Sage Therapeutics™

SAGE-217 MOUNTAIN Study Topline Results

December 5, 2019

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,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “opportunity”, “potential,” “confident”, or “continue,” and other similar expressions.

Forward-looking statements in this presentation include statements regarding: our views as to the potential of SAGE-217 in the treatment of major depressive disorder (MDD) and other indications; our views as to the need for additional treatment options in MDD and the potential profile and benefit of SAGE-217; our plans and expectations related to ongoing development of SAGE-217, the potential pathway for approval and next steps; the potential timing and results of our ongoing and future development efforts; our estimates as to the number of people affected by MDD; and other statements regarding the goals, opportunity and expectations for our business.

These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risk that:

- We may not be successful in our development of SAGE-217 or of any of our other current or future product candidates in any indication we are currently pursuing or may in the future pursue. Success in pre-clinical studies or in earlier clinical trials of SAGE-217 may not be repeated or observed in ongoing or future studies, and future non-clinical and clinical results may not support further development or regulatory approval on the timelines we expect or at all or may require additional clinical trials or nonclinical studies.
- Even if our planned development programs are successful, we still may not achieve review or approval, despite prior regulatory advice, and regulatory authorities may ask for additional trials or data.
- 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.
- Even if our products are successfully developed and approved, the number of patients with MDD or any of the other 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 encounter unexpected safety or tolerability issues with respect to SAGE-217 or any of our other product candidates or marketed products.
- We may face competition from others developing products for similar uses as those for which SAGE-217 or our other product candidates are being developed.
- Funding to support operations may not be available, when needed, on reasonable terms or at all, or may result in significant dilution to existing shareholders;
- We may face other unexpected hurdles in the manufacture and development of our products.

For additional disclosure regarding these and other risks Sage faces, see the disclosure contained in the "Risk Factors" section of our most recent quarterly 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™

Major Depressive Disorder
Innovation Needed to Give People Treatment Choices

- Major depressive disorder (MDD), commonly referred to as depression, is a brain health disorder that affects an estimated 17 million adults in the U.S. each year
- MDD causes significant impairment in daily life and can limit a person's ability to fulfill work, school, family, or social responsibilities; enjoy leisure activities; or maintain health and hygiene
- While antidepressants are widely used to treat MDD, large-scale studies have demonstrated that there is a need for new therapeutic options
- Standard-of-care pharmacotherapies (e.g., SSRIs, SNRIs, TCAs) are suboptimal across the MDD treatment cycle, from initiation (low remission rates, slow onset of action) to maintenance (no treatment-free days, significant side effects) to discontinuation (recognition of Antidepressant Discontinuation Syndrome in DSM-5)
- An 'as needed' antidepressant simplifies therapy across treatment phases, reduces unnecessary chronic medication use to support wellness, and eliminates stigma-related concerns about 'never coming off pills'
- Current therapies require too long to achieve maximal response, underscoring the need for a reliable, rapid response in depressive symptoms

LANDSCAPE Program

Broad Program Underway Across Numerous Studies, Indications

STUDY	MDD-201	PPD-201	MDD-301	MDD-302	MDD-303	MDD-304
		ROBIN STUDY	MOUNTAIN STUDY	REDWOOD STUDY	SHORELINE STUDY	RAINFOREST STUDY
Indication	MDD	Postpartum Depression (PPD)	MDD	MDD	MDD	Co-morbid MDD and Insomnia
Phase	Pivotal Ph. 2	Pivotal Ph. 2	Pivotal Ph. 3	Pivotal Ph. 3	Pivotal Ph. 3	Pivotal Ph. 3
Objectives	Efficacy in the treatment of MDD compared to placebo	Efficacy in the treatment of PPD compared to placebo	Efficacy in the treatment of MDD compared to placebo	Efficacy of a fixed, repeated treatment regimen in the prevention of relapse	Safety, tolerability of re-treatment(s) over a 1-year period	Effectiveness (polysomnography) on insomnia symptoms
Status	Completed	Completed	Completed	Enrollment ongoing	Enrollment complete	Enrollment ongoing

Sage Therapeutics™

MOUNTAIN Study (SAGE-217 MDD-301)

Pivotal Phase 3 Efficacy and Safety Study

Treatment of a major depressive episode in the context of MDD, studied at 55 sites in the U.S.

