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

March 30, 2020
Date of report (Date of earliest event reported)

Axsome Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-37635**	**45-4241907**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

200 Broadway, 3rd Floor **New York, New York**	**10038**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code **(212) 332-3241**

(Former name or former address, if changed since last report)

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	AXSM	The Nasdaq Global Market

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

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

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

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

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

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 8.01. Other Events.

On March 30, 2020, Axsome Therapeutics, Inc. (the "Company") issued a press release announcing topline results of the Company's STRIDE-1 Phase 3 trial of AXS-05 in treatment resistant depression ("TRD"). The Company will host a conference call at 8:00 a.m. ET on March 30, 2020 to discuss the results of the STRIDE-1 trial.

The full text of the press release is filed as Exhibit 99.1 hereto and is incorporated herein by reference. A copy of the presentation that the Company will use in connection with the conference call is filed as Exhibit 99.2 hereto and is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release dated March 30, 2020.
99.2	STRIDE-1 Presentation.

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.

Axsome Therapeutics, Inc.

Dated: March 30, 2020

By: /s/ Herriot Tabuteau, M.D.
Name: Herriot Tabuteau, M.D.
Title: President and Chief Executive Officer

Exhibit 99.1

Axsome Therapeutics Announces Topline Results of the STRIDE-1 Phase 3 Trial in Treatment Resistant Depression and Expert Call to Discuss Clinical Implications

Achieves key secondary endpoints demonstrating rapid and statistically significant improvements in depressive symptoms on MADRS versus active comparator at Weeks 1, 2, and overall (key secondary endpoints, p=0.02, 0.035, and 0.031)

Demonstrated numerical improvement on primary endpoint (MADRS at Week 6) versus active comparator, but did not reach statistical significance (p=0.12)

Rapid and statistically significant remission of depression achieved versus active comparator starting at Week 1 (p=0.001, QIDS-SR-16)

Statistically significant improvement in cognitive function (p=0.011) and anxiety (p=0.009, HAM-A) versus active comparator

Data support continued development in TRD with initiation of second Phase 3 trial anticipated 3Q 2020

NDA filing for Breakthrough Therapy-designated AXS-05 in MDD on track for 4Q 2020

Topline results for ADVANCE-1 pivotal trial of AXS-05 in Alzheimer's disease agitation on track for early 2Q 2020

Company to host conference call with Dr. Maurizio Fava today at 8:00 AM ET

NEW YORK, March 30, 2020 (Globe Newswire) – Axsome Therapeutics, Inc. (NASDAQ: AXSM), a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders, today announced that AXS-05, a novel, oral, investigational NMDA receptor antagonist with multimodal activity, met key secondary endpoints in the STRIDE-1 trial by rapidly and statistically significantly improving symptoms of depression on the Montgomery-Åsberg Depression Rating Scale (MADRS), as early as Week 1 and for the overall 6-week treatment period, as compared to the active comparator bupropion in patients with treatment resistant depression (TRD). The STRIDE-1 trial did not reach statistical significance on the Week 6 primary endpoint on MADRS. STRIDE-1 was a randomized, double-blind, active-controlled, multi-center, U.S. trial, in which 312 adult patients with confirmed TRD, who had failed two or three prior treatments, were randomized to treatment with either AXS-05 (45 mg dextromethorphan/105 mg bupropion) or 150 mg bupropion, twice daily for 6 weeks.

AXS-05 rapidly and significantly improved symptoms in patients with TRD as measured by MADRS averaged over the entire 6-week treatment period, a key secondary endpoint, with mean reductions of 8.6 for AXS-05 versus 6.7 for bupropion (p=0.031). The rapid onset of action with AXS-05 treatment was demonstrated with statistically significant mean MADRS reductions at Week 1, the earliest time point measured, of 5.2 versus 3.6 respectively for AXS-05 and bupropion (p=0.02), and at Week 2 of 8.0 versus 6.1 respectively for AXS-05 and bupropion (p=0.035), both time points being key secondary endpoints. At Week 6, the primary endpoint, AXS-05 demonstrated a numerically greater improvement in MADRS, with mean reductions of 11.6 for AXS-05 versus 9.4 for bupropion (p=0.117).

AXS-05 rapidly and significantly improved depressive symptoms in patients with TRD as measured by the Quick Inventory of Depressive Symptomatology-Self-Rated (QIDS-SR-16) averaged over the entire 6-week treatment period, with mean reductions of 3.3 for AXS-05 versus 2.3 for bupropion (p=0.013). Rates of remission from depression (defined as QIDS-SR-16 ≤5) were statistically significantly greater for AXS-05 compared to bupropion at Week 1 (p=0.001) and at every time point thereafter, being achieved by 18.2% of AXS-05 patients compared to 8.2% of bupropion patients at Week 6 (p=0.012).

AXS-05 significantly improved cognitive function in patients with TRD as compared to bupropion, assessed using the Cognitive subscale of the Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire (CPFQ) (p=0.011). Cognitive dysfunction is well documented in the different phases of major depression, and plays an important role in functional recovery from major depression. The improvement in cognitive function with AXS-05 was rapid as compared to bupropion, reaching statistical significance as early as Week 2 (p=0.01) and at every time point thereafter. The Cognitive subscale of the CPFQ assesses sharpness/mental acuity, and the ability to focus/maintain attention, to remember/recall information, and to find words. Statistical significance for the superiority of AXS-05 versus bupropion was also achieved for the entire CPFQ (p=0.014), which assesses physical in addition to cognitive functioning.

AXS-05 rapidly and significantly reduced anxiety symptoms in patients with TRD as compared to bupropion, assessed using the Hamilton Anxiety Scale (HAM-A) (p=0.009). AXS-05 demonstrated numerical improvement versus the active comparator bupropion for all other efficacy variables assessed.

“In patients with depression that is resistant to current treatments, AXS-05 demonstrated a rapid and clinically meaningful improvement in depressive symptoms and in cognitive function. The results with AXS-05 in this trial are especially notable in light of the well-known low level of response in treatment resistant depression, the use of an active comparator administered at a higher dose, and the administration of the active comparator for twice the duration of AXS-05 administration,” said Professor Maurizio Fava, MD, Psychiatrist-in-Chief at Massachusetts General Hospital (MGH), Director of the Division of Clinical Research of the MGH Research Institute, and Associate Dean for Clinical & Translational Research at Harvard Medical School. “The results of the STRIDE-1 trial add to the growing body of evidence for the anti-depressant effects of AXS-05, an NMDA receptor antagonist with multimodal activity. These data suggest that AXS-05 may represent a novel approach both for the frontline treatment of major depressive disorder, and for treatment resistant depression.”

