UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): January 10, 2022

Sage Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

DELAWARE	001-36544	27-4486580
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

215 First Street Cambridge, MA	02142
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code (617) 299-8380

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	**SAGE**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On January 10, 2022, Sage Therapeutics, Inc. (the "Company") made available an updated corporate presentation, which it plans to use for meetings with investors and analysts at the 40th Annual J.P. Morgan Healthcare Conference, to be held virtually. A copy of the presentation is being furnished hereto as Exhibit 99.1 and is incorporated herein by reference.

The information in this Current Report on Form 8-K and Exhibit 99.1 attached hereto is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Corporate Presentation dated January 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: January 10, 2022

SAGE THERAPEUTICS, INC.

By: /s/ Jennifer Fitzpatrick
Jennifer Fitzpatrick
Vice President, Corporate Counsel

Sage Therapeutics®

Exhibit 99.1

J.P. Morgan Healthcare Conference

January 2022

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 and our expectations as to potential results; our belief that we have sufficient data to file an NDA for zuranolone, the potential regulatory pathways for filing and approval of zuranolone, expected timelines for filings and the potential for approval and launch, including anticipated timelines; our belief in the potential benefit and profile of zuranolone and in its potential to be successful and to meet an unmet need in the treatment of MDD; the potential for commercialization of zuranolone and our commercialization plans, including plans to help enable access; our expectations as to the types of MDD patients who may benefit from zuranolne, if approved; the potential for success of our other product candidates in various indications, including the potential profile and benefit of our other product candidates; our 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; the goals, opportunity, mission and vision for our Company, including our goals for generating new INDs and new products or indications and the 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 research engine; our belief in the potential for upcoming catalysts and milestones to support our mission and goals; and our belief in our ability to become the leading brain health company and top-tier pharmaceutical company in 5 years.
- 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. 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 our other 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. We may not meet our expected time-lines for filing an NDA for zuranolone or for approval. 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 INDs or new products or new indications from our research and development efforts that we expect in the future. We may not be successful in our goal to become the leading brain health company or a top tier biopharmaceutical company.
  - 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 or on the terms we expect. 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 our products, or to defend our 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. 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 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's vision is to fearlessly lead the way to create a world with better brain health

- Expertise in brain circuitry
- Rich pipeline across 3 franchises
  - First and only product approved specifically for postpartum depression
  - 3 late-stage programs
  - 7 clinical phase NCE development programs across 12+ potential indications
  - Strong intellectual property strategy
- Product platform to drive goals for ongoing growth
  - 2 or more INDs per year by 2023
  - Launch a new product or indication every 12-24 months starting in 2023
- $1.8B+ capital/collaborations to fund efforts to accelerate and advance medicines
- Potential to impact an estimated >450M patients globally

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Patient, economic, societal impact of brain health disorders in the U.S. demonstrates urgent need for innovation

COGNITIVE & MOTOR DISEASES

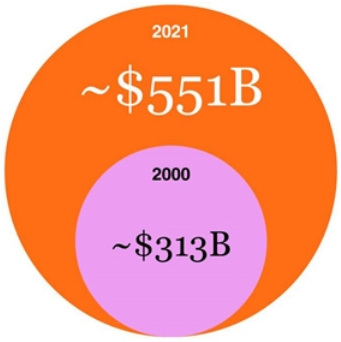
Huntington's Disease (HD)

Parkinson's Disease (PD)

Epilepsy

Essential Tremor (ET)

Alzheimer's Disease (AD)



DEPRESSIVE DISORDERS

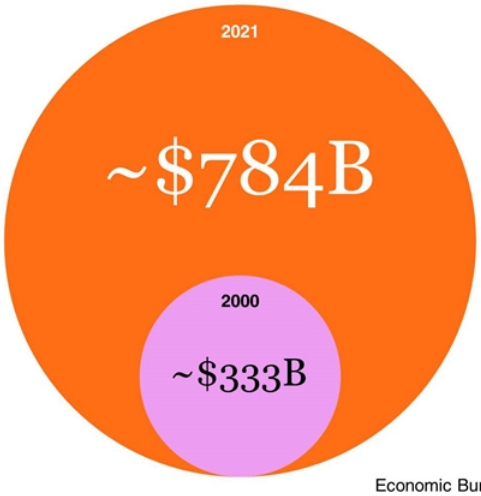
Major Depressive Disorder (MDD)

Postpartum Depression (PPD)

General Anxiety Disorder (GAD)

Treatment Resistant Depression (TRD)

Bipolar Depression (BPD)



Economic Burden in the US ($B)

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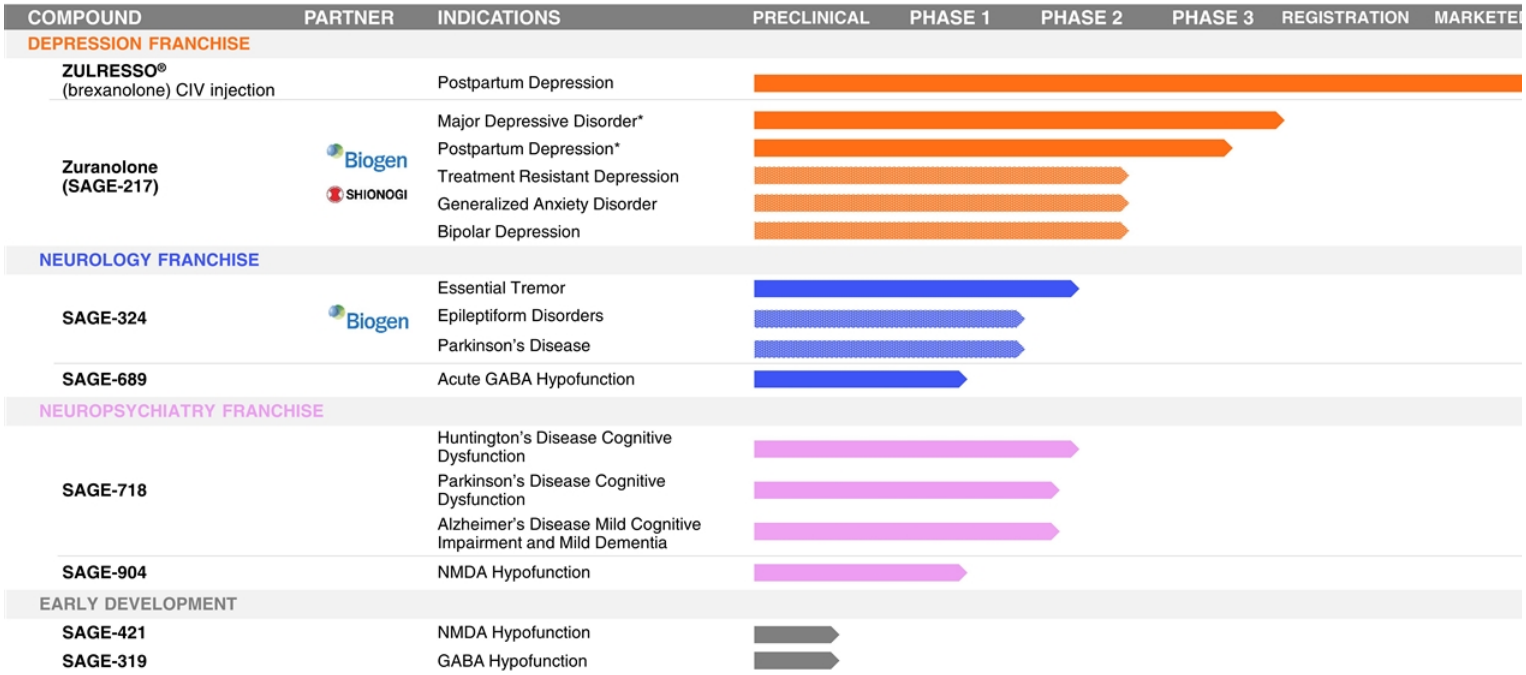
BLS CPI (Consumer Price Index) Calculator was used to estimate 2000 and 2021 economic burden amounts using U.S. specific studies in respect to the indications noted.