Inclusion

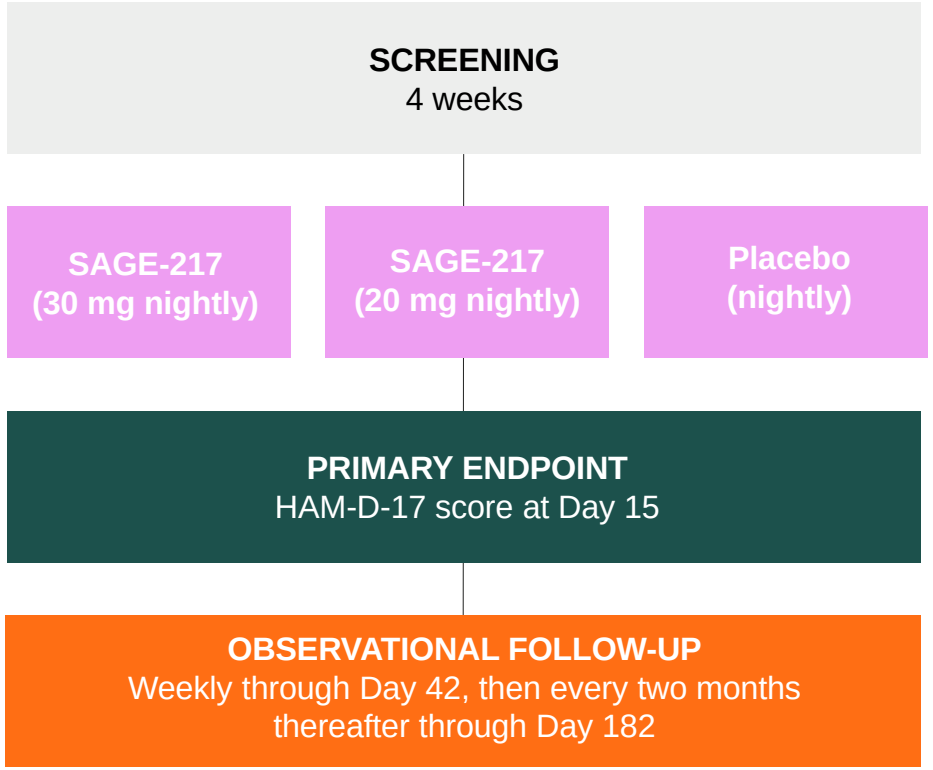
- Males and females; 18 to 65 years
- SCID diagnosis of MDD
- MADRS≥32 and HAM-D-17≥22
- Stable baseline antidepressants permitted

Exclusion

- Attempted suicide in current episode
- Uncontrolled medical conditions
- Clinically significant safety/medical abnormalities
- Failure of 2 or more antidepressants (treatment-resistant depression)

Assessments included

- Efficacy (HAM-D, MADRS, CGI-I, HAM-A, ISI)
- Safety (vital signs, laboratories, ECG, C-SSRS)
- Patient-reported outcomes (fatigue, sexual functioning, SF-36v2, PHQ-9)



Abbreviations: SCD = Structured Clinical Interview for DSM-IV Diagnosis; MADRS = Montgomery-Asberg Depression Rating Scale; HAM-D-17 or HAM-D = Hamilton Depression Rating Scale, 17-item; CGI-I = Clinical Global Impression – Improvement scale; HAM-A = Hamilton Anxiety Rating Scale; ISI = Insomnia Severity Index; C-SSRS = Columbia-Suicide Severity Rating Scale, SF-36x2 = 36-Item Short-Form Survey, version 2.0; PHQ-9 = Patient Health Questionnaire-9