The positive findings with AXS-05 in patients with TRD build upon the rapid and statistically significant improvements in depressive symptoms in patients with MDD previously demonstrated in two pivotal trials, the ASCEND active-controlled trial and the GEMINI placebo-controlled trial. AXS-05 was granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) for the treatment of MDD in March 2019. Based on the outcome of the FDA Breakthrough Therapy meeting, Axsome believes the positive results of the GEMINI and ASCEND trials are sufficient to support submission of a New Drug Application (NDA) for AXS-05 for the treatment of MDD, as previously disclosed. Axsome remains on track to submit the NDA in the fourth quarter of 2020.

AXS-05 was well tolerated in the trial. The most commonly reported adverse events in the AXS-05 arm were dizziness and nausea. The rates of discontinuation due to adverse events were low in both treatment groups (2.6% for AXS-05 and 1.9% for bupropion). There were 3 serious adverse events in the AXS-05 arm, consisting of migraine; overdose; and suicidal ideation, which occurred more than one week after the cessation of treatment. Treatment with AXS-05 was not associated with psychotomimetic effects, weight gain, or sexual dysfunction.

“These STRIDE-1 results provide the first evidence of clinical activity of AXS-05 in patients with treatment depression, an area of high unmet medical need. Although the primary endpoint at week 6 did not reach statistical significance, we are encouraged by the overall results as they continue to demonstrate a rapid, statistically significant onset of action for AXS-05 which, in this study, has translated through to even the most difficult-to-treat population,” said Herriot Tabuteau, MD, Chief Executive Officer of Axsome. “The differentiated profile of AXS-05 demonstrated in the STRIDE-1 trial, including rapid induction of remission, and positive effects on cognition and anxiety, support the continued development of AXS-05 in treatment resistant depression, and initiation of a second Phase 3 trial in this indication is anticipated in the third quarter. Separately, we remain on track to file an NDA in the fourth quarter for AXS-05 in the treatment of major depressive disorder, based on the previously completed positive GEMINI and ASCEND trials. We expect data readouts from our INTERCEPT Phase 3 trial of AXS-07 in early treatment of migraine imminently, and from our ADVANCE-1 Phase 2/3 trial of AXS-05 in Alzheimer’s disease agitation in early second quarter.”

“STRIDE-1 is now the third efficacy trial in which AXS-05 has demonstrated a rapid, statistically significant onset of action in patients with depression and it is the second trial against the active comparator bupropion in which AXS-05 has demonstrated statistically significant improvement in depressive symptoms,” said Cedric O’Gorman, MD, Senior Vice President of Clinical Development and Medical Affairs of Axsome. “The novel NMDA mechanism and multimodal action of AXS-05 may be especially relevant to patients with TRD given the growing evidence for the importance of glutamatergic modulation in depression. The observed improvements in both cognition and anxiety with AXS-05 are also noteworthy and expand AXS-05’s therapeutic profile in CNS disorders.”

Based on the results of the STRIDE-1 trial, Axsome intends to initiate a second Phase 3 trial of AXS-05 in patients with treatment resistant depression in the third quarter of 2020. Detailed study results, including additional secondary endpoints, will be submitted for presentation at upcoming medical meetings and for publication. AXS-05 is also being evaluated in the ADVANCE-1 trial in patients with Alzheimer's disease agitation. AXS-05 was granted Fast Track designations by the FDA for the treatment of TRD and for the treatment of Alzheimer's disease agitation.

Summary of Topline Results of the STRIDE-1 Trial

Effect on Depressive Symptoms

- AXS-05 was associated with a statistically significant mean reduction from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score over the entire 6-week treatment period (key secondary endpoint), with mean reductions of 8.6 for AXS-05 versus 6.7 for bupropion (p=0.031).

- AXS-05 was associated with a statistically significant mean reduction from baseline in the Quick Inventory of Depressive Symptomatology-Self-Rated (QIDS-SR-16) total score over the entire 6-week treatment period, with mean reductions of 3.3 for AXS-05 versus 2.3 for bupropion (p=0.013).

- Remission from depression (defined as QIDS-SR-16 ≤5) was statistically significantly greater for AXS-05 compared to bupropion, being achieved by 18.2% of AXS-05 patients compared to 8.2% of bupropion patients at Week 6 (p=0.012).

Time Course of Effect on Depressive Symptoms

- At Week 1 (key secondary endpoint), the earliest time point assessed, AXS-05 demonstrated a statistically significant mean reduction from baseline in the MADRS total score of 5.2 versus 3.6 for bupropion (p=0.02).

- At Week 2 (key secondary endpoint), AXS-05 demonstrated a statistically significant mean reduction from baseline in the MADRS total score of 8.0 versus 6.1 for bupropion (p=0.035).

- At Week 6 (primary endpoint), AXS-05 demonstrated a numerically greater improvement in MADRS, with mean reductions of 11.6 for AXS-05 versus 9.4 for bupropion (p=0.117).

- At Week 1, remission rates (defined as QIDS-SR-16 ≤5) were statistically significantly greater with AXS-05 versus bupropion (p=0.001), with statistical significance maintained at every time point thereafter.

Cognitive Function

- AXS-05 was associated with a statistically significant improvement in cognitive function in patients as compared to bupropion, assessed using the Cognitive subscale of the Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire (CPFQ) (p=0.011).

- The improvement in cognitive function with AXS-05 was rapid as compared to the active comparator bupropion, reaching statistical significance as early as Week 2 (p=0.01) and at every time point thereafter.

Anxiety Symptoms

- AXS-05 rapidly and significantly reduced anxiety symptoms as compared to bupropion, assessed using the Hamilton Anxiety Scale (HAM-A) (p=0.009).

Safety and Tolerability

- AXS-05 was well tolerated in the trial.
- The most commonly reported adverse events in the AXS-05 arm were dizziness and nausea. There were 3 serious adverse events in the AXS-05 arm, consisting of migraine; overdose; and suicidal ideation, which occurred more than one week after the cessation of treatment.
- The rates of discontinuation due to adverse events were low in both treatment groups (2.6% for AXS-05 and 1.9% for bupropion).
- Treatment with AXS-05 was not associated with psychotomimetic effects, weight gain, or sexual dysfunction.