Sage has a leading brain health portfolio



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Light shades indicate trials in the planning or evaluation stage
**NDA submission planned for zuranolone*

Sage's Mission:

Pioneer solutions to deliver life-changing brain health medicines so every person can thrive

Paucity of innovation plagues MDD disease landscape

- Prevalence and impact continue to increase globally
  - 62% of MDD respondents in the U.S. were severely impaired by their depression in a survey conducted by the World Health Organization[1]
  - Depression has generational impact as well as direct impact on caregivers (e.g., caregivers/ partners unable to work full time, increasing economic burden exponentially)
- MDD may present in various phenotypes, such as MDD with elevated anxiety
  - MDD with elevated anxiety is known to be associated with poorer short- and long-term outcomes in relation to SSRI/SNRI pharmacotherapy[2]
  - PPD presents as depression with elevated anxiety[3]

In a survey of MDD patients conducted by Sage:

68% reported that they were not satisfied with the amount of time they take medication[4]

75% reported being frustrated with the need to switch and try multiple options to treat their MDD[4]

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[1]Bromet 2018
[2]Wu et al., 2013; Papakostas et al., 2008; Souery et al., 2007; Fava et al., 2006; Fava et al, 1997; Fava et al 2008; Ionescu et al, 2013, 2014; Papakostas et al, 2011
[3]Fairbrother N, Janssen P, Antony MM, et al. J Affect Disord. 2016;200:148-155; Postpartum Depression: Action Towards Causes and Treatment (PACT) Consortium. Lancet Psychiatry. 2015;2(1):59-67
[4]Sage Therapeutics, Inc. Data on file.

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

Rapid Onset & Sustained

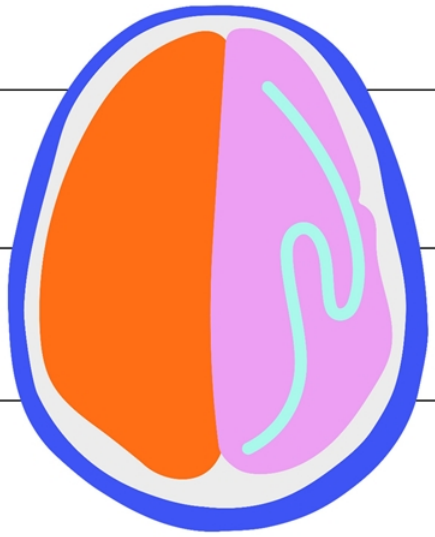
- Rapid response
- Sustained effects lasted beyond completion of treatment

Well-Tolerated

- Favorable tolerability profile
- Differentiated side effect profile

Improved Feel/Functioning

- Improvements across domains of quality of life
- Benefits that patients are looking for from depression treatment



Short Course

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

Novel MOA

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

Flexible Approach

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

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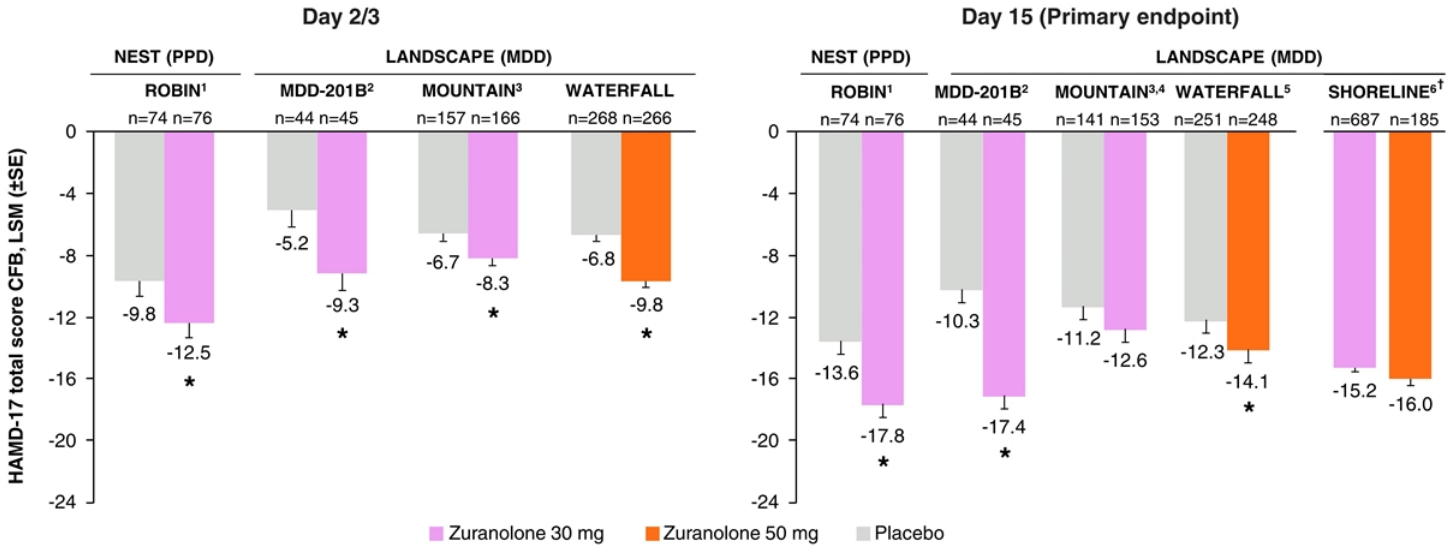
Profile based on data demonstrated in clinical studies with zuranolone to date
Note: Success of zuranolone and the product profile depend on the clinical development program and regulatory approval.
[1]Antonoudiou, P. et al. Allopregnanolone mediates affective switching through modulation of oscillatory states in the basolateral amygdala. Biological Psychiatry, 2021.2003.2008.434156, doi:10.1016/j.biopsych.2021.07.017 (2021).

Zuranolone has consistently demonstrated rapid improvement in depressive symptoms in clinical trials



The clinical trials above differ in sample size, patient population, entry criteria, study sites as well as other design elements. No direct comparison can be made across these clinical trials based on the graph above. ROBIN enrolled patients with PPD; MDD-201B, MOUNTAIN, and WATERFALL enrolled patients with MDD. Studies with Day 3 data: ROBIN, MOUNTAIN, WATERFALL; Study with Day 2 data: MDD-201B. The SHORELINE Study is an ongoing, open-label study. In the SHORELINE Study, the Day 15 measurement refers to the initial treatment course and was not the primary endpoint of the study. It was designed to evaluate efficacy in an observational manner only. No statistical inferences can be drawn from the efficacy outcome data.

*p<0.05 vs placebo. p values for Day 2/3 LSM treatment difference are not adjusted for multiplicity and are nominal. †HAMD-17 raw mean change from baseline.

CFB = change from baseline; HAMD-17 = 17-item Hamilton Rating Scale for Depression total score; LSM = least squares mean; MDD = major depressive disorder; PPD = postpartum depression.

1. Deligiannidis KM et al. *JAMA Psychiatry.* 2021 Sep 1;78(9):951-959. 2. Gunduz-Bruce H et al. *N Engl J Med.* 2019;381(10):903-911. 3. Mittal A, et al. Poster presented at the American Academy of Neurology Annual Meeting. Toronto, Canada. April 25-May 1, 2020. 4. Data on file. 217-MDD-301 MOUNTAIN CSR. 5. Clayton A, et al. Oral presentation at the European College of Neuropsychopharmacology Annual Meeting (New Medications Symposium). 2021. 6. Lasser R, et al. Poster presented at: Psych Congress Annual Meeting; 29 Oct-1 Nov 2021; San Antonio, TX. 6. Cutler AJ, et al. Poster presented at: The Society of Biological Psychiatry Annual Meeting; 2021.

Zuranolone demonstrated sustained effects in the SHORELINE Study

Patients had the opportunity to be followed for up to 12 months

50 mg*

~80% of patients who responded to initial course received 1 or 2 treatment courses

3 Treatment Courses	4 Treatment Courses	5 Treatment Courses
10.3% (n = 15)	6.8% (n = 10)	3.4% (n = 5)

30 mg*

~70% of patients who responded to initial course received 1 or 2 treatment courses

3 Treatment Courses	4 Treatment Courses	5 Treatment Courses
11.9% (n = 58)	10.8% (n = 53)	8.8% (n = 43)

- Number of additional treatment courses was similar in patients using zuranolone as monotherapy or add-on therapy (without or with pre-existing antidepressants).[1]
- The SHORELINE Study was designed to evaluate efficacy in an observational manner, and therefore, statistical inferences cannot be drawn from efficacy outcome data.[2]

Only responders (≥50% reduction in HAMD-17 total score from baseline) at Day 15 of the initial treatment period can continue in the SHORELINE Study. Need for repeat treatment courses is first assessed by PHQ-9 every 2- weeks. If PHQ-9 ≥10, a HAMD-17 assessment is performed within 1 week. If HAMD-17 total score ≥20, a repeat treatment course may be initiated. There is a minimum of 8 weeks between treatment periods, to allow for a maximum of 5 treatment courses for the 1-year study period; a new repeat treatment course cannot start after Week 48.[1] *30 mg Cohort includes a 30 mg Only Group (patients who received repeat treatment courses with zuranolone 30 mg) and a 30 mg Dose Switch Group (patients who received repeat treatment courses with zuranolone 50 mg). [1]De novo patients who enrolled into the 50 mg Cohort by September 2020 and had the opportunity to complete 1-year follow-up. The full analysis set consisted of 146 patients who were responders at Day 15 and completed the initial treatment cycle.[1]

1. Data on file. SHORELINE Topline results memo (November 2021). 2. Cutler AJ et al. Presented at Society of Biological Psychiatry Annual Meeting, 2021 Virtual Meeting; April 29-May 1, 2021.

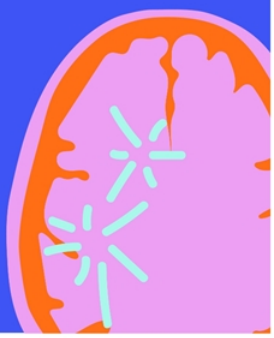
Zuranolone demonstrated improvements across domains of quality of life in clinical trials

LANDSCAPE and NEST integrated SF-36 patient-reported outcome of functioning and well-being[†]

~40-60%

improvement in mental health domains

- Vitality
- Social Functioning
- Role-Emotional
- Mental Health



~8-12%

improvement in physical and general health domains

- Physical Functioning
- Role-Physical
- Bodily Pain
- General Health

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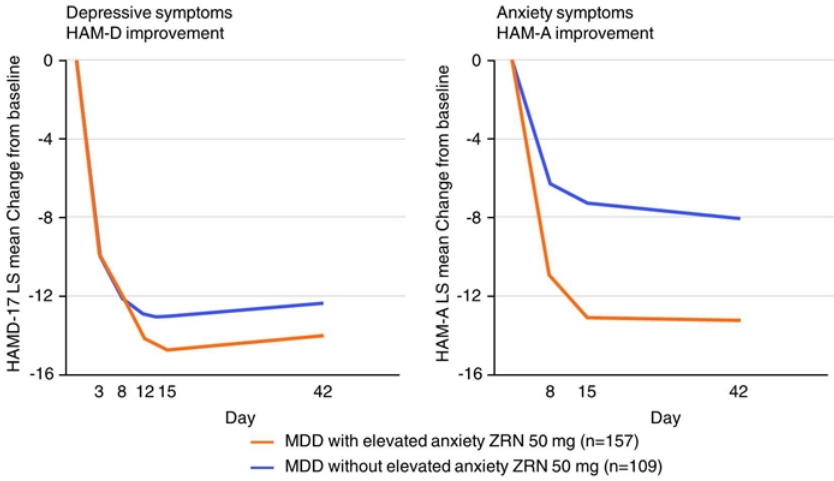
[†]Integrated analyses of SF-36 patient-reported outcomes data combined doses from the ROBIN Study, MDD-201B Study, MOUNTAIN Study (≥24 HAMD-17 subgroup), and WATERFALL Study. SF-36v2 = 36-Item Short Form Health Survey (version 2). Results reported for zuranolone-treated patients.

Zuranolone has the potential to address MDD patient populations for whom standard of care doesn't fully address unmet need

- Continued unmet need evidenced by majority of LANDSCAPE program participants meeting criteria for MDD with elevated anxiety
  - Assessed at baseline by elevated anxiety and somatization symptoms in the setting of MDD (e.g., HAMD-17, HAM-A scales)
  - Improvements in depression and anxiety symptoms observed when elevated anxiety is – or is not – present
- Well-established that MDD with elevated anxiety as a symptom is associated with:
  - More severe illness
  - More difficulty tolerating antidepressants, potentially impacting adherence
  - Higher rates of non-response to treatment, and greater need for additional interventions and resources

WATERFALL Study: Zuranolone Significantly Improved Depression and Anxiety Symptoms



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Fava et al, 1997; Fava et al, 2006; Fava et al 2008; Ionescu et al, 2013, 2014; Papakostas et al, 2011
MDD with elevated anxiety is defined as a person with MDD who has a baseline HAM-A ≥20

Zuranolone has demonstrated a consistent and differentiated tolerability profile in clinical trials

"The AEs frequently associated with current antidepressant therapies such as weight gain, sexual dysfunction, euphoria and sleep disruption have not been seen to date with zuranolone. These are the adverse effects I have to deal with to help my patients be able to continue to take their standard of care antidepressants and they affect a significant percentage of patients. These symptoms also are typically the cause of treatment discontinuation with standard of care antidepressant drugs."

Anita Clayton, M.D., Chair of Psychiatry and Neurobehavioral Sciences, University of Virginia School of Medicine

- The most common TEAEs* across zuranolone pivotal studies were headache (6-18%), somnolence (7-16%), dizziness (6-15%), nausea (4-11%), sedation (4-10%), URTI (1-8%†), diarrhea (0-7%), insomnia (7%†), fatigue (7%‡), dry mouth (4-6%), tremor (5%†)
- Most TEAEs across the zuranolone clinical development program were mild or moderate in severity
- Discontinuation rates due to AEs of less than or equal to 6.5% across controlled and uncontrolled studies

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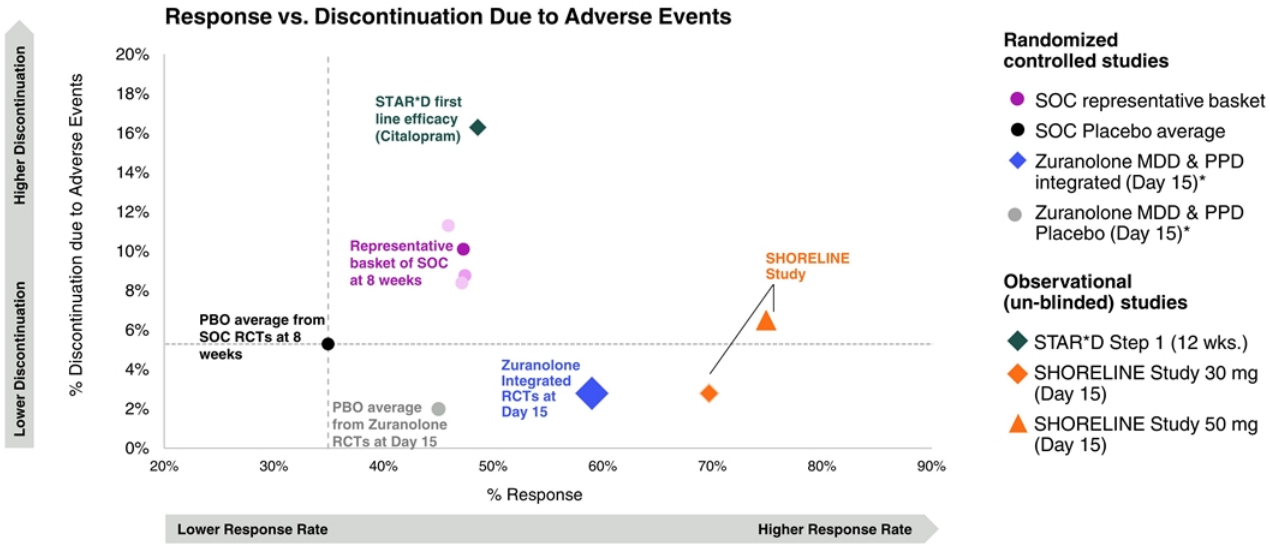
AE = adverse event; TEAE = treatment-emergent adverse event; URTI = upper respiratory tract infection; *Most common defined as ≥ 5% of patients in either zuranolone (30 or 50 mg) arm, excluding dose switch. †Reported at ≥ 5% in any arm only in SHORELINE study. ‡Reported at ≥ 5% in any arm only in MOUNTAIN study.

Potential benefit-risk profile of zuranolone may be distinct from current antidepressants



- Methods: Average response (>50% reduction from baseline) and discontinuation due to side effects rates for SOC were obtained from Cipriani et al. 2018 (average placebo for SOC trials and representative basket of SOC products), and for zuranolone from an integrated analysis of zuranolone clinical data; SHORELINE Study and STAR*D, which was included for real-world context.
- The clinical trials above differ in sample size, patient population, entry criteria, study sites as well as other design elements. No direct comparison can be made across these clinical trials based on the graph above.

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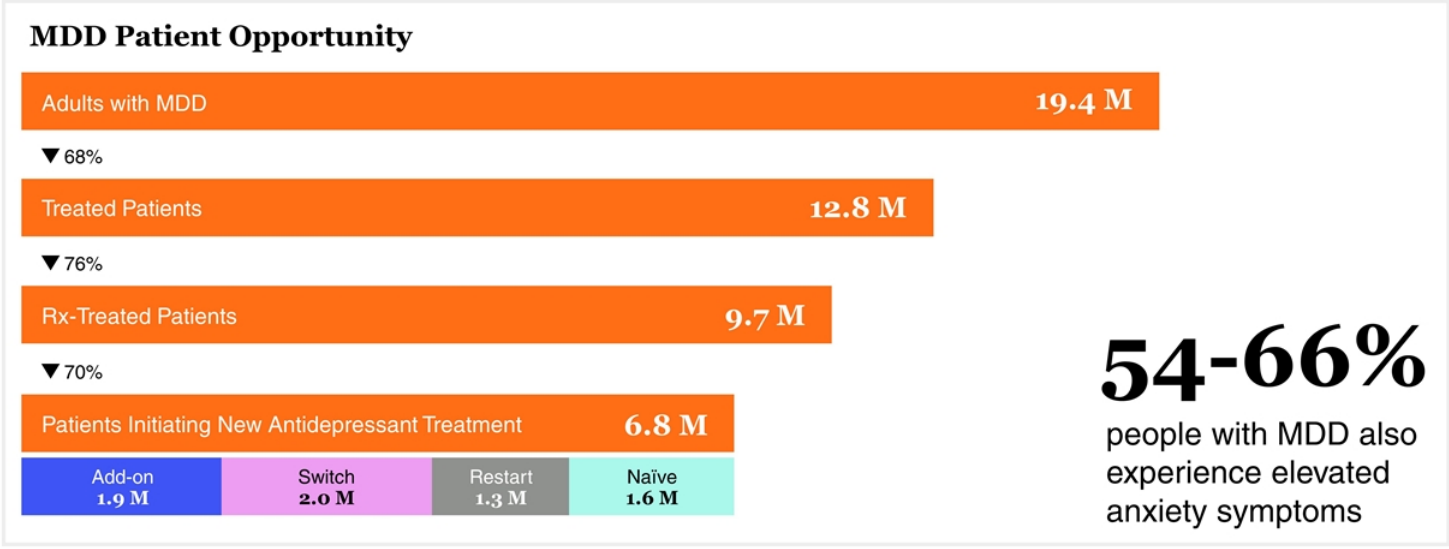
*Integrated analyses combine doses from ROBIN Study, MDD-201B Study, MOUNTAIN Study (≥24 HAMD-17 subgroup), and WATERFALL Study.

Sage's planned commercialization approach designed to educate and engage stakeholders

Stakeholder Needs		Strategic Imperatives
Patients	Rapid, durable therapy without stigmatizing side effects often associated with chronic treatments (e.g., sexual dysfunction/weight gain)	**Inspire** people with MDD and PPD to talk to their HCP about zuranolone
HCPs	Rapid, durable, well-tolerated therapy for a range of patients with MDD and PPD with low/no access hurdles	**Mobilize** targeted HCPs to identify and treat zuranolone patient types in MDD and PPD
Payors	Efficacious, cost-effective solution for MDD and PPD patient types associated with poorer outcomes	**Connect** treatment outcomes in MDD and PPD with zuranolone performance through innovative proactive Value Based Agreements to drive at-launch access
Patient Advocacy and **Policy Makers**	Education to advocate for and advance the standard of care for those who need more from MDD and PPD treatment	**Raise** treatment expectations in MDD and PPD through grassroots efforts, leveraging policy interventions that have been proven effective in addressing access to treatment

The MDD landscape presents significant opportunity for a new therapy to help patients at various points in their treatment journey



54-66%

people with MDD also experience elevated anxiety symptoms

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Numbers represent estimates based on cited data.
Sources: [1] Sage Epidemiology Data on File (June 2021), [2] HEOR Truven Claims Analysis 2019-2020- 29% of patients are stable, 17% are new starts,21% are switching Rx, 20% are adding on Rx, and 13% are restarting treatment

Potential clinical use scenarios for zuranolone in MDD

Across these different clinical scenarios, *MDD with elevated anxiety is a common presentation*

"Major depressive disorder with elevated anxiety is a common presentation of depression and is associated with a more prolonged and severe disease course and poor response to current treatments. Data from the LANDSCAPE and NEST clinical development programs indicate that, if approved, zuranolone may offer the potential for patients with MDD and PPD with or without elevated anxiety to experience rapid improvements."

Maurizio Fava, M.D.
Psychiatrist-In-Chief, Department of Psychiatry
Director, Division of Clinical Research, Mass General Research Institute; Executive Director, Clinical Trials Network & Institute Associate Dean for Clinical & Translational Research, Slater Family Professor of Psychiatry, Harvard Medical School

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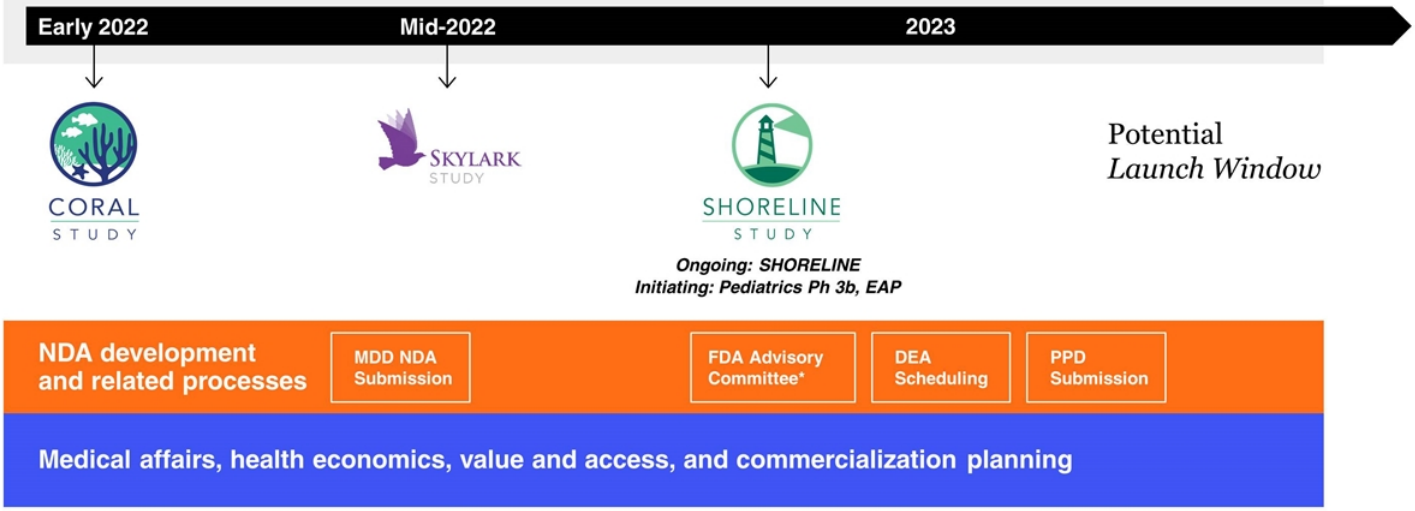
Zuranolone development plans over next 24 months include two Phase 3 readouts and NDA submissions

Planned activities and anticipated timelines



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* Anticipated not scheduled

Neuropsychiatric disorders

Preserving independence through the treatment of cognitive impairment

- Globally, disorders involving cognitive dysfunction continue to increase
- These disorders represent one of the greatest areas of unmet need
- Significant impact on patients' ability to work, live independently, adhere to medical care, and interact with family
- Sage is forging new pathways

~188K	~8.8M	~134M
Huntington's Disease	Parkinson's Disease	Alzheimer's Disease

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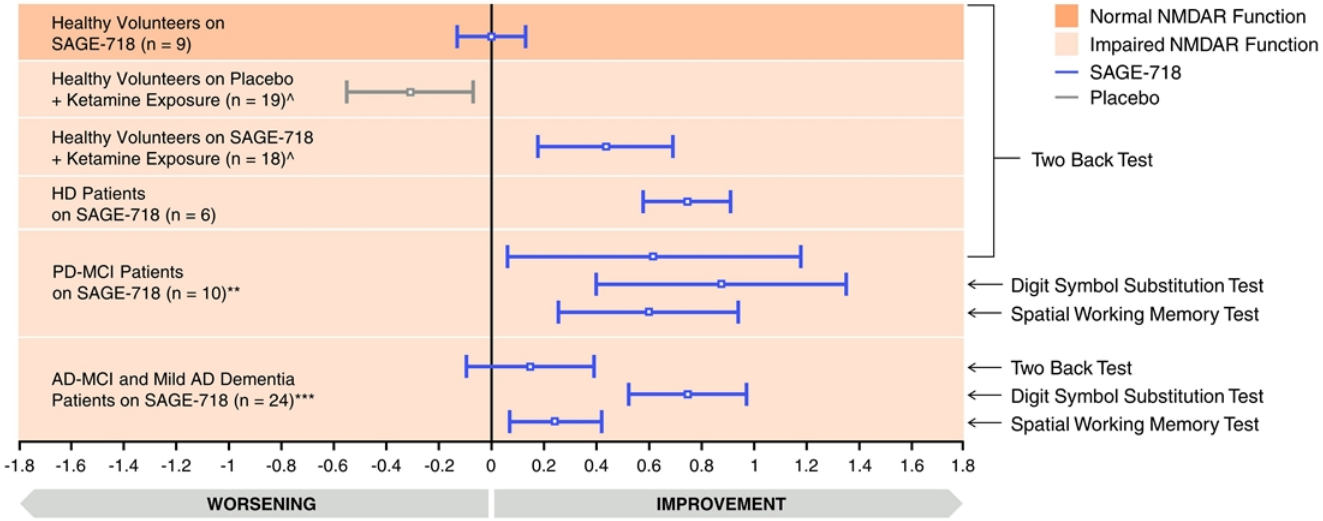
SAGE-718 demonstrated improvements in cognitive function in early clinical trials

Performance on Executive Tasks in Healthy Volunteers and Patients with Huntington's, Parkinson's, and Alzheimer's Diseases

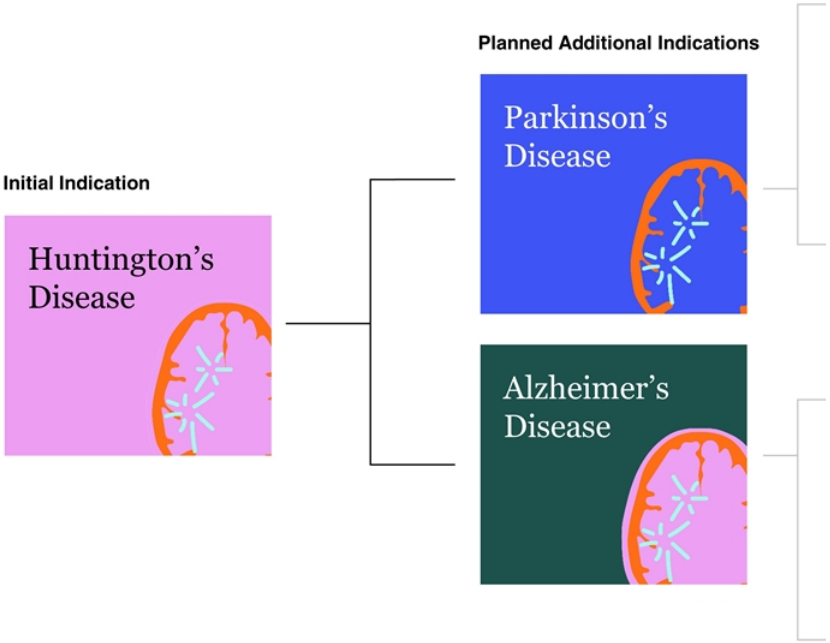
Z-Transformed Change from Baseline to Last Assessment* (Mean ± SE Plotted)



*Last assessment at day 14 for HV study, day 10 for HV ketamine study, day 14 for HD study, day 14 for PD/AD 2-back, and day 28 for PD/AD DSST and SWM
**n=6 for Two-Back, n=9 for DDST
***n=21 for Two-Back, n=23 for SWM

SAGE-718 clinical development program designed with goal to de-risk opportunities in multiple indications

- Huntington's disease is the initial indication for SAGE-718 development
- Fast Track Designation for SAGE-718 in Huntington's disease enables interactions to define an efficient potential path to registration in an orphan disease
- Plans for further development including in Parkinson's and Alzheimer's disease
- Leveraging learnings across indications designed to help de-risk program



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SAGE-718 planned clinical development program designed to define potential benefits and leverage learnings

Huntington's Disease & CogNEXT Clinical Signal-Finding Studies

Huntington's
Parkinson's
Alzheimer's
FDA Fast-track Designation

Phase 1

CLP-102-B
Completed
Open-label study in HD

Phase 2

DIMENSION (CIH-201)
Enrolling
Randomized study in HD

PARADIGM (CNP-201)
Enrolling
Open-label study in PD

LUMINARY (CNA-201)
Completed
Open-label study in AD

SURVEYOR (CIH-202)
Planned Mid-2022 (Start)
Randomized Study in HD

CNP-202
Planned Mid-2022 (Start)
Randomized Study in PD

CNA-202
Planned Late 2022 (Start)
Randomized Study in AD

Phase 3

CIH-301
Planned Late 2022 (Start)
Open-label study in HD

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Abbreviations: HD = Huntington's Disease, PD = Parkinson's Disease, AD = Alzheimer's Disease, PBO = Placebo, PK = Pharmacokinetics, MRI = Magnetic Resonance Imaging

Movement and neurological disorders

Gaps remain in bringing effective treatments to people with movement disorders

- An estimated 136.4 million people globally suffer from essential tremor (ET) or Parkinson's disease (PD)
- Standards of care are inadequate for many people suffering from movement disorders
- Substantial mental health impact and caregiver burden

ET is strongly linked to impairment in Activities of Daily Living (ADL)

In patients with severe ADL impairment:

>90% of patients have difficulty with writing, eating, drinking, and self-care

79% of employed patients have reduced hours or changed jobs due to ET

56% of patients require caregiving from family, friends, or professionals

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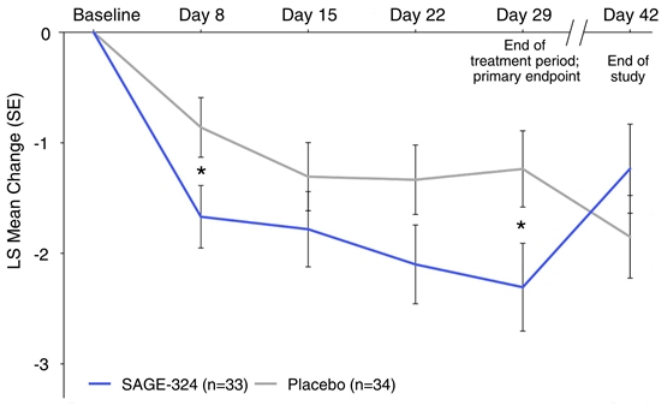
Sources: 1) Data from HEOR survey of 108 US ET-treating physicians, 1,003 patient records, 476 patient reports, and 253 caregiver reports

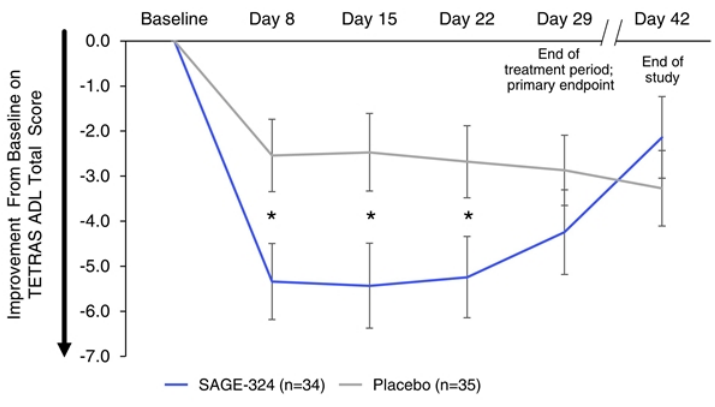
Improvement in tremor control and ADL score observed in the KINETIC Study

Change From Baseline for TETRAS Performance Subscale Upper Limb Tremor Total Score in SAGE-324 and Placebo Treatment Groups



Baseline mean (SD) TETRAS Performance Subscale Upper Limb Tremor Total Score: placebo 12.28 (1.69); SAGE-324 12.82 (1.73)

Change From Baseline for TETRAS ADL Subscale Total Score in SAGE-324 and Placebo Treatment Groups



Baseline mean (SD) TETRAS ADL Subscale Total Score: placebo 26.7 (6.84); SAGE-324 26.3 (8.50)

The most frequently reported adverse events reported by at least 10% of participants on SAGE-324 in the KINETIC Study were somnolence (68%), dizziness (38%), balance disorder (15%), fatigue (15%), diplopia (12%), dysarthria (12%), and gait disturbance (12%).

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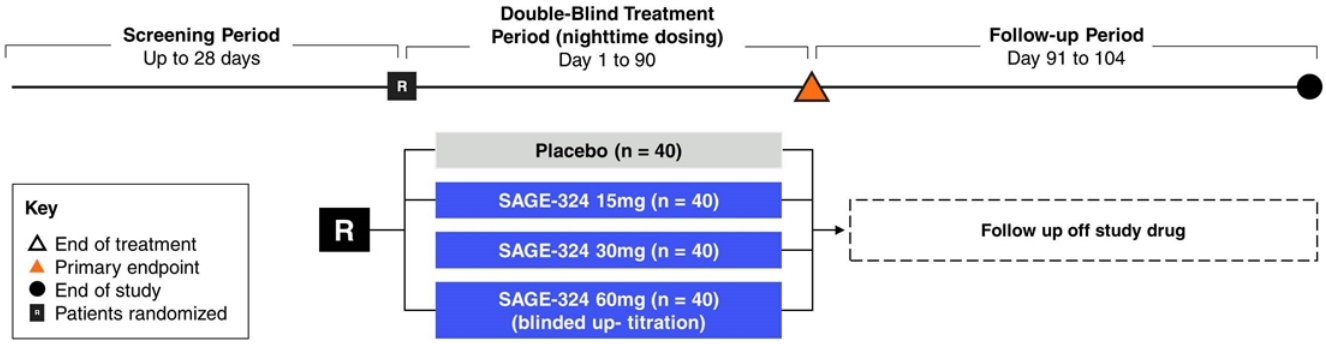
*p<0.05 (Secondary/other endpoints were not adjusted for multiplicity; p-values are nominal)
Sage Therapeutics, Inc. Data on file.

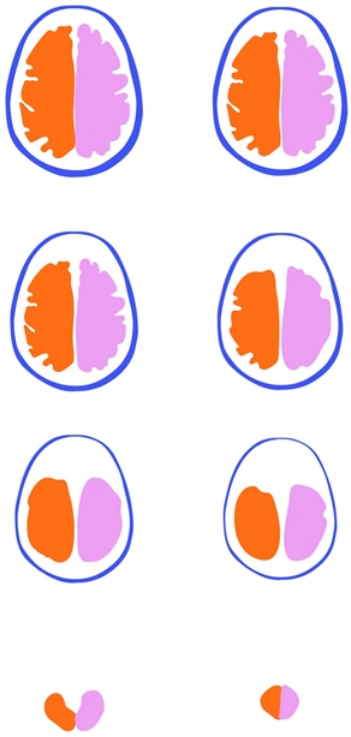
324-ETD-202: Phase 2 double-blind, randomized, placebo-controlled, dose–response study of SAGE-324 for the treatment of patients with essential tremor



- Patients with moderate to severe essential tremor
- Primary aim is to identify a dose-response
- Primary endpoint is change from baseline in TETRAS Performance Subscale Item 4 total score at Day 91
- Dose(s) selected for potential pivotal studies will balance efficacy with tolerability

Proactive, predictive, productive and patient-focused drug development approach

- Sage is pairing deep GABA and NMDA domain expertise with leadership in neuroactive steroids
  - >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 rapidly into clinical proof-of-concept
- Dedicated to improving patients' lives by focusing on the things that matter most to them



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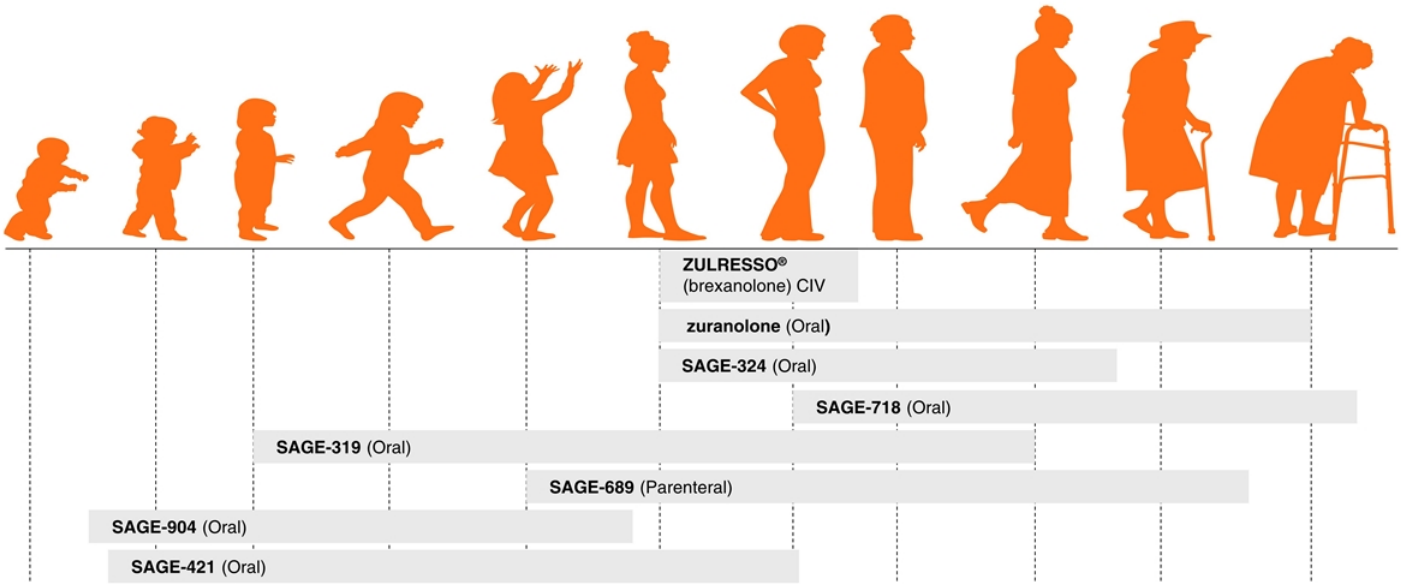
Sage's robust portfolio features NCEs with differentiated target profiles that are suited for study across the lifespan



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Anticipated 2022 Milestones

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

	Early	Mid	Late	
DEPRESSION FRANCHISE				
Zuranolone (SAGE-217)	●			Report topline data from CORAL Study in MDD
	●	●		Rolling submission of NDA filing package for the treatment of MDD
		●		Report topline data from SKYLARK Study in PPD
			●	Submit NDA filing package for the treatment of major depressive disorder (2H 2022)
	●	●	●	Present additional analyses of data from LANDSCAPE and NEST clinical programs, including health economics and patient reported outcomes
NEUROLOGY FRANCHISE				
SAGE-324		●		Initiate Phase 2/3 safety study
			●	Complete enrollment in Phase 2b KINETIC 2 Study
	●	●	●	Present additional analyses of data from clinical development program
NEUROPSYCHIATRY				
SAGE-718		●		Initiate placebo-controlled Phase 2 Study in Parkinson's disease
		●		Initiate SURVEYOR Study in Huntington's disease
			●	Initiate Huntington's disease open label extension study
			●	Initiate placebo-controlled Phase 2 Study in Alzheimer's disease cognitive impairment
	●	●	●	Present additional analyses of data from clinical development program
ADDITIONAL CLINICAL PROGRAMS				
Additional Pipeline Programs		●		Present data on early-phase studies for pipeline programs
			●	Provide update on next steps for pipeline programs

Sage's goal is to become the leader in brain health

Fearlessly leading the way to create a world with better brain health

Data rich 2021 sets up potential for long-term value creation through 2022 and beyond

Deep domain expertise paired with neuroactive steroid capability generating the leading brain health pipeline

Expect to progress four ongoing Phase 2 studies in 2022 and submit NDA filing seeking approval for second marketed product

Focused on plans for potential commercialization for later-stage programs

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

Seeing the brain differently *makes a world of difference*

Sage Therapeutics