MOUNTAIN Study in MDD
Demographics

	SAGE-217 30 mg (n=166)	**SAGE-217 20 mg** (n=159)	**Placebo** (n=157)
Age, years – mean, years (SD)	42.3 (12)	41.9 (12)	41.4 (12)
Female sex – n (%)	121 (73)	112 (70)	106 (68)
Race or ethnic group – n (%)			
Asian	2 (1.2)	3 (1.9)	3 (1.9)
Black/African-American	64 (38.6)	56 (35.1)	54 (34.4)
Multiple	4 (2.4)	1 (0.6)	3 (1.9)
White	94 (56.6)	99 (62.3)	96 (61.1)
Other	2 (1.2)	0	1 (0.6)
Ethnicity – n (%)			
Hispanic/Latino	27 (16.3)	31 (19.5)	26 (16.6)
Weight – mean, kg (SD)	89.7 (22.4)	87.3 (20.2)	89.5 (22.9)
Baseline HAM-D-17 score – mean (SD)	25.9 (2.9)	25.8 (2.8)	25.8 (3.1)
Use of antidepressants at baseline – n (%)	47 (28)	46 (29)	49 (31)

Sage Therapeutics™

MOUNTAIN Study in MDD
Disposition

- Low rate of discontinuation from adverse events (AEs)
- AEs leading to study medication discontinuation were similar across all treatment groups: 2.1% for SAGE-217 30 mg (n=4), 1.6% for SAGE-217 20 mg (n=3), and 3.2% for placebo (n=6)

	SAGE-217 30 mg	SAGE-217 20 mg	Placebo	Total
Screened – n				1351
Randomized – n	194	194	193	581
Received study medication – n	192	188	190	570
Completed Day 42 – n (%)	164 (85.4)	171 (91.0)	167 (87.9)	502 (88.1)
Discontinued by Day 42 – n (%)	28 (14.6)	17 (9.0)	23 (12.1)	68 (11.9)
Adverse event - n (%)	3 (1.6)	1 (0.5)	5 (2.6)	9 (1.6)
Lost to follow-up	4 (2.1)	5 (2.7)	3 (1.6)	12 (2.1)
Non-compliance with study drug	1 (0.5)	0	1 (0.5)	2 (0.4)
Physician decision	1 (0.5)	0	2 (1.1)	3 (0.5)
Withdrawal by subject	17 (8.9)	9 (4.8)	11 (5.8)	37 (6.5)
Other	2 (1.0)	2 (1.1)	1 (0.5)	5 (0.9)

Sage Therapeutics™

MOUNTAIN Study in MDD
Safety Through Day 42

- Overall reports of AEs during the 14-day treatment period and 28 day follow-up were similar between all treatment groups (SAGE-217 30 mg 54.2%, SAGE-217 20 mg 50.0%, placebo 48.9%)
- Serious adverse events (SAEs) were reported in 5 patients during the double-blind phase:
  - During treatment period: Two patients receiving SAGE-217 30 mg reported SAEs, including one suicide attempt on Day 5 in a patient with a longstanding history of MDD and a past suicide attempt, and one report of a bile duct stone after Day 2 requiring removal in a patient with a prior bile duct repair
  - During follow-up period: Three patients, one in each treatment group, reported SAEs during follow-up, all occurring at least one week following cessation of treatment: syncope and associated injuries which occurred with dehydration and orthostatic hypotension during exercise in a patient with a history of bradycardia (SAGE-217 30 mg, Day 28), multiple SAEs related to medical complications of cocaine ingestion (SAGE-217 20 mg, Day 39) and suicidal ideation (placebo, Day 22)
- No adverse events of loss of consciousness reported
- No signal for increased suicidal ideation or suicidal behavior compared to baseline, as measured by C-SSRS
- No clinically significant changes in vital signs or clinical laboratory parameters or ECGs, based on adverse events

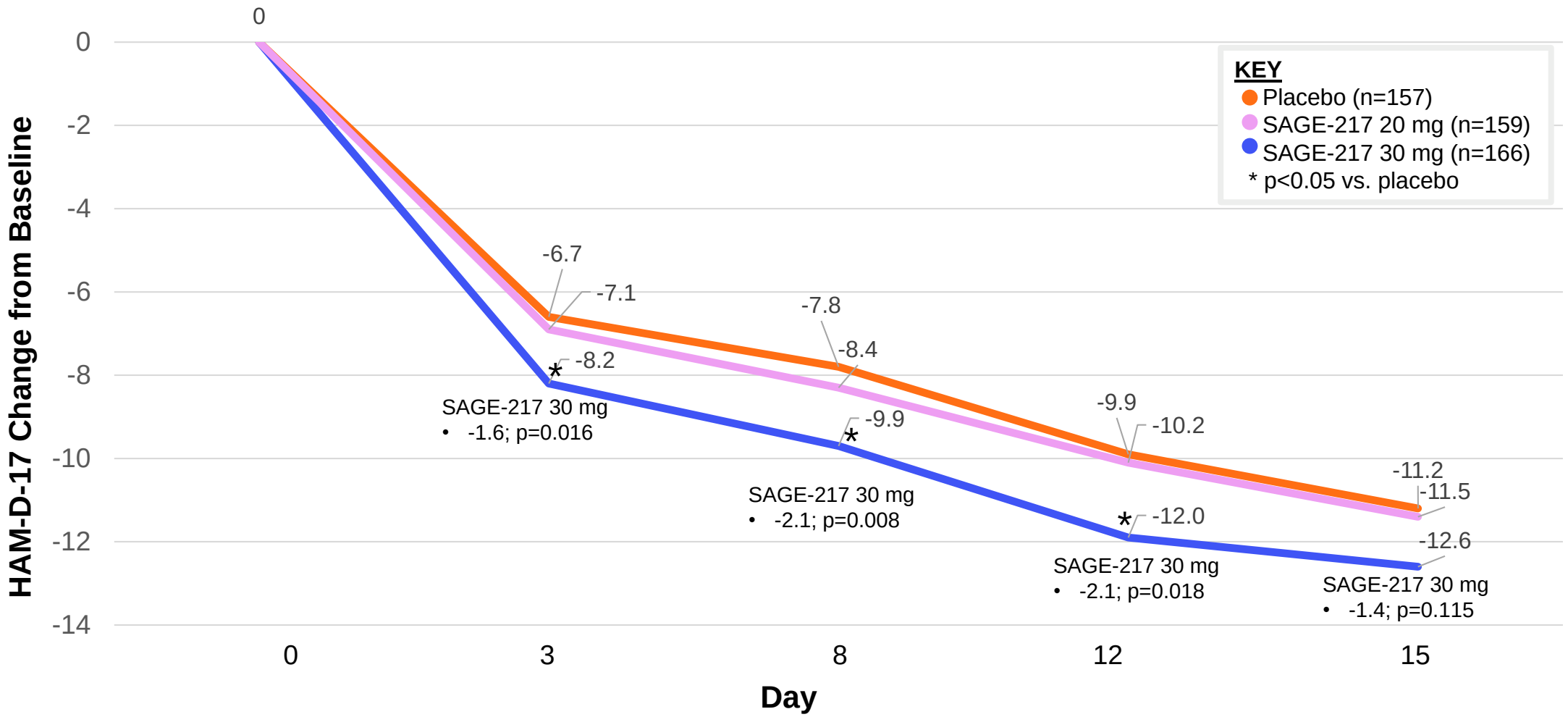
Adverse Events ≥5% Through Day 42

	SAGE-217 30 mg (n=192)	SAGE-217 20 mg (n=188)	Placebo (n=190)
Any – n (%)	104 (54.2)	94 (50.0)	93 (48.9)
Headache	12 (6.3)	21 (11.2)	14 (7.4)
Dizziness	11 (5.7)	14 (7.4)	7 (3.7)
Somnolence	13 (6.8)	11 (5.9)	8 (4.2)
Fatigue	13 (6.8)	3 (1.6)	5 (2.6)
Diarrhea	12 (6.3)	11 (5.9)	10 (5.3)
Sedation	9 (4.7)	11 (5.9)	6 (3.2)
Nausea	7 (3.6)	10 (5.3)	9 (4.7)

Sage Therapeutics™

SAGE-217 Primary Efficacy Measure

HAM-D Total Score LS Mean Change From Baseline Through Day 15

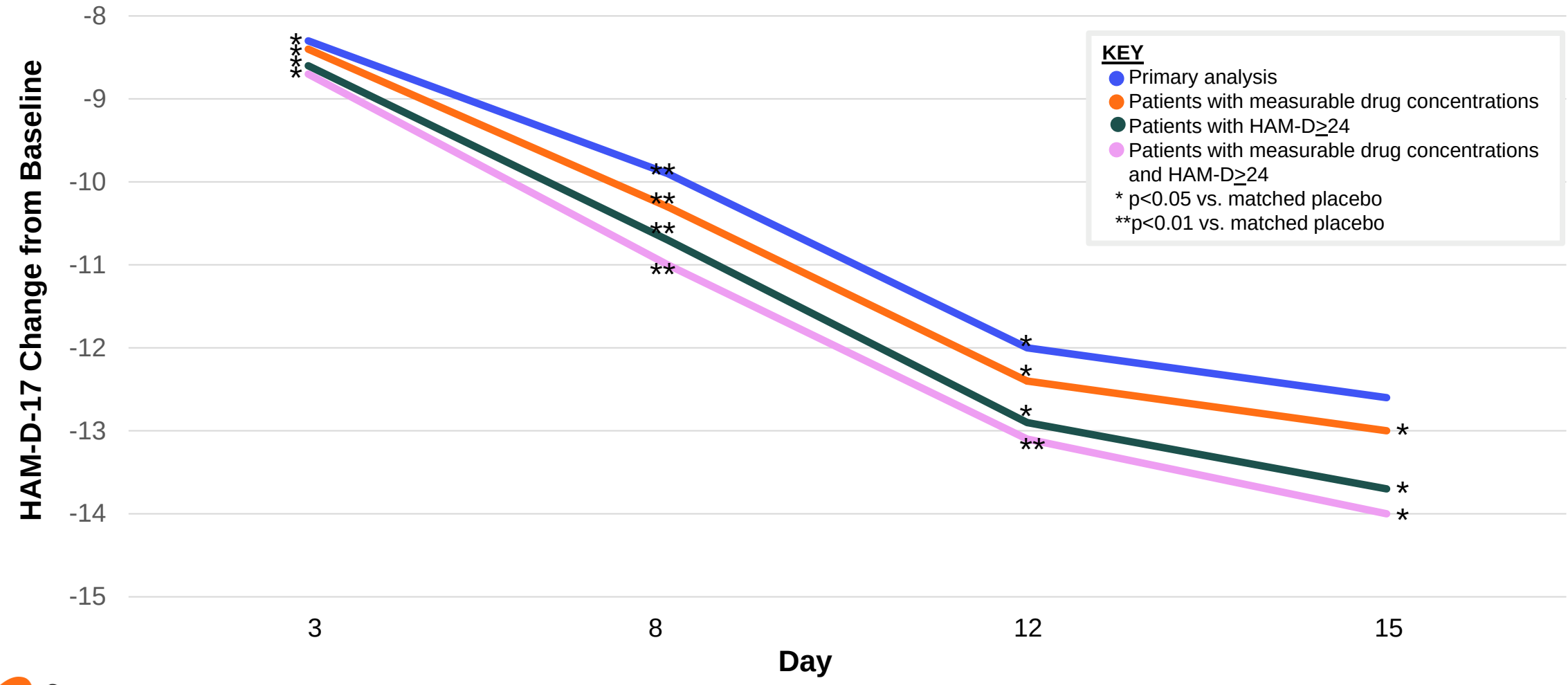


Rapid onset of effect for SAGE-217 30 mg was seen beginning at Day 3 with maintenance of effect through Day 15; statistical separation from placebo observed Days 3 – 12

Sage Therapeutics™

Post-Hoc Analysis: SAGE-217 30 mg Performance by Factors

Primary Efficacy Through End of Treatment at Day 15



Post-Hoc Analysis: SAGE-217 30 mg Performance by Factors

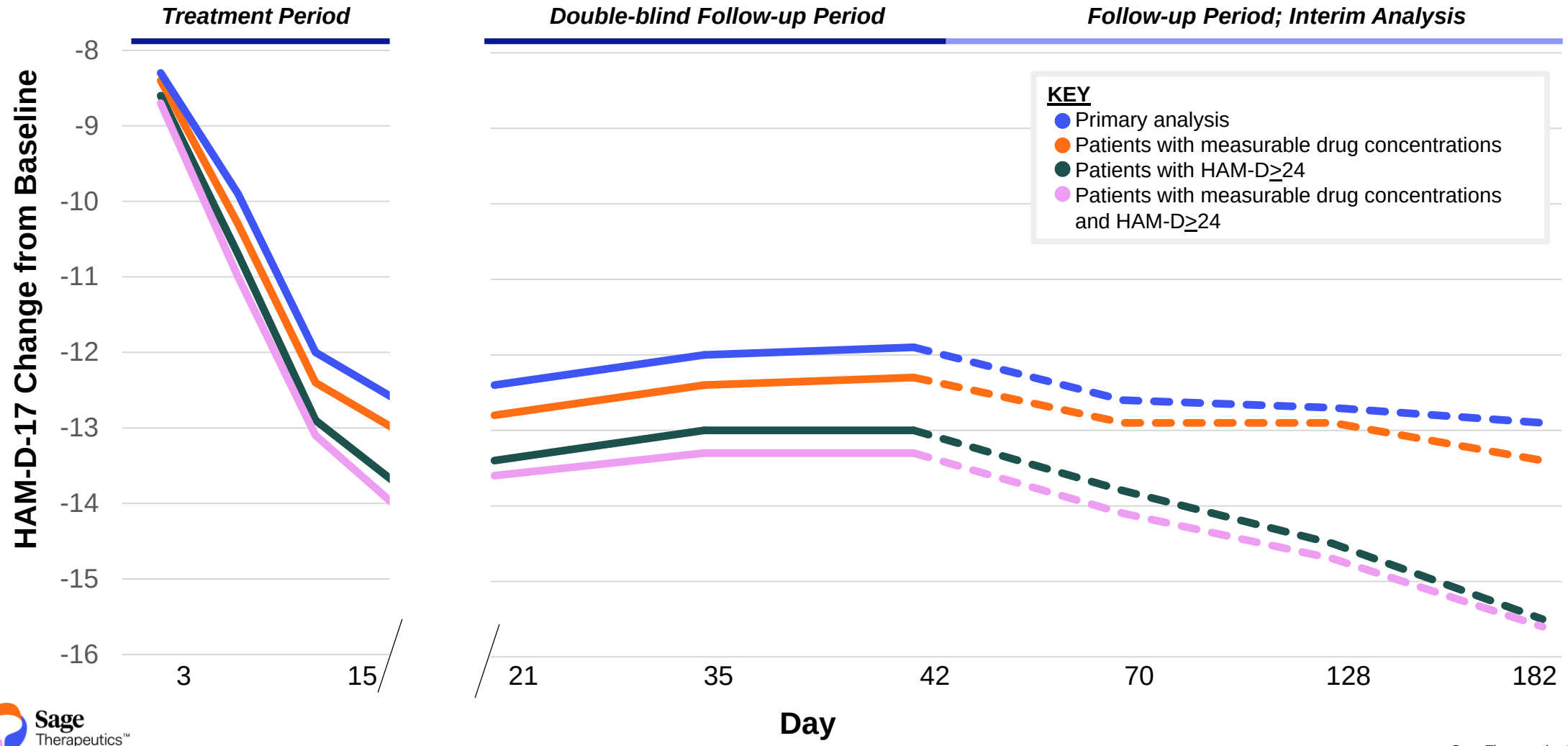
Primary Efficacy Through End of Treatment at Day 15

Impact Analysis HAM-D-17 change from baseline; p-value vs. matched placebo (sample size)				
Day	**Primary analysis**	**Patients with measurable drug concentrations**	**Patients with HAM-D≥24**	**Patients with measurable drug concentrations and HAM-D≥24**
3	-8.3; p=0.016 (n=163)	-8.4; p=0.011 (n=148)	-8.6; p=0.015 (n=122)	-8.7; p=0.015 (n=113)
8	-9.9; p=0.008 (n=160)	-10.3; p=0.002 (n=145)	-10.7; p=0.005 (n=121)	-11.0; p=0.003 (n=112)
12	-12.0; p=0.018 (n=154)	-12.4; p=0.006 (n=140)	-12.9; p=0.007 (n=116)	-13.1; p=0.005 (n=108)
15	-12.6; p=0.115 (n=153)	-13.0; p=0.048 (n=139)	-13.7; p=0.032 (n=115)	-14.0; p=0.017 (n=107)

Sage Therapeutics™

Post-Hoc Analysis: SAGE-217 30 mg Performance by Factors

Primary Analysis Up to Day 182



Sage Therapeutics™

Post-Hoc Analysis: SAGE-217 30 mg Performance by Factors

Primary Analysis Days 21 to 182

Impact Analysis HAM-D-17 change from baseline; p-value vs. matched placebo (sample size)				
Day	**Primary analysis**	**Patients with measurable drug concentrations**	**Patients with HAM-D≥24**	**Patients with measurable drug concentrations and HAM-D≥24**
21	-12.4; p=0.195 (n=149)	-12.8; p=0.089 (n=136)	-13.4; p=0.048 (n=111)	-13.6; p=0.030 (n=104)
35	-12.0; p=0.559 (n=142)	-12.4; p=0.361 (n=129)	-13.0; p=0.119 (n=105)	-13.3; p=0.079 (n=98)
42	-11.9; p=0.807 (n=136)	-12.3; p=0.534 (n=124)	-13.0; p=0.265 (n=100)	-13.3; p=0.178 (n=94)
70	-12.6; p=0.335 (n=72)	-12.9; p=0.227 (n=67)	-13.8; p=0.085 (n=53)	-14.1; p=0.059 (n=49)
128	-12.7; p=0.568 (n=44)	-12.9; p=0.440 (n=44)	-14.5; p=0.146 (n=30)	-14.7; p=0.108 (n=30)
182	-12.9; p=0.619 (n=20)	-13.4; p=0.380 (n=20)	-15.5; p=0.099 (n=14)	-15.6; p=0.039 (n=14)

Sage Therapeutics™

Summary and Next Steps

- **MOUNTAIN Study did not meet its primary endpoint (Day 15)**
  - Statistical significance achieved at all earlier treatment timepoints
- **Two observations to put results in perspective**
  - “No drug detected” issue limited to small number of sites but impacted results
  - Study population included more patients with milder severity of symptoms than previous studies of SAGE-217
- **Data consistent and supportive of results in two earlier positive pivotal SAGE-217 studies**
- **Next steps**
  - Continue data analysis
  - Data to inform ongoing and other potential studies
  - Ongoing discussions with U.S. Food and Drug Administration to discuss breakthrough program
  - Present additional data at an upcoming medical congress

Sage Therapeutics™