Conference Call Information

Axsome will host a conference call and webcast with slides today at 8:00 AM Eastern to discuss the topline results of the STRIDE-1 trial of AXS-05 in treatment resistant depression. Professor Maurizio Fava, MD, Psychiatrist-in-Chief at Massachusetts General Hospital (MGH), Director of the Division of Clinical Research of the MGH Research Institute, and Associate Dean for Clinical & Translational Research at Harvard Medical School will join the call and will be available to answer questions. To participate in the live conference call, please dial (844) 698-4029 (toll-free domestic) or (647) 253-8660 (international), and use the passcode 4166236. The live webcast can be accessed on the "Webcasts & Presentations" page of the "Investors" section of the Company's website at axsome.com. A replay of the webcast will be available for approximately 30 days following the live event.

About the STRIDE-1 Trial

STRIDE-1 (Symptom Treatment in Resistant Depression 1) was a Phase 3, randomized, double-blind, active controlled trial to assess the efficacy and safety of AXS-05 in the treatment of treatment resistant depression (TRD). Patients with major depressive disorder (MDD) who had previously failed one or two antidepressant treatments were treated in an open-label fashion with 150 mg bupropion twice daily (300 mg total daily dose) (n=799) during a 6-week lead-in period. Patients who failed to respond to bupropion during this lead-in period were randomized in a 1:1 ratio to treatment with bupropion at this same total daily dose (n=156), or to treatment with AXS-05 (45 mg dextromethorphan/105 mg bupropion) twice daily (90 mg dextromethorphan/210 mg bupropion total daily dose) (n=156), for 6 weeks. The change in depressive symptoms over time was measured using the Montgomery-Åsberg Depression Rating Scale (MADRS) and the Quick Inventory of Depressive Symptomatology-Self-Rated (QIDS-SR-16). The primary endpoint was the change from baseline in the MADRS after 6 weeks of treatment. The key secondary endpoints were the change from baseline in the MADRS after 1 week of treatment, after 2 weeks of treatment, the average change over entire 6-week double-blind treatment period, and the Sheehan Disability Scale (SDS). Other pre-specified secondary efficacy variables included the Cognitive subscale of the Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire (CPFQ), and the Hamilton Anxiety Scale (HAM-A).

About Treatment Resistant Depression (TRD)

Patients diagnosed with major depressive disorder (MDD) are defined as having TRD if they have failed two or more antidepressant therapies. MDD is a serious condition characterized by depressed mood or a loss of interest or pleasure in daily activities consistently for at least a two-week period, and which impairs social, occupational, educational, or other important functioning. According to the National Institute of Health, an estimated 7.1% of U.S. adults experience MDD each year. Nearly two-thirds of diagnosed and treated patients do not experience adequate treatment response with first-line therapy, and the majority of these initial failures also fail second-line treatment.

About the Montgomery-Åsberg Depression Rating Scale (MADRS)

The Montgomery-Åsberg Depression Rating Scale (MADRS) is a well-established, 10-item, validated rating scale used to provide an assessment of depression, and as a guide to evaluate recovery. This scale is an accepted regulatory endpoint for depression. The scale is used in clinical research to rate the severity of a patient's depression by probing mood, feelings of guilt, suicide ideation, insomnia, agitation, anxiety, weight loss, and somatic symptoms.

About AXS-05

AXS-05 is a novel, oral, patent-protected, investigational NMDA receptor antagonist with multimodal activity under development for the treatment of major depressive disorder and other central nervous system (CNS) disorders. AXS-05 consists of a proprietary formulation and dose of dextromethorphan and bupropion and utilizes Axsome's metabolic inhibition technology. The dextromethorphan component of AXS-05 is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, also known as a glutamate receptor modulator, which is a novel mechanism of action, meaning it works differently than currently approved therapies for major depressive disorder. The dextromethorphan component of AXS-05 is also a sigma-1 receptor agonist, nicotinic acetylcholine receptor antagonist, and inhibitor of the serotonin and norepinephrine transporters. The bupropion component of AXS-05 serves to increase the bioavailability of dextromethorphan, and is a norepinephrine and dopamine reuptake inhibitor, and a nicotinic acetylcholine receptor antagonist. AXS-05 is covered by more than 40 issued U.S. and international patents which provide protection out to 2034. AXS-05 has been granted U.S. Food and Drug Administration (FDA) Breakthrough Therapy designation for the treatment of MDD as well as Fast Track designations for the treatment of treatment resistant depression and for the treatment of Alzheimer's disease agitation. AXS-05 is not approved by the FDA.

About Axsome Therapeutics, Inc.

Axsome Therapeutics, Inc. is a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system (CNS) disorders for which there are limited treatment options. Axsome's core CNS product candidate portfolio includes four clinical-stage candidates, AXS-05, AXS-07, AXS-09, and AXS-12. AXS-05 is being developed for major depressive disorder (MDD), treatment resistant depression (TRD), Alzheimer's disease (AD) agitation, and for smoking cessation treatment. AXS-07 is being developed for the acute treatment of migraine. AXS-12 is being developed for the treatment of narcolepsy. AXS-14 is being developed for the treatment of fibromyalgia. AXS-05, AXS-07, AXS-09, AXS-12, and AXS-14 are investigational drug products not approved by the FDA. For more information, please visit the Company's website at axsome.com. The Company may occasionally disseminate material, nonpublic information on the company website.

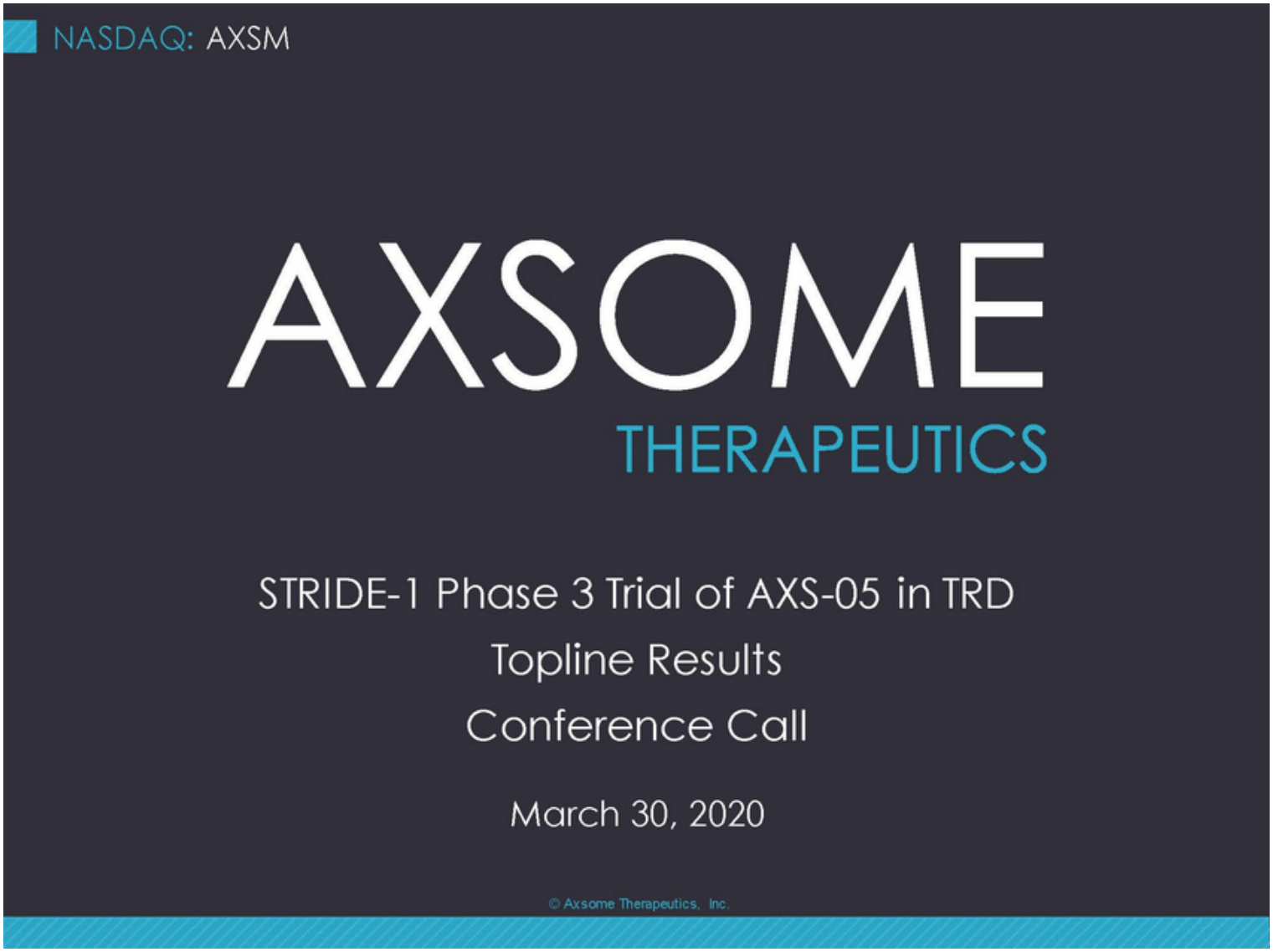
Forward Looking Statements

Certain matters discussed in this press release are "forward-looking statements". We may, in some cases, use terms such as "predicts," "believes," "potential," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. In particular, the Company's statements regarding trends and potential future results are examples of such forward-looking statements. The forward-looking statements include risks and uncertainties, including, but not limited to, the success, timing and cost of our ongoing clinical trials and anticipated clinical trials for our current product candidates, including statements regarding the timing of initiation, pace of enrollment and completion of the trials (including our ability to fully fund our disclosed clinical trials, which assumes no material changes to our currently projected expenses), futility analyses and receipt of interim results, which are not necessarily indicative of the final results of our ongoing clinical trials, and the number or type of studies or nature of results necessary to support the filing of a new drug application ("NDA") for any of our current product candidates; our ability to fund additional clinical trials to continue the advancement of our product candidates; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration ("FDA") or other regulatory authority approval of, or other action with respect to, our product candidates (including, but not limited to, FDA's agreement with the Company's plan to discontinue the bupropion treatment arm of the ADVANCE-1 study in accordance with the independent data monitoring committee's recommendations); the potential for the MOMENTUM clinical trial to provide a basis for approval of AXS-07 for the acute treatment of migraine in adults with or without aura, pursuant to our special protocol assessment; the potential for the ASCEND clinical trial, combined with the GEMINI clinical trial results, to provide a basis for approval of AXS-05 for the treatment of major depressive disorder and accelerate its development timeline and commercial path to patients; the Company's ability to successfully defend its intellectual property or obtain the necessary licenses at a cost acceptable to the Company, if at all; the successful implementation of the Company's research and development programs and collaborations; the success of the Company's license agreements; the acceptance by the market of the Company's product candidates, if approved; the Company's anticipated capital requirements, including the Company's anticipated cash runway; unforeseen circumstances or other disruptions to normal business operations arising from or related to COVID-19; and other factors, including general economic conditions and regulatory developments, not within the Company's control. The factors discussed herein could cause actual results and developments to be materially different from those expressed in or implied by such statements. The forward-looking statements are made only as of the date of this press release and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstance.

Axsome Contact:

Mark Jacobson
Chief Operating Officer
Axsome Therapeutics, Inc.
200 Broadway, 3rd Floor
New York, NY 10038
Tel: 212-332-3243
Email: mjacobson@axsome.com
www.axsome.com

Exhibit 99.2


NASDAQ: AXSM
AXSOME
THERAPEUTICS
STRIDE-1 Phase 3 Trial of AXS-05 in TRD
Topline Results
Conference Call
March 30, 2020
© Axsome Therapeutics, Inc.

AXS-05 in Treatment Resistant Depression (TRD)
STRIDE-1 Phase 3 Trial Topline Results

Introduction	**Mark Jacobson**, Chief Operating Officer
Overview and Summary	**Herriot Tabuteau, MD**, Chief Executive Officer
STRIDE-1 Trial Design & Results	**Cedric O'Gorman, MD**, Senior Vice President, Clinical Development & Medical Affairs
KOL Perspective of STRIDE-1 Data	**Maurizio Fava, MD,** Psychiatrist-in-Chief at Massachusetts General Hospital (MGH), Director of the Division of Clinical Research of the MGH Research Institute, Associate Dean for Clinical & Translational Research at Harvard Medical School
Q&A	**Presenters, Nick Pizzie**, Chief Financial Officer and **Dave Marek,** Chief Commercial Officer
Concluding Remarks	**Herriot Tabuteau, MD**, Chief Executive Officer

Forward-Looking Statements & Safe Harbor

Certain information contained in this presentation may include "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. We may, in some cases, use terms such as "predicts," "believes," "potential," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. In particular, the Company's statements regarding trends and potential future results are examples of such forward-looking statements. The forward-looking statements include risks and uncertainties, including, but not limited to, the success, timing and cost of our ongoing clinical trials and anticipated clinical trials for our current product candidates, including statements regarding the timing of initiation, pace of enrollment and completion of the trials (including our ability to fully fund our disclosed clinical trials, which assumes no material changes to our currently projected expenses), futility analyses and receipt of interim results, which are not necessarily indicative of the final results of our ongoing clinical trials and the number or type of studies or nature of results necessary to support the filing of a new drug application for any of our current product candidates; our ability to fund additional clinical trials to continue the advancement of our product candidates; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration ("FDA") or other regulatory authority approval of, or other action with respect to, our product candidates (including, but not limited to, FDA's agreement with the Company's plan to discontinue the bupropion treatment arm of the ADVANCE-1 study in accordance with the independent data monitoring committee's recommendations); the Company's ability to obtain additional capital necessary to fund its operations; the Company's ability to generate revenues in the future; the potential for the MOMENTUM clinical trial to provide a basis for approval of AXS-07 for the acute treatment of migraine in adults with or without aura, pursuant to our special protocol assessment; the potential for the ASCEND clinical trial, combined with the GEMINI clinical trial results, to provide a basis for approval of AXS-05 for the treatment of major depressive disorder and accelerate its development timeline and commercial path to patients; the Company's ability to successfully defend its intellectual property or obtain the necessary licenses at a cost acceptable to the Company, if at all; the successful implementation of the Company's research and development programs and collaborations; the enforceability of the Company's license agreements; the acceptance by the market of the Company's product candidates, if approved; the Company's anticipated capital requirements, including the Company's anticipated cash runway; and other factors, including general economic conditions and regulatory developments, not within the Company's control. These factors could cause actual results and developments to be materially different from those expressed in or implied by such statements. Forward-looking statements are not guarantees of future performance, and actual results may differ materially from those projected. The forward-looking statements are made only as of the date of this presentation and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstance.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. In addition, these projections, assumptions and estimates are necessarily subject to a high degree of uncertainty and risk.

Summary and Overview

Herriot Tabuteau, MD

AXSOME THERAPEUTICS

Chief Executive Officer
Axsome Therapeutics, Inc.

Summary of Topline Results:
Rapid and Significant Effects with AXS-05 in TRD Patients

- AXS-05: a novel, oral, investigational NMDA receptor antagonist with multimodal activity
- Rapid and statistically significant improvements in MADRS versus bupropion at Weeks 1, 2, and overall (key secondary endpoints)
- Numerical separation from bupropion at all timepoints, statistical significance not reached on primary endpoint (Week 6)
- Rapid and highly statistically significant induction of remission on the QIDS-SR-16 (score of ≤ 5) as compared to bupropion starting at Week 1, with significance maintained at every point thereafter
- AXS-05 demonstrated statistically significant improvements in cognitive function and reduction in anxiety symptoms versus bupropion
- AXS-05 was generally safe, well tolerated, and not associated with psychotomimetic effects, weight gain or sexual dysfunction
- These results support continued development in TRD with initiation of second Phase 3 trial anticipated 3Q 2020
- On track for planned NDA filing for Breakthrough Therapy designated AXS-05 in MDD for 4Q 2020

Treatment Resistant Depression (TRD): Urgent Unmet Medical Need

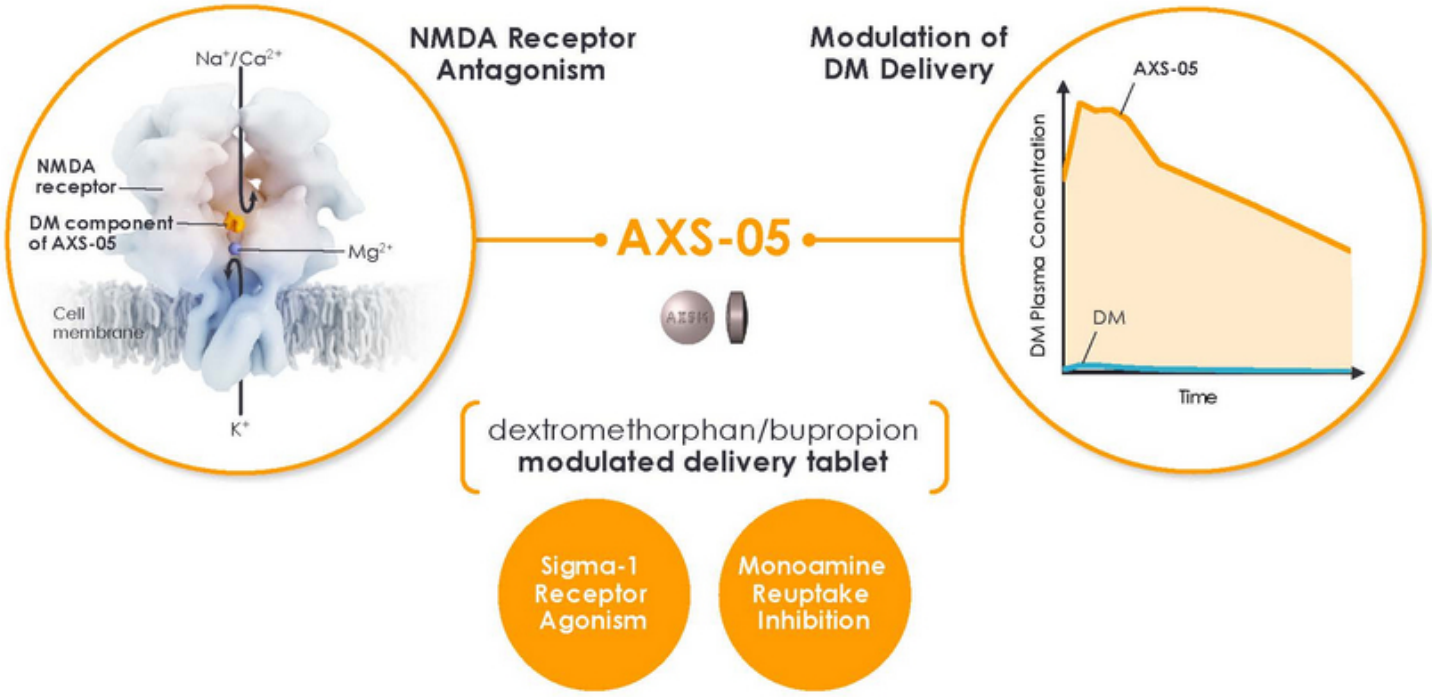
- Depression is a disabling and potentially life-threatening, biologically-based disorder
- 17 million U.S. adults experience major depressive episodes each year and at least one-third of them are considered treatment resistant[1,2]
- Patients are considered treatment resistant if they have not responded adequately to at least 2 different anti-depressants of adequate dose and duration in the current depressive episode[2]
- Treatment resistant depression is a chronic disorder associated with high economic burden, significantly impacted quality of life and various comorbid conditions[3]
- Limited treatment options are available
- Urgent need exists for new treatments that have rapid and significant efficacy, are safe and well tolerated, and offer convenient administration

17 million U.S. adults experience major depressive episodes each year[1]

At least **5.7 million** Of them are considered treatment resistant[2]

1. National Survey on Drug Use and Health (NSDUH). (2017).
2. Rush AJ, et al. *Am J Psychiatry* 2006;163:1905-1917.
3. Mrazek DA et al. *Psychiatr Serv*. 2014;65(8):977-987.

AXS-05: Novel, Oral, NMDA Receptor Antagonist with Multimodal Activity



Abbreviations: DM = Dextromethorphan; Mg2+=magnesium ion; Na+=sodium ion; Ca+2=calcium ion; K+=potassium ion. Axsome data on file

STRIDE-1 Phase 3 Trial Design & Results

Cedric O'Gorman MD, MBA

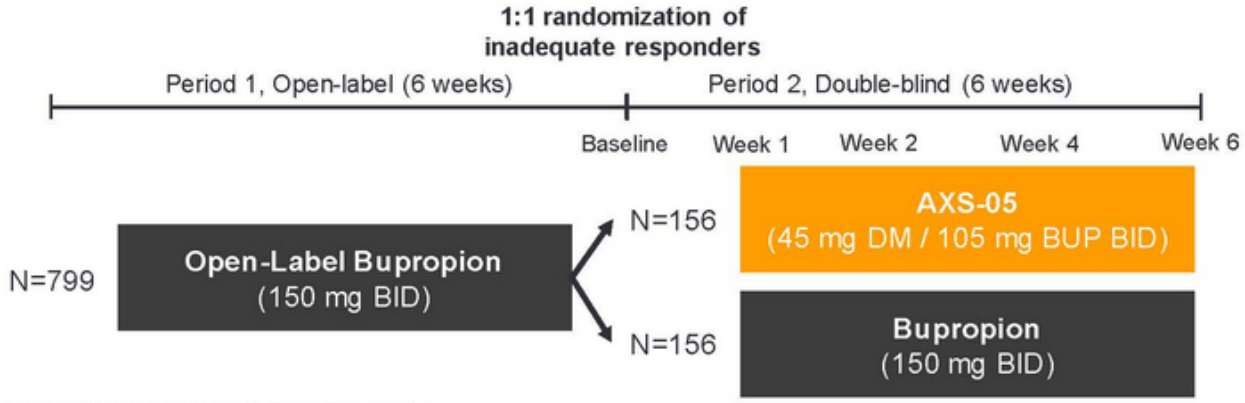
AXSOME THERAPEUTICS

Senior Vice President, Clinical Development and Medical Affairs
Axsome Therapeutics, Inc.

STRIDE-1 Phase 3 Trial: Design Summary

Stride1Study AXS-05

A Phase 3 trial to assess the efficacy and safety of AXS-05 in the treatment of TRD



BID = twice daily; BUP = Bupropion; DM = Dextromethorphan.

- **Primary Endpoint:** Change in depression score from randomization to end of study, measured using the Montgomery-Åsberg Depression Rating Scale (MADRS)

- **Key Secondary Endpoints:**
  - Change from baseline in MADRS at week 2 post-randomization
  - Change from baseline in MADRS at week 1 post-randomization
  - Overall treatment effect on MADRS total score
  - Change from baseline in Sheehan Disability Scale (SDS) at week 6 post-randomization

STRIDE-1 Phase 3 Trial: Key Entry Criteria

Inclusion criteria included:

Open-label Period

- Male or female 18-65 years of age inclusive
- History of inadequate response to 1 or 2 prior antidepressant treatments, established by ATRQ
- Hamilton Depression Rating Scale (HAMD-17) total score of ≥ 18

Double-blind Period

- Inadequate response to 2 or 3 prior antidepressant treatments, including open-label period failure

Exclusion criteria included:

- History of electroconvulsive therapy, vagus nerve stimulation, transcranial magnetic stimulation or any experimental central nervous system treatment during the current episode or in the past 6 months
- Schizophrenia, bipolar disorder, obsessive compulsive disorder
- Psychiatric symptoms secondary to any other general medical condition

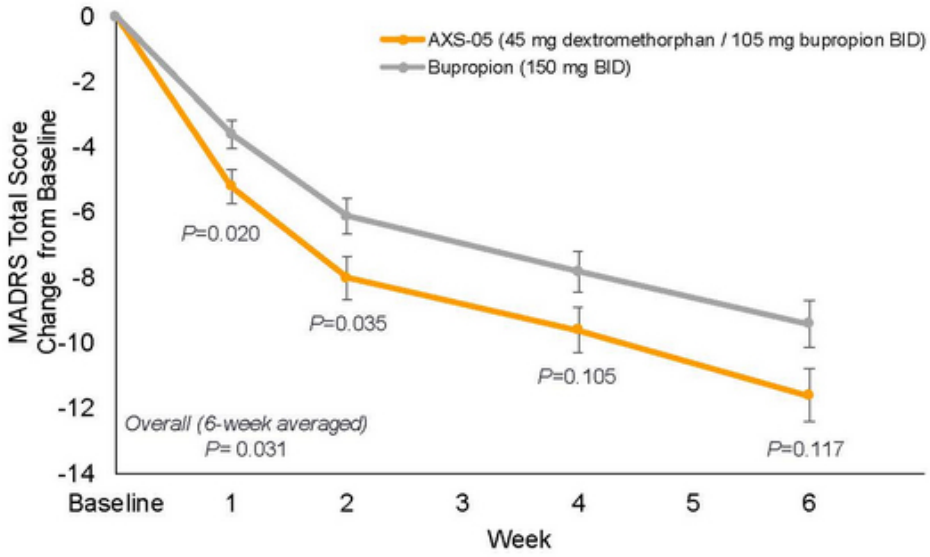
STRIDE-1 Phase 3 Trial:
Demographics and Baseline Characteristics

	AXS-05 (45 mg DM / 105 mg BUP)	Bupropion (150 mg)
Age (years)	44.3 (12.19)	45.1 (12.56)
Female Gender, n (%)	101 (65.6%)	97 (62.6%)
Race, n (%)		
White	100 (64.9%)	106 (68.4%)
Black or African American	41 (26.6%)	39 (25.2%)
Asian	2 (1.3%)	6 (3.9%)
Other or Not Reported	11 (7.1%)	4 (2.6%)
BMI (mg/kg^2)	29.9 (5.85)	29.5 (5.64)
MADRS Total Score	33.4 (5.61)	33.2 (5.17)
CGI-S Score	4.6 (0.61)	4.6 (0.54)

Data are mean (SD) unless otherwise stated.
Abbreviations: BMI = Body Mass Index; BUP = bupropion; CGI-S = Clinical Global Impression – Severity; DM = dextromethorphan; MADRS = Montgomery-Åsberg Depression Rating Scale

- Demographics and baseline characteristics were similar across both treatment groups
- Study completion rates were similar across both treatment groups, 89% for AXS-05 and 94% for bupropion

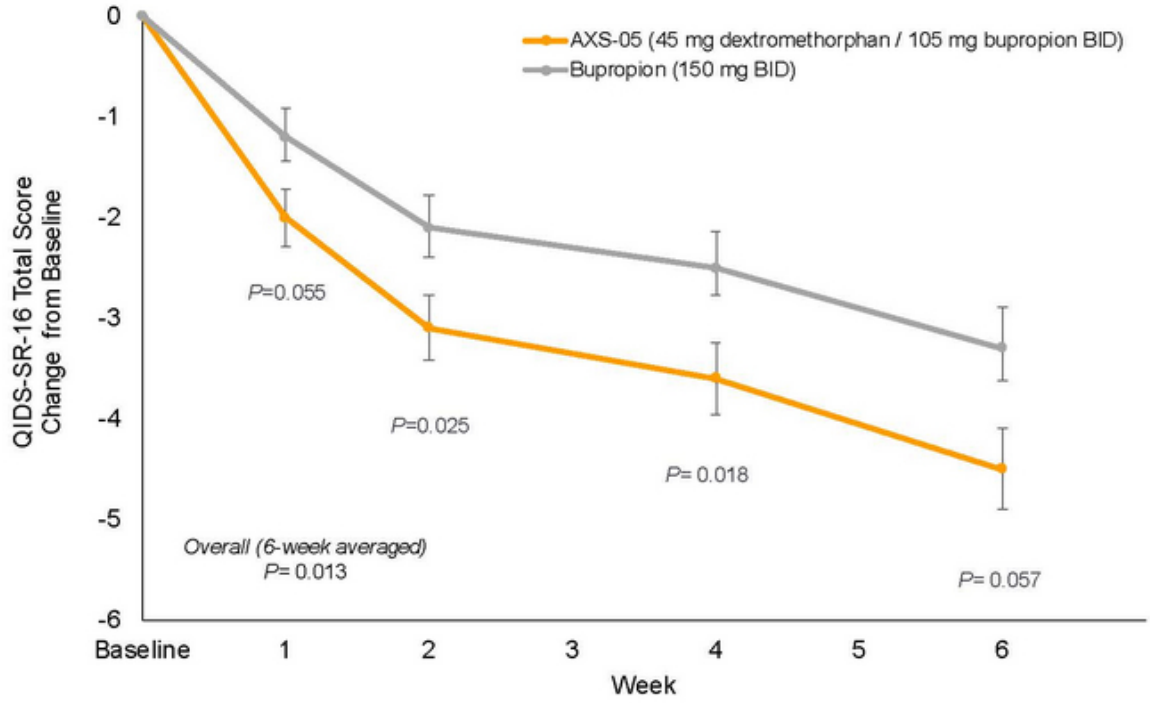
Improvement in Depressive Symptoms:
Change in MADRS Total Score



	AXS-05 (n=154)	Bupropion (n=155)	Difference	*P*-Value
Primary Endpoint: Change in MADRS Total Score at Week 6	-11.6	-9.4	-2.2	NS
Key Secondary Endpoints:				
Change in MADRS Total Score at Week 1	-5.2	-3.6	-1.6	0.020
Change in MADRS Total Score at Week 2	-8.0	-6.1	-2.1	0.035
Overall treatment effect on MADRS Total Score	-8.6	-6.7	-1.9	0.031

Notes: P-values calculated from LSMean. Abbreviations: BID = twice daily; MADRS = Montgomery-Åsberg Depression Rating Scale

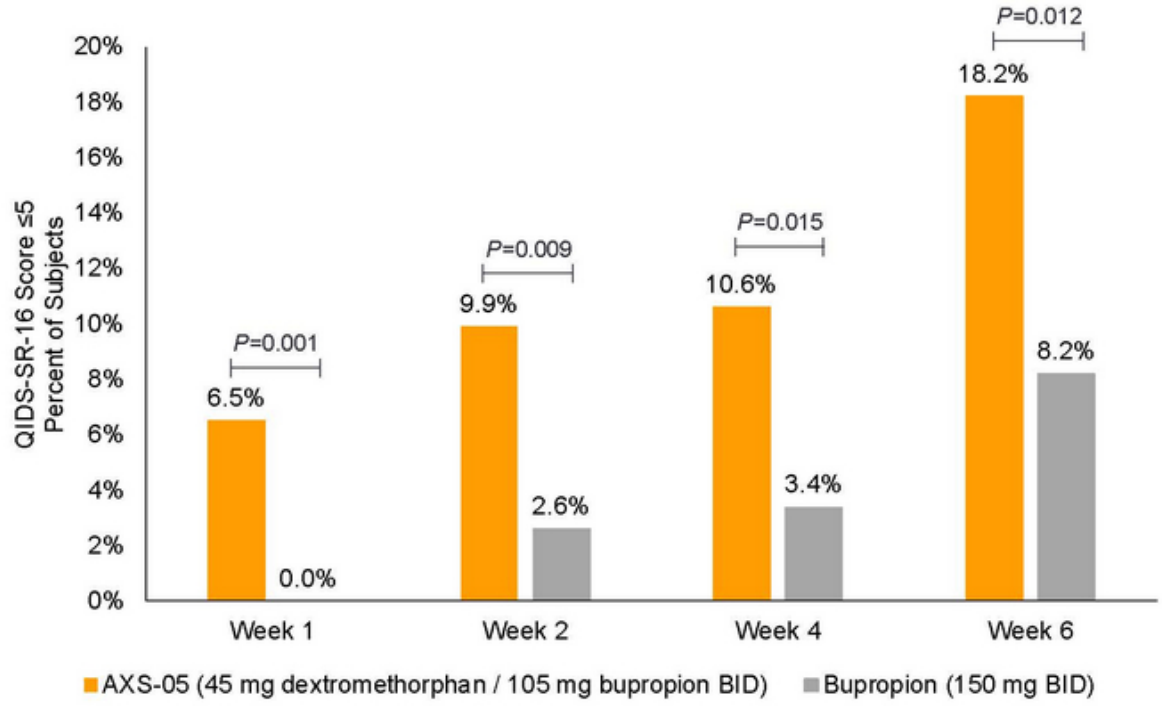
Improvement in Depressive Symptoms: Change in the QIDS-SR-16



Notes: P-values calculated from LSMean.
Abbreviations: BID = twice daily; QIDS-SR-16 = Quick Inventory of Depressive Symptomatology-Self-Report-16 Item

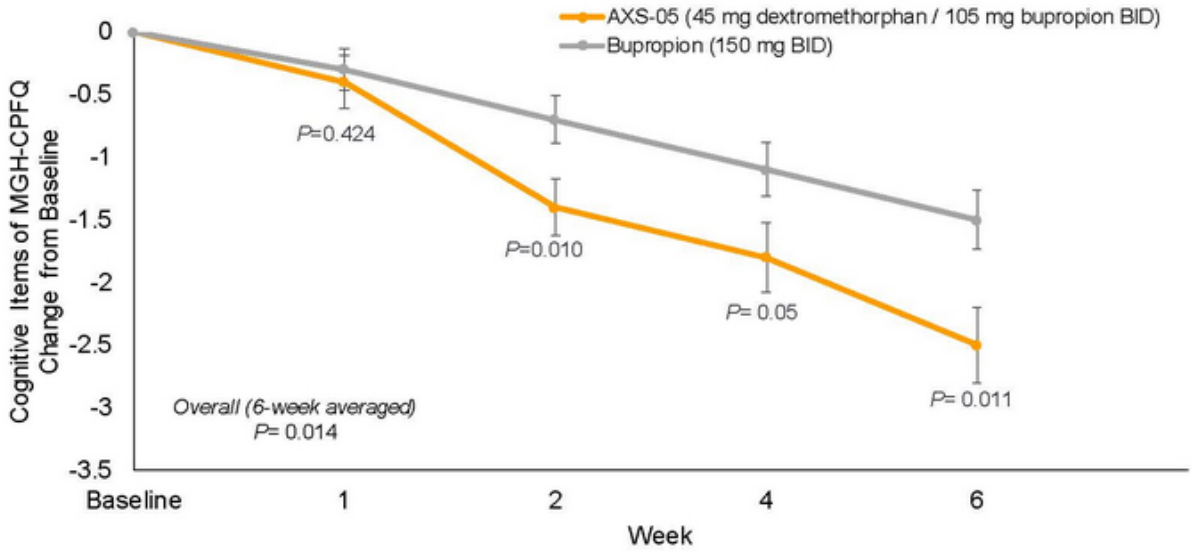
AXSOME THERAPEUTICS

Improvement in Depressive Symptoms:
Achievement of Remission (QIDS-SR ≤ 5)



Notes: P-values calculated from LSMean. Remission cut-off score of ≤5
Abbreviations: BID = twice daily; QIDS-SR-16 = Quick Inventory of Depressive Symptomatology-Self-Report-16 Item

Improvement in Cognitive Function:
Change in MGH-CPFQ-Cognitive Dimension



- Cognitive items of the CPFQ assess sharpness/mental acuity, and the ability to focus/maintain attention, to remember/recall information, and to find words
- Each of the 4 items on the cognitive dimension of the CPFQ are scored 1-6, with lower scores representing improvements in cognitive functioning

Notes: P-values calculated from LSMean.
Abbreviations: BID = twice daily; MGH-CPFQ = Massachusetts General Hospital -Cognitive and Physical Functioning Questionnaire

Safety Profile of AXS-05 in TRD:
Treatment-Emergent Adverse Events

	Double-blind Period[b]		Open-label Period
	AXS-05 (N = 154)	Bupropion (N = 156)	Bupropion (n=310)
Any TEAE[a]	**67 (43.5%)**	**61 (39.1%)**	**135 (43.5)**
Dizziness	13 (8.4%)	0	9 (2.9%)
Nausea	8 (5.2%)	3 (1.9%)	22 (7.1%)
Dry mouth	6 (3.9%)	3 (1.9%)	13 (4.2%)
Headache	4 (2.6%)	7 (4.5%)	14 (4.5%)
Insomnia	3 (1.9%)	5 (3.2%)	19 (6.1%)
Constipation	3 (1.9%)	3 (1.9%)	13 (4.2%)
Anxiety	2 (1.3%)	0	11 (3.5%)
Irritability	0	2 (1.3%)	10 (3.2%)

Abbreviations: AE = adverse event. Data presented as number of subjects (% of subjects)
a. Treatment-emergent AEs occurring in ≥3% of subjects during the open-label period or ≥5% of subjects during the double-blind period are reported
b. In double-blind period, treatment-emergent AE is defined as any AE with an onset on or after date of randomization and prior to or on visit 9 date or period 2 early termination date

- Rates of discontinuation due to adverse events were low in both groups; 2.6% for AXS-05 and 1.3% for bupropion
- Three serious adverse events occurred in the AXS-05 arm: migraine, overdose, and suicidal ideation (8 days after subject completed treatment)

STRIDE-1 Phase 3 Trial Results: Summary

- AXS-05 met key secondary endpoints by rapidly improving symptoms of depression in patients with treatment resistant depression (TRD)
- AXS-05 demonstrated numerical improvement on primary endpoint (MADRS at Week 6) versus active comparator, but did not reach statistical significance
- Statistically significant greater rates of remission on the QIDS as compared to bupropion
- Statistically significant improvements with AXS-05 compared to bupropion in cognition and anxiety
- AXS-05 was generally safe and well tolerated in this trial, consistent with our prior experience with AXS-05

KOL Perspective on STRIDE-1 Data

Professor Maurizio Fava, MD

AXSOME THERAPEUTICS

Psychiatrist-in-Chief at Massachusetts General Hospital (MGH)
Director of the Division of Clinical Research of the MGH Research Institute
Associate Dean for Clinical & Translational Research at Harvard Medical School

Q&A

AXSOME THERAPEