfront payment and equity investment

$1.6B

Potential development & commercial milestones

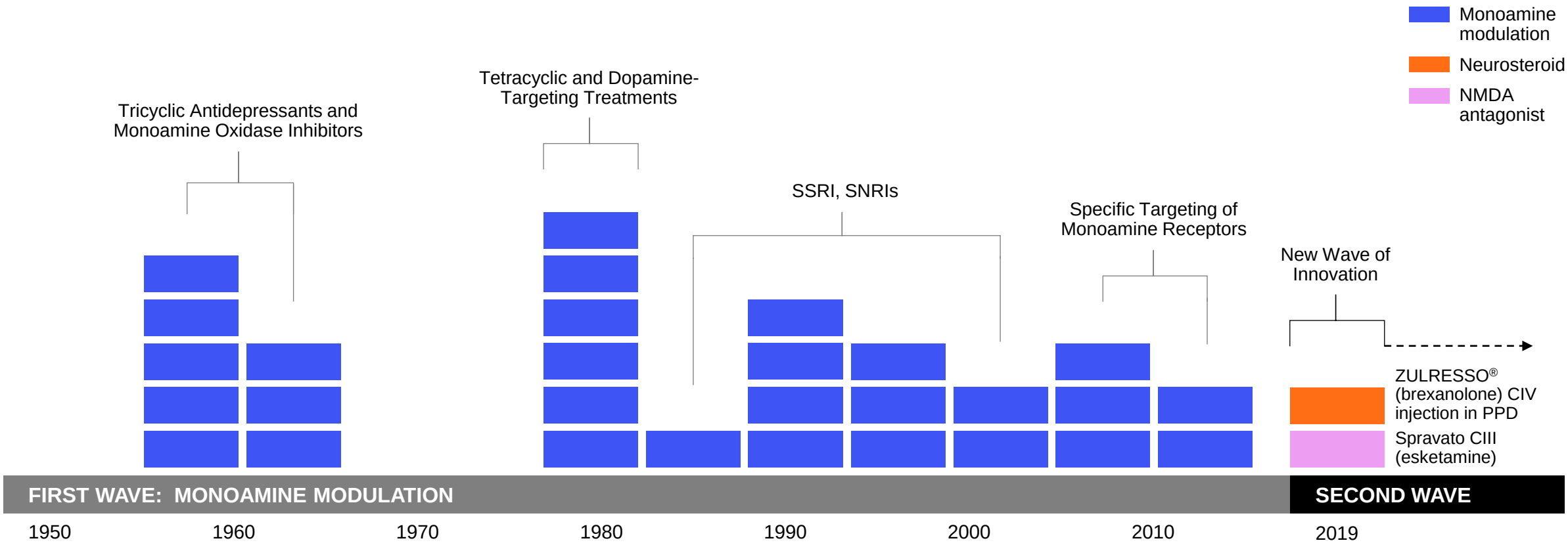
Clinical Relevance of Delta from Placebo in Clinical Trials

- A paper published in the *Journal of Psychopharmacology* suggests that using HAMD-17 delta from placebo-controlled trials as an estimation of the clinical relevance of antidepressant treatment may be misleading.
- In randomized controlled clinical trials (RCTs) placebo groups tend to have a greater response than watchful waiting in real life.
- Similarly, there is a blunting effect on the antidepressant response in RCTs.
- Therefore, the outcome difference between being treated with antidepressant versus watchful waiting or treatment as usual in daily practice is likely to be much larger than that between antidepressant versus placebo within RCTs.

Hegerl, U., & Mergl, R. (2009). The clinical significance of antidepressant treatment effects cannot be derived from placebo-verum response differences. Journal of Psychopharmacology, 24(4), 445–448. https://doi.org/10.1177/0269881109106930

Sage Leading Second Wave of Neuropsych Innovation

First new MOA in 60 years



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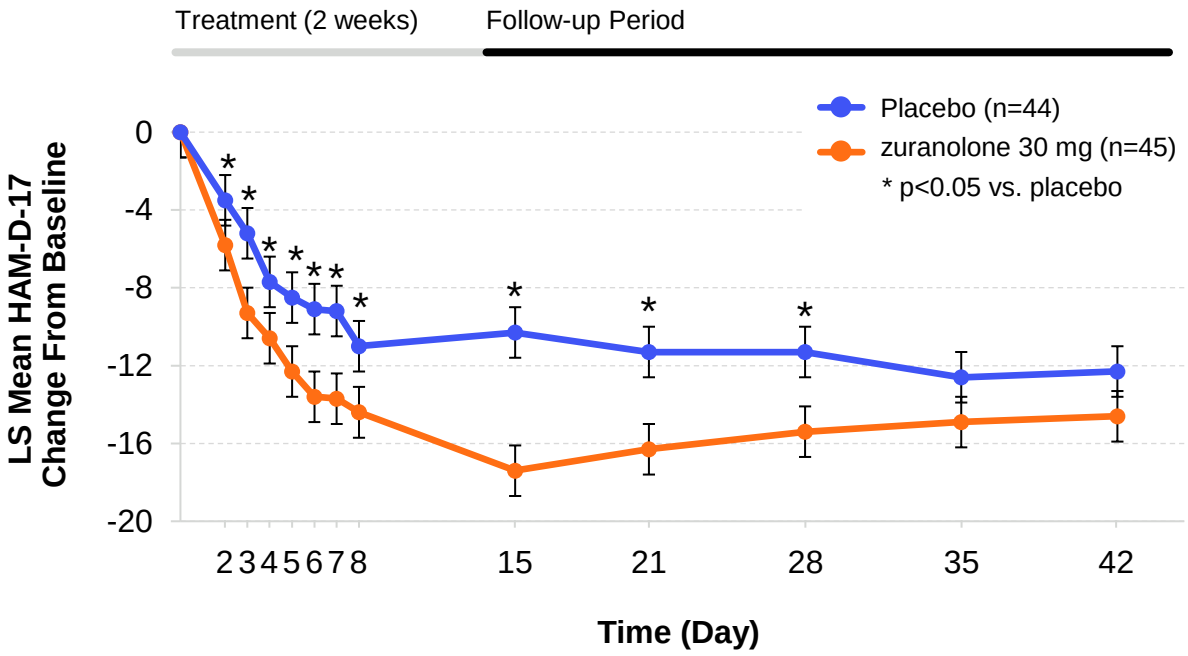
Source: Thomas, D., & Wessel, C. (2017). The State of Innovation in Highly Prevalent Chronic Diseases: Volume I: Depression Therapeutics. BIO.

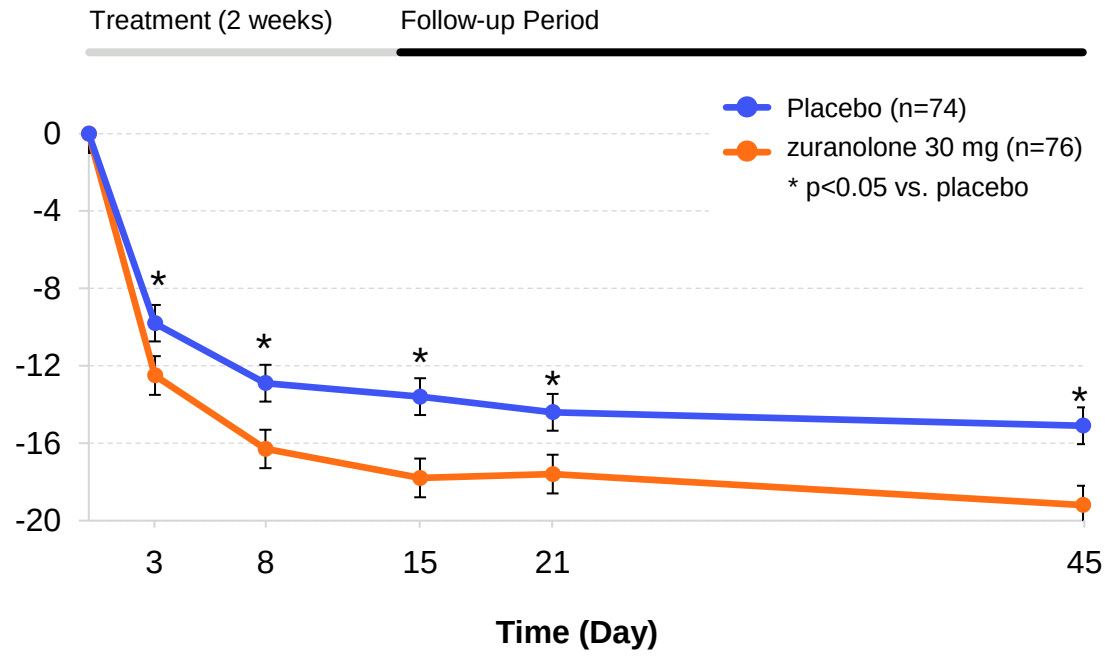
MDD-201 & ROBIN Studies

Rapid onset of activity with generally well-tolerated safety profile

MDD-201



ROBIN (PPD-201)



Zuranolone was generally well-tolerated in both studies

The most common AEs (≥5%) in the MDD-201 study included headache, dizziness, nausea, and somnolence

The most common AEs (≥5%) in the PPD-201 study included somnolence, headache, dizziness, upper respiratory tract infection, diarrhea, and sedation

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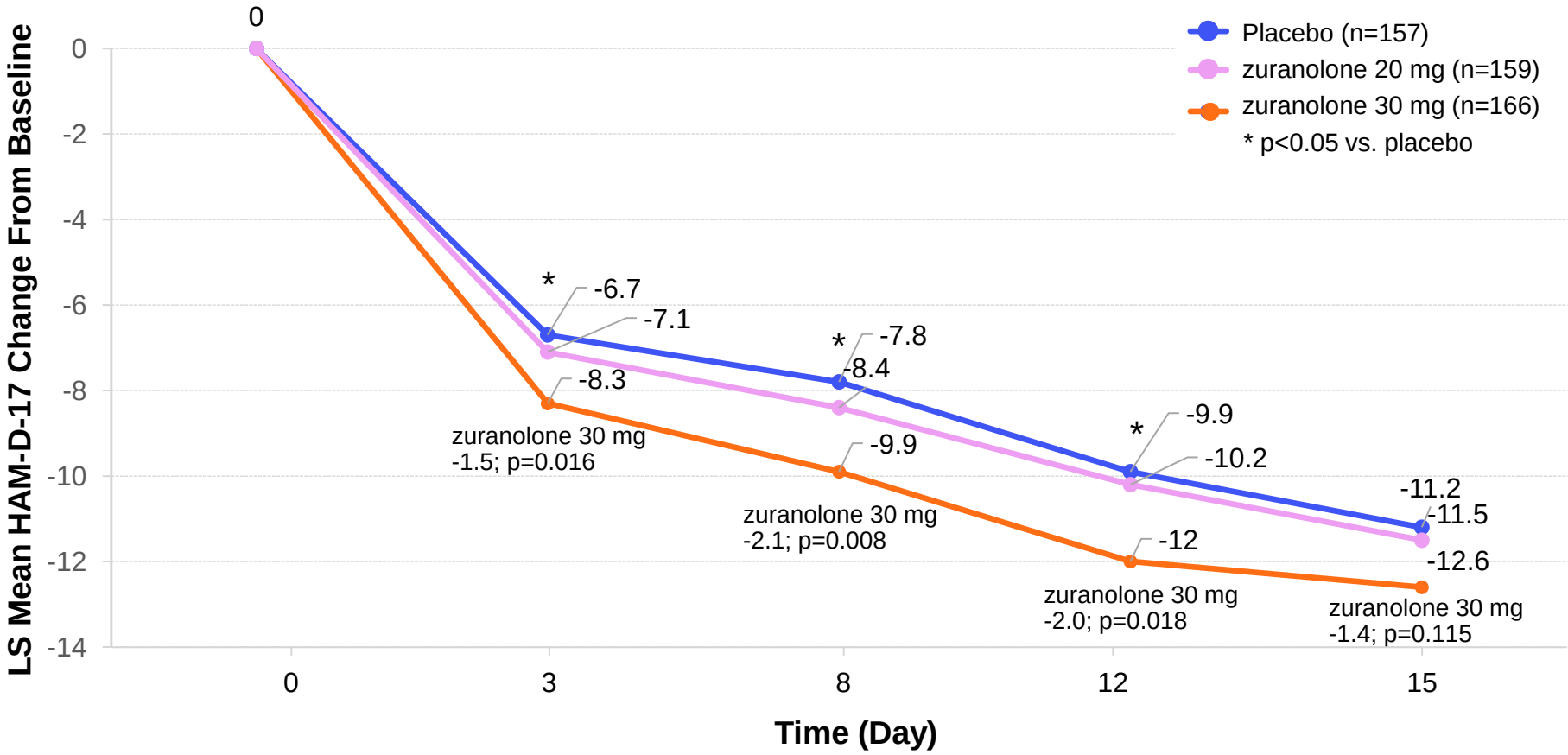
Abbreviations: AEs = adverse events

MOUNTAIN (MDD-301) Study

Displayed rapid, robust onset similar to prior pivotal studies



Zuranolone was generally well-tolerated in the study

The most common AEs (≥5%) included headache dizziness, somnolence, fatigue, diarrhea, sedation and nausea

Rapid onset of effect for zuranolone 30 mg was seen beginning at Day 3 with maintenance of effect through Day 15; statistical separation from placebo observed Days 3 – 12 although primary endpoint at Day 15 was not met

Sage Therapeutics™

Abbreviations: AEs: = adverse events

ZULRESSO® (brexanolone) CIV Injection

Commercial efforts primarily focused on geographies that have existing, active treating sites

- **Support in existing geographies:** Primary focus on working with healthcare providers and supporting women with PPD in geographies with active ZULRESSO treating sites

- **Customized case management:** Sage Central, Sage's national patient support center, continuing to provide customized case management support to women with PPD

SAGE CENTRAL™
PATIENT SUPPORT

Please see Boxed Warning and Important Safety Information

ZULRESSO is only available at certified healthcare settings through a restricted program called the ZULRESSO REMS due to the risk of serious harm resulting from excessive sedation or sudden loss of consciousness

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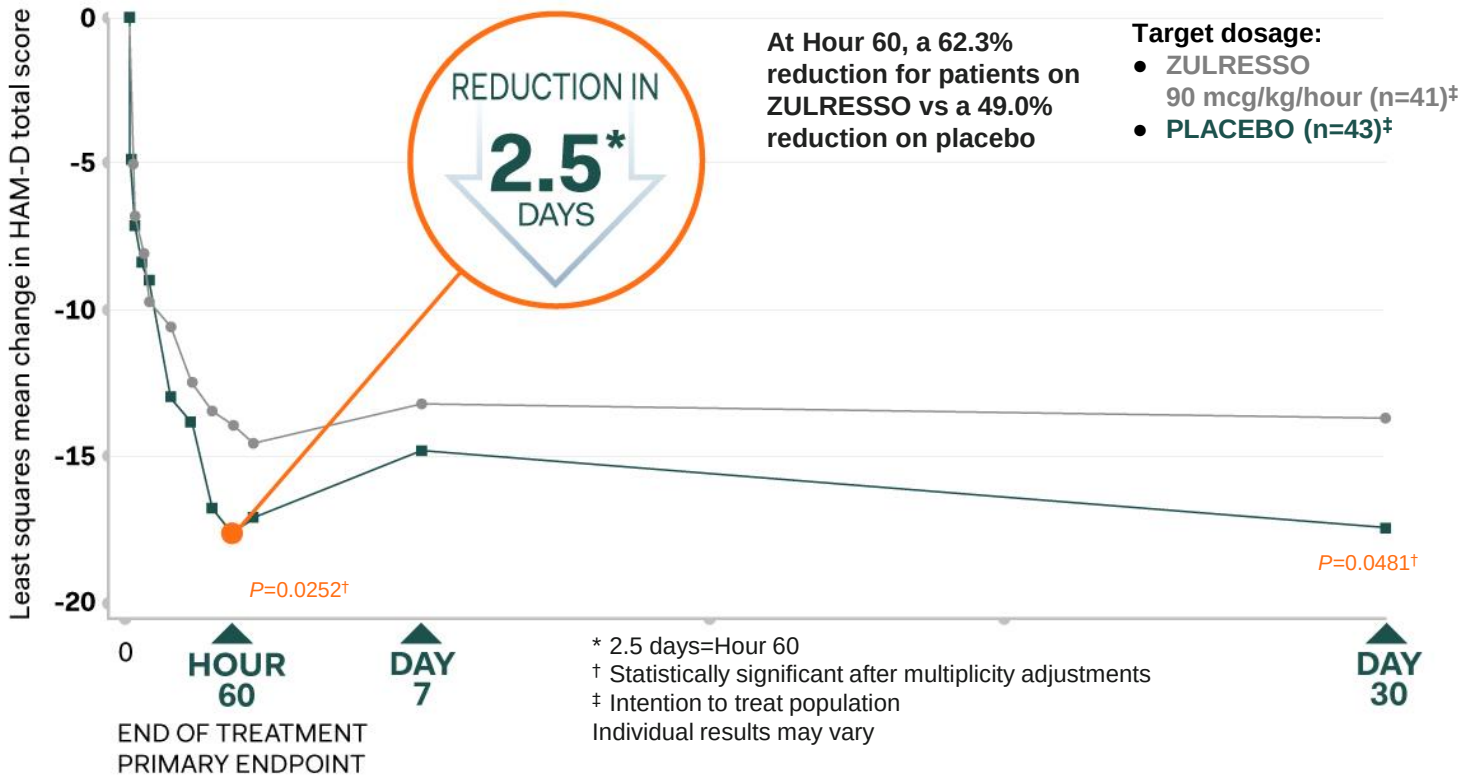
ZULRESSO® (brexanolone) CIV Injection

Treated patients experienced rapid improvement of depressive symptoms

Change from baseline in HAM-D total score over time in Study 1 with the recommended target dosage of ZULRESSO (90 mcg/kg/h)[i,ii]



Durable therapeutic effect

A prespecified secondary efficacy endpoint was the mean change from baseline in HAM-D total score at Day 30[i]

In Study 1, significantly greater symptom reduction vs placebo was observed at Day 30[i,ii]

In Study 2, the 90 mcg/kg/hour arm maintained therapeutic effect at Day 30, but did not show a greater reduction vs placebo

The most common adverse reactions (incidence of ≥5% and at least twice the rate of placebo):

- Sedation/somnolence
- Dry mouth
- Loss of consciousness
- Flushing/hot flush

ZULRESSO is only available through the ZULRESSO Risk Evaluation and Mitigation Strategy (REMS), a safety program to manage the risk of serious harm resulting from excessive sedation and sudden loss of consciousness during the ZULRESSO infusion. To administer ZULRESSO, sites of care must be certified in the ZULRESSO REMS[iii]

Please see full Prescribing Information, including Boxed Warning available with this presentation

Sage Therapeutics™

Sources: i. ZULRESSO Prescribing Information. Cambridge, MA: Sage Therapeutics, Inc., ii. Meltzer-Brody S et al. Lancet. 2018;392(10152):1058-1070, iii. ZULRESSO REMS. https://zulressorems.com/#Public

ZULRESSO® (brexanolone) CIV Injection
Boxed warning

WARNING: EXCESSIVE SEDATION AND SUDDEN LOSS OF CONSCIOUSNESS

See full prescribing information for complete boxed warning.

- Patients are at risk of excessive sedation or sudden loss of consciousness during administration of ZULRESSO. (5.1)
- Because of the risk of serious harm, patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring. Patients must be accompanied during interactions with their child(ren). (5.1)
- ZULRESSO is available only through a restricted program called the ZULRESSO REMS. (5.1, 5.2)

ZULRESSO® (brexanolone) CIV injection

Select Important Safety Information

These are not all the side effects of ZULRESSO.

ZULRESSO can cause serious side effects, including:

- **Excessive sedation and sudden loss of consciousness.** ZULRESSO may cause you to feel very sleepy (excessive sedation) or pass out (loss of consciousness). Your healthcare provider should check you for symptoms of excessive sleepiness every 2 hours while you are awake.
  - During your infusion, tell your healthcare provider right away if you feel like you cannot stay awake during the time you are normally awake or if you feel like you are going to pass out. Your healthcare provider may lower your dose or stop the infusion until symptoms go away
  - You must have a caregiver or family member with you to help care for your child(ren) during your infusion
- Because of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness, ZULRESSO is only available through a restricted program called the ZULRESSO REMS.

ZULRESSO can cause other serious side effects, including:

- **Increased risk of suicidal thoughts or actions.** ZULRESSO and other antidepressant medicines may increase suicidal thoughts and actions in some people 24 years of age and younger. **Pay close attention to and tell your healthcare provider right away if you have any of the following symptoms, especially if they are new, worse, or worry you:**
  - Attempts to commit suicide, thoughts about suicide or dying, new or worse depression, other unusual or sudden changes in behavior or mood
  - Keep all follow-up visits and call your healthcare provider between visits as needed, especially if you have concerns about symptoms.

The most common side effects of ZULRESSO include:

- Sleepiness, dry mouth, passing out, flushing of the skin or face.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Before receiving ZULRESSO, tell your healthcare provider about all your medical conditions including if you drink alcohol, have kidney problems, are pregnant or think you may be pregnant, or are breastfeeding or plan to breastfeed. It is not known if ZULRESSO will harm your unborn baby. If you become pregnant during treatment, talk with your healthcare provider about enrolling with the National Pregnancy Registry for Antidepressants at 1-844-405-6185.

While receiving ZULRESSO, avoid the following:

- Driving a car or doing other dangerous activities after your ZULRESSO infusion until your feeling of sleepiness has completely gone away
- Do not drink alcohol

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

Especially tell your healthcare provider if you take other antidepressants, opioids, or Central Nervous System (CNS) depressants (such as benzodiazepines).

Please see the patient Medication Guide, including information about serious side effects, for ZULRESSO in the full Prescribing Information.

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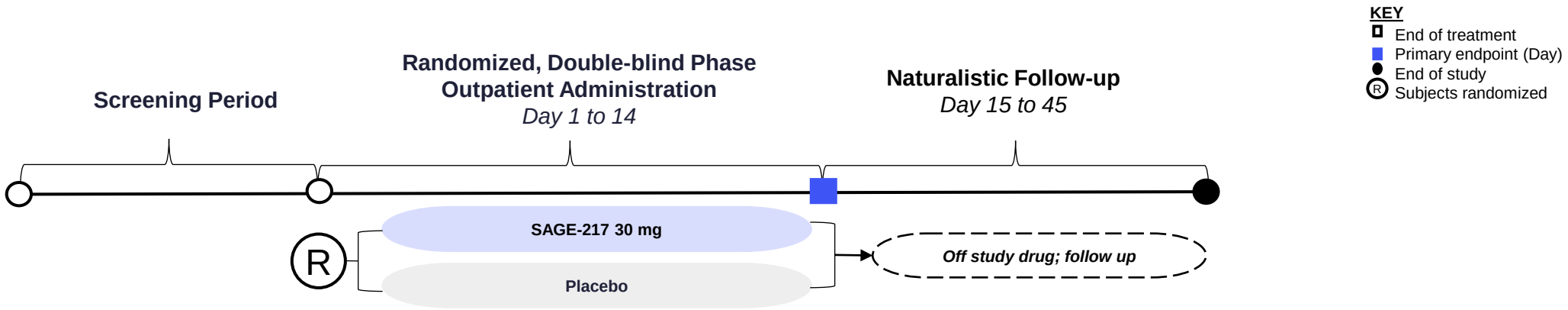
Study Design:

Completed Studies

Completed SAGE-217 Studies

Pivotal Ph. 2 in PPD (ROBIN; PPD-201)



STUDY OVERVIEW

Arms	Randomization: 1:1 • SAGE-217 30 mg • Placebo	**Key Inclusion Criteria**	• Major Depressive Episode that began no earlier than the third trimester and no later than the first 4 weeks following delivery, as diagnosed by the SCID-I • Subject is ≤ six months postpartum • Ceased lactating at screening or, if still lactating or actively breastfeeding at screening, must agree to temporarily cease giving breast milk to her infant(s)	**Primary Endpoint**	• Change from baseline in HAM-D total score*

Dosing Regimen	2-week, once-nightly	**Key Exclusion Criteria**	• Active psychosis
			• Attempted suicide associated with current episode of PPD (Note, suicidal ideation is not an exclusion; other protocol-defined inclusion/exclusion criteria may apply)
			• Medical history of seizures, bipolar disorder, schizophrenia, and/or schizoaffective disorder
				Secondary Endpoints	• Safety and tolerability compared with placebo as assessed by:
					  • Incidence of AEs, vital signs, clinical laboratory evaluations, ECG parameters**
					  • C-SSRS**

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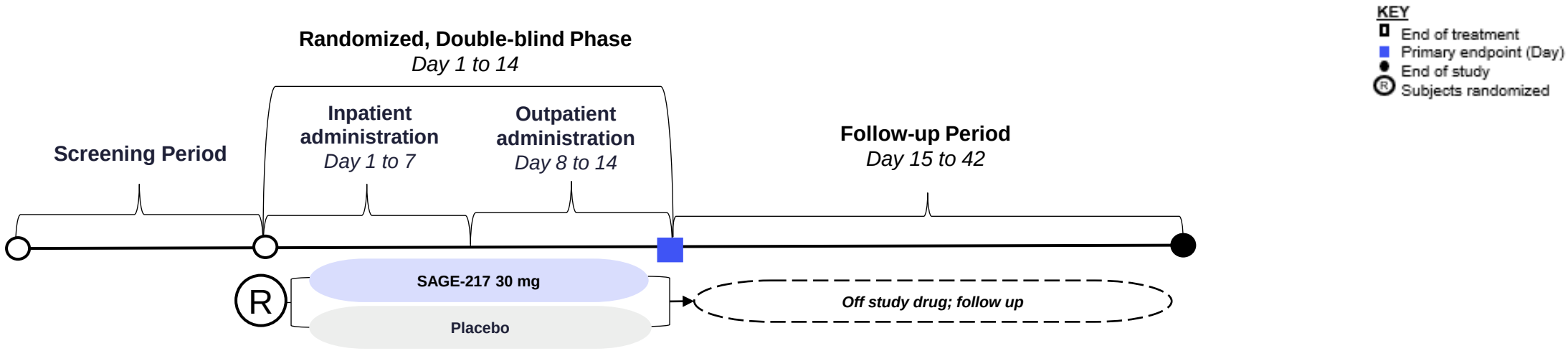
*During double-blind phase; **During double-blind and follow-up periods |NCT02978326. Available from: clinicaltrials.gov [accessed November 2019]

Completed SAGE-217 Studies

Pivotal Ph. 2 in MDD (MDD-201)



STUDY OVERVIEW

Arms	Randomization: 1:1 • SAGE-217 30 mg • Placebo	**Inclusion Criteria**	• Diagnosis of MDD with symptoms that have been present for at least a 4-week period	**Primary Endpoint**	• Change from baseline in HAM-D*
Dosing Regimen	2-week, once-nightly	**Exclusion Criteria**	• History of suicide attempt • Active psychosis • Medical history of seizures, bipolar disorder, schizophrenia, and/or schizoaffective disorder • History of treatment-resistant depression, defined as persistent depressive symptoms despite treatment with adequate doses of antidepressants from two different classes for an adequate amount of time	**Secondary Endpoints**	• Safety and tolerability of SAGE-217 as assessed by: ○ Frequency and severity of AE/SAE** ○ Physical examination** ○ Clinical laboratory measures, vital signs, electrocardiograms, suicidal ideation using C-SSRS* ○ Stanford Sleepiness Scale (SSS) score* • Reduction in depressive symptoms, compared to placebo, as assessed by: ○ Change in the 17-item HAM-D total score from baseline at all time points** ○ HAM-D response, HAM-D remission** ○ Change from baseline in MADRS total score, HAM-A total score, at Day 15 and all other time points** ○ HAM-D subscale and individual item scores at all time points** ○ CGI-I response**

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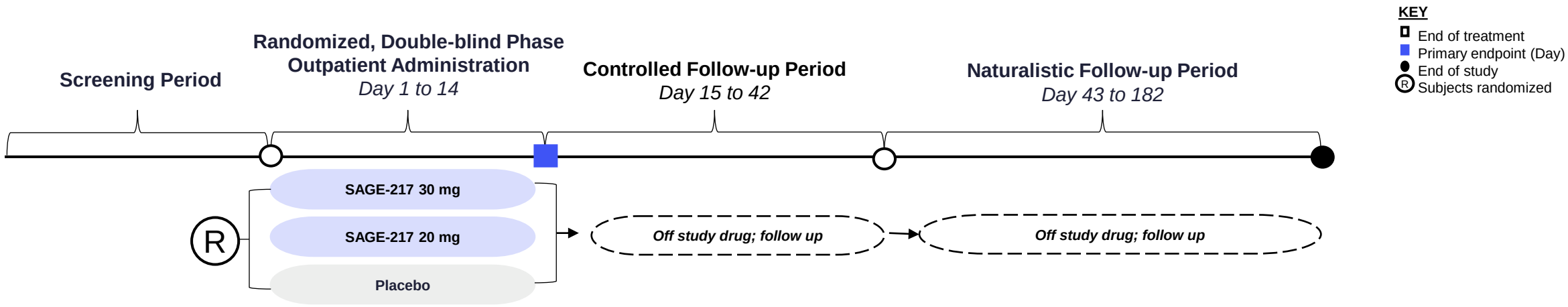
*During double-blind phase; **During double-blind and follow-up periods | NCT03000530. Available from: clinicaltrials.gov [accessed November 2019]

Completed SAGE-217 Studies

Phase 3 MOUNTAIN (MDD-301)



STUDY OVERVIEW

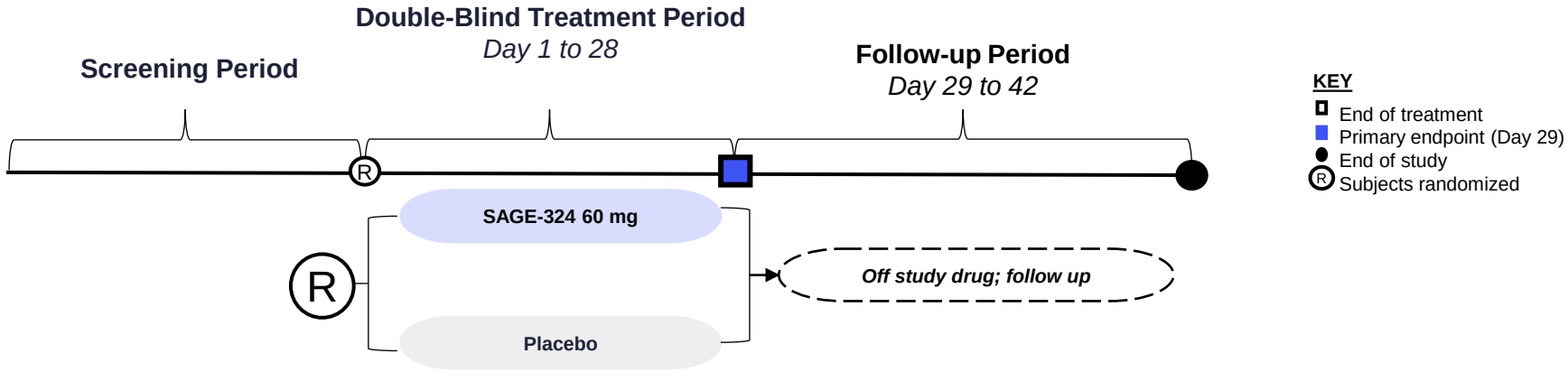
Status	Complete	**Inclusion Criteria**	• Diagnosis of MDD with symptoms that have been present for at least a 4-week period • MADRS total score ≥32 and HAM-D total score ≥22 at screening and Day 1 (prior to dosing)
Indication	MDD		
Phase	Phase 3	**Exclusion Criteria**	• Active psychosis • Attempted suicide associated with the current episode of MDD • Medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder
Start/End Date* *topline data announced	Sep. 2018; Dec. 2019		
Arms	Double-blind, randomized: 1:1:1 • SAGE-217 20 mg, SAGE-217 30 mg, placebo	**Primary Endpoint**	• Change from baseline in HAM-D total score*
Dosing Regimen	2-week, once-nightly	**Secondary Endpoints**	• Change from baseline in HAM-D, HAM-A*, MADRS, CGI-I, CGI-S** • Incidence and severity of AE/SAE**

Use of antidepressants, antianxiety or insomnia medications restricted during controlled follow-up period; however, these medications may be used during the naturalistic follow up period as indicated by clinical judgement of the Investigators

*During double-blind phase; **During double-blind and follow-up periods; NCT03672175. Available from: clinicaltrials.gov [accessed January 2020]

Completed SAGE-324

*Placebo-controlled **Essential Tremor** study - KINETIC (324-ETD-201)*



STUDY OVERVIEW

Status	Complete
Indication	Essential Tremor (ET)
Phase	Phase 2
Start/End Date	1Q 2020 / Apr. 2021
Arms	Double-blind, randomized: 1:1 • SAGE-324 60 mg: placebo
Dosing Regimen	28 days, once-daily

Inclusion Criteria	• Diagnosis of ET consisting of
	  • bilateral upper limb action tremor
	  • at least 3 years duration
	  • with or without tremor in other locations
	  • absence of other neurological signs, sudden onset or evidence of stepwise deterioration of tremor
	• Score of at least 1.5 for each TETRAS performance subscale part 4 items with total score for the dominant upper limb of at least 5.5

Exclusion Criteria	• Presence of known causes of enhanced physiological tremor • Recent exposure to tremorgenic drugs or presence of alcohol withdrawal state • Direct or indirect injury or trauma to the nervous system within 3 months before the onset of tremor • Previous procedure for the treatment of ET, deep brain stimulation, brain lesioning, or magnetic resonance guided procedure
Primary Endpoint	• Change from baseline in TETRAS performance subscale part 4 upper limb tremor score on Day 29
Secondary Endpoints	• Change from baseline in TETRAS performance subscale part 4 upper limb tremor score at all other timepoints • Change from baseline in Kinesia ONE accelerometer scores

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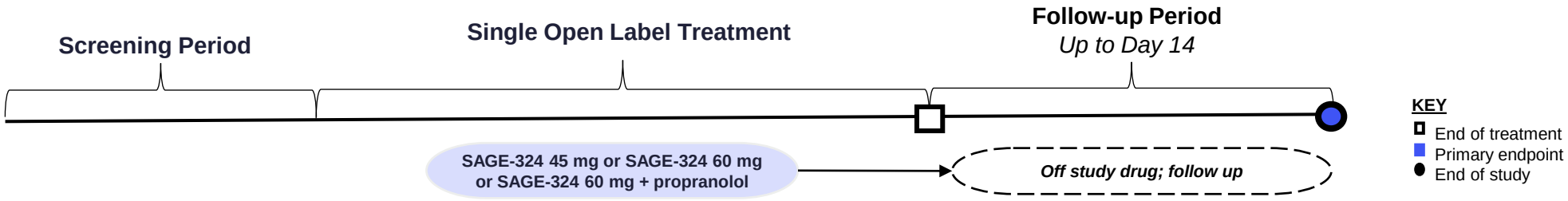
Completed SAGE-324 Study

Open-label essential tremor study (324-CLP-101E)



STUDY OVERVIEW

Status	Complete	**Inclusion Criteria**	• Diagnosis of ET consisting of
			  • bilateral upper limb action tremor
			  • at least 3 years duration
			  • with or without tremor in other locations
			  • absence of other neurological signs
			• Combined TETRAS upper limb total score of ≥ 8 on the performance subscale part 4

Indication	Essential Tremor (ET)		
Phase	Phase 1	**Exclusion Criteria**	• History or evidence of clinically relevant medical disorders (with exception of ET) • Current or recent exposure to tremorgenic drugs or drug withdrawal state • Previous surgery for the treatment of ET
Start/End Date	Aug. 2018 / Dec. 2019		
Cohorts	Open-label study: • SAGE-324 45 mg • SAGE-324 60 mg • SAGE-324 60 mg + propranolol	**Primary Endpoint**	• Safety and tolerability as assessed by frequency and severity of AE/SAE
Dosing Regimen	Single dose	**Secondary Endpoints**	• PK profile of SAGE-324
		Exploratory Endpoint	• Change from baseline over time in TETRAS performance subscale and Kinesia™ accelerometer scores

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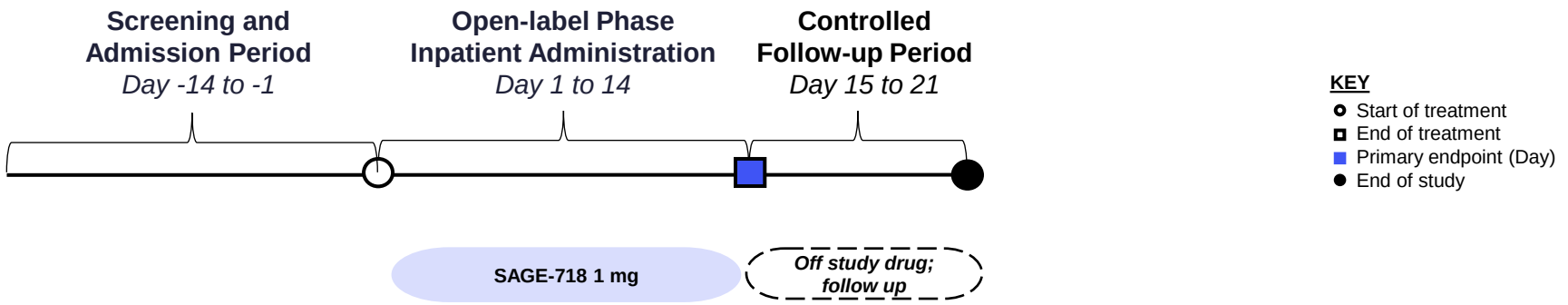
Completed SAGE-718 Study

Open-label Cohort of Patients with Huntington's Disease (CLP-102 Part B)



STUDY OVERVIEW

Status	Complete
Indication	Huntington's Disease Cognitive Impairment
Phase	Phase 1
Start/End Date* *topline data announced	Jan. 2019 / Dec. 2019
Arms	Open-label SAGE-718 1 mg oral solution
Dosing Regimen	2-week, once daily

Inclusion Criteria	• Positive for mutant *HTT* (documented CAG repeats ≥ 36 units) • Total Functional Capacity (TFC) score > 6 • Score 28 or less on the MoCA at Screening
Exclusion Criteria	• Unstable co-morbid medical conditions
Primary Endpoint	• Incidence of adverse events and serious adverse events, and changes from baseline in vital signs, safety EEGs, ECGs, laboratory parameters, and Columbia-Suicide Severity Rating Scale (C-SSRS).
Secondary and Other Endpoints	• PK profile of SAGE-718 following administration of multiple doses of SAGE-718 oral solution • Change from baseline on a computerized cognitive battery

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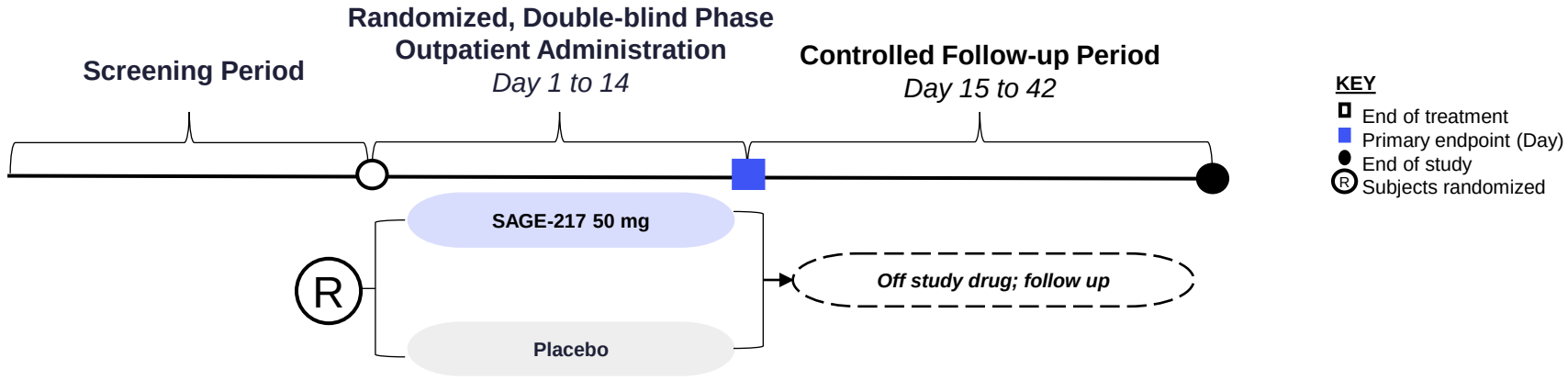
Completed Zuranolone (SAGE-217) - 50 mg

*New placebo-controlled **MDD** study - WATERFALL (MDD-301B)*



STUDY OVERVIEW

Status	Active	**Inclusion Criteria**	• Diagnosis of MDD with symptoms that have been present for at least a 4-week period • HAM-D total score ≥24 at screening and Day 1 (prior to dosing)
Indication	MDD		
Phase	Phase 3	**Exclusion Criteria**	• Active psychosis • Attempted suicide associated with the current episode of MDD • Medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder
Data Timing	Topline data announced June 2021		
Arms	Double-blind, randomized: 1:1 • SAGE-217 50 mg, placebo	**Primary Endpoint**	• Change from baseline in HAM-D total score at Day 15
Dosing Regimen	2-week, once-nightly	**Secondary Endpoints**	• Change from baseline in HAM-D, HAM-A, MADRS, CGI-I, CGI-S • Incidence and severity of AE/SAE

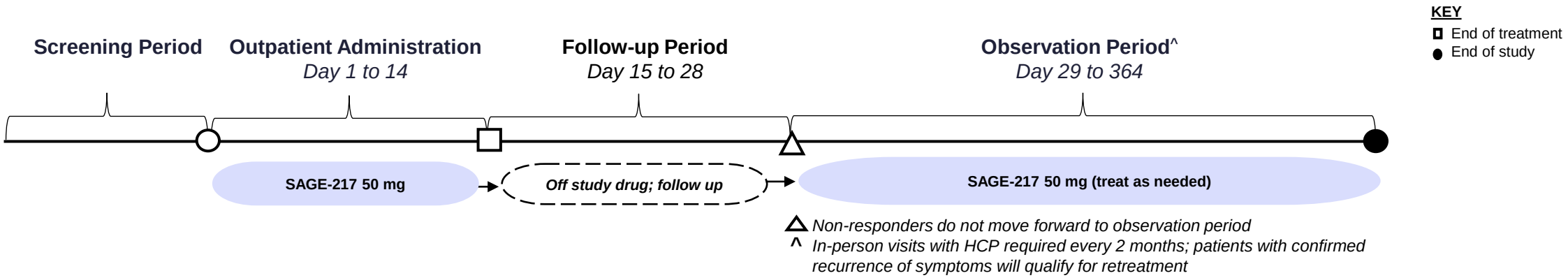
Use of antidepressants, antianxiety or insomnia medications restricted during controlled follow-up period

Study Design:

Planned / Ongoing Studies

Zuranolone (SAGE-217) - 50 mg

*SHORELINE (**MDD**-303; 50 mg cohort)*



50 mg will be examined in subjects having already received 30 mg, as well as enrollment of a new cohort of 50 mg only subjects

STUDY OVERVIEW

Status	Active	**Inclusion Criteria**	• MDD, as diagnosed by SCID-5-CT, with symptoms that have been present for at least a 4-week period • Subject is in good physical health and has no clinically significant findings, as determined by the Investigator, on physical examination, 12-lead ECG, or clinical laboratory tests
Data Timing	Data Cut Late 2021	**Exclusion Criteria**	• Attempted suicide associated with the current episode of MDD • Medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder • Subject has had vagus nerve stimulation, electroconvulsive therapy, or has taken ketamine (including esketamine) within the current major depressive episode
Arms	Non-randomized; SAGE-217 50 mg	**Primary Endpoint**	• Safety and tolerability of the initial treatment and re-treatment as assessed by: incidence and severity of AEs; suicidal ideation and behavior using C-SSRS*

Dosing Regimen	2-week, once-nightly	**Secondary Endpoints**	• Need for re-treatment, as assessed by time to first re-treatment, number of subjects achieving the requirements for re-treatment, number of re-treatment cycles for each subject*
			• Response of initial treatment and/or retreatment, as assessed by:
			  • Change from baseline in HAM-D, CGI-S*
			  • Percent of subjects achieving: HAM-D response (≥50% reduction) and HAM-D remission (HAM-D total score ≤7) at the end of each 14-day treatment period*
			  • Percent of subjects achieving CGI-I*

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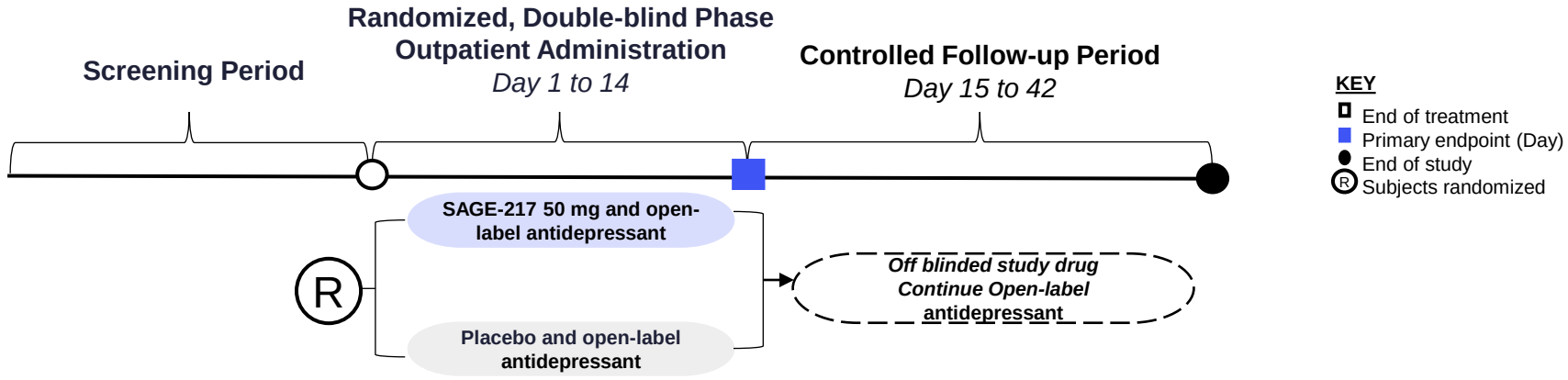
*During double-blind and follow-up periods | NCT03864614. Available from: clinicaltrials.gov [accessed November 2019]

Zuranolone (SAGE-217) - 50 mg

*New active-controlled RRT when co-initiated with new ADT in **MDD** study – CORAL (MDD-305)*



STUDY OVERVIEW

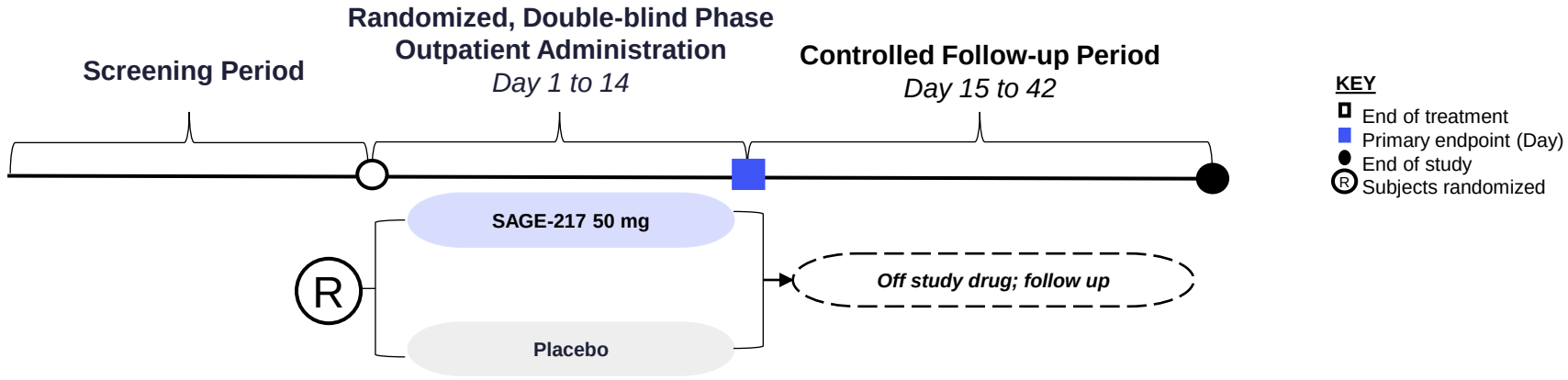
Status	Active	**Inclusion Criteria**	• Diagnosis of MDD with symptoms that have been present for at least a 4-week period • HAM-D total score ≥24 at screening and Day 1 (prior to dosing)
Indication	MDD		
Phase	Phase 3	**Exclusion Criteria**	• Active psychosis • Attempted suicide associated with the current episode of MDD • Medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder
Data Timing	Late 2021		
Arms	Double-blind, randomized: 1:1 • SAGE-217 50 mg, placebo added to open-label antidepressant	**Primary Endpoint**	• Change from baseline in HAM-D total score at Day 15
Dosing Regimen	2-week, once-nightly	**Secondary Endpoints**	• Change from baseline in HAM-D, HAM-A, MADRS, CGI-I, CGI-S • Incidence and severity of AE/SAE

Use of antidepressants, antianxiety or insomnia medications restricted during controlled follow-up period

RRT = rapid response therapy

Zuranolone (SAGE-217) - 50 mg

*New placebo-controlled **PPD** study - SKYLARK (PPD-301)*



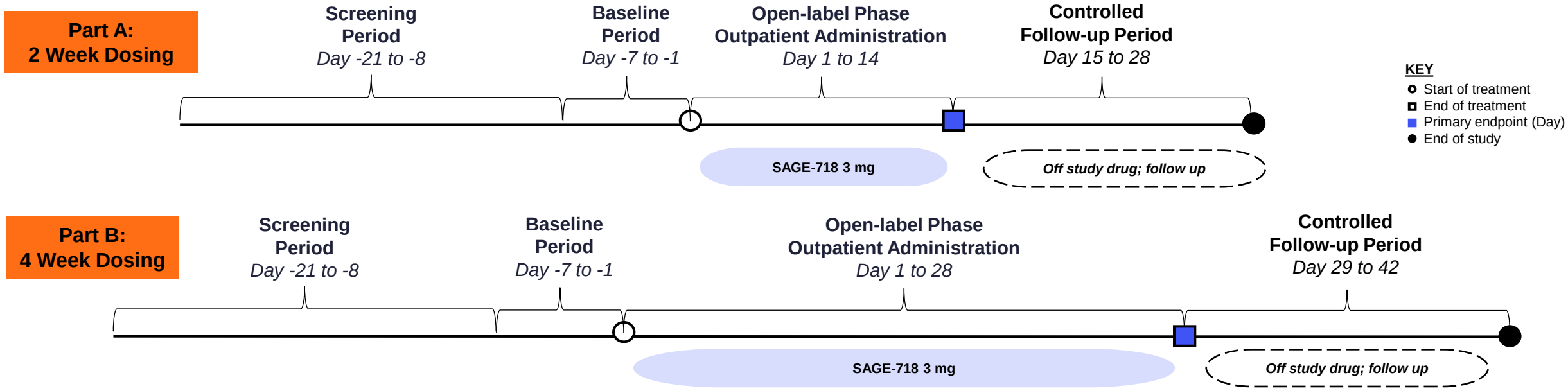
STUDY OVERVIEW

Status	Active	**Inclusion Criteria**	• Diagnosis of MDD with symptoms that have been present for at least a 4-week period • HAM-D total score ≥26 at screening and Day 1 (prior to dosing)
Indication	PPD		
Phase	Phase 3	**Exclusion Criteria**	• Active psychosis • Attempted suicide associated with the current episode of PPD • Medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder
Data Timing	Mid-2022		
Arms	Double-blind, randomized: 1:1 • SAGE-217 50 mg, placebo	**Primary Endpoint**	• Change from baseline in HAM-D total score at Day 15
Dosing Regimen	2-week, once-nightly	**Secondary Endpoints**	• Change from baseline in HAM-D, HAM-A, MADRS, CGI-I, CGI-S • Incidence and severity of AE/SAE

Use of antidepressants, antianxiety or insomnia medications restricted during controlled follow-up period

SAGE-718

*New Open-label **Parkinson's Mild Cognitive Impairment** Study – PARADIGM (CNP-201)*



STUDY OVERVIEW

Status	Active	**Inclusion Criteria**	• Diagnosis of Parkinson's Disease Mild Cognitive Impairment • Score 20 to 25 (inclusive) on the MoCA at Screening
Indication	PD-MCI		
Phase	Phase 2	**Exclusion Criteria**	• Diagnosis of dementia of any etiology • Experiencing fluctuations in motor and/or non-motor symptoms of Parkinson's disease
Data Timing	Part A: 2021		
Arms	Open-label SAGE-718 3 mg oral tablet	**Primary Endpoint**	• Incidence of treatment-emergent adverse events (TEAEs)
Dosing Regimen	Part A: 2-week, once daily Part B: 4-week, once daily	**Secondary and Other Endpoints**	• Change from baseline in vital signs, clinical laboratory analytes, electrocardiograms, and responses on the Columbia–Suicide Severity Rating Scale (C-SSRS) • Change from baseline on comprehensive neurocognitive and neuropsychiatric batteries

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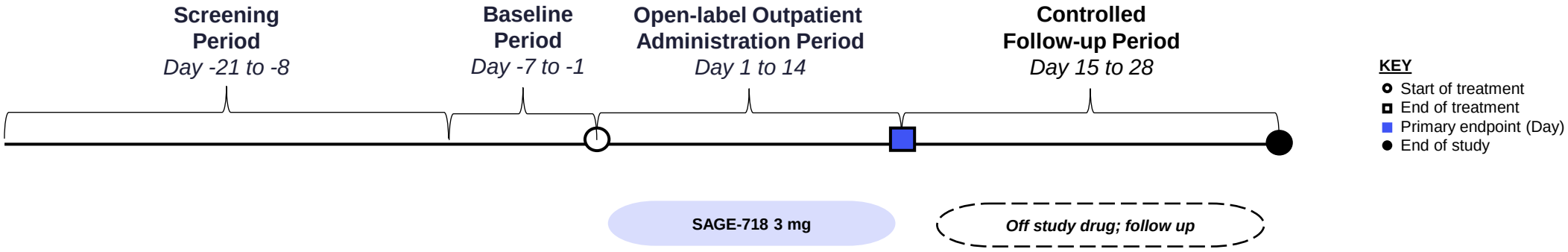
SAGE-718

New Open-label Alzheimer's Mild Cognitive Impairment and Mild Dementia Study – LUMINARY (CNA-201)



STUDY OVERVIEW

Status	Active	**Inclusion Criteria**	• Diagnosis of MCI or mild dementia due to Alzheimer's Disease • Score 15 to 24 (inclusive) on the MoCA at Screening
Indication	AD-MCI and Mild AD Dementia		
Phase	Phase 2	**Exclusion Criteria**	• Have any medical or neurological condition (other than AD) that might be contributing to the participant's cognitive impairment or history of cognitive decline
Data Timing	Late 2021		
Arms	Open-label SAGE-718 3 mg oral tablet	**Primary Endpoint**	• Incidence of treatment-emergent adverse events (TEAEs)
Dosing Regimen	2-week, once daily	**Secondary and Other Endpoints**	• Change from baseline in vital signs, clinical laboratory analytes, electrocardiograms, and responses on the Columbia–Suicide Severity Rating Scale (C-SSRS) • Change from baseline on comprehensive neurocognitive and neuropsychiatric batteries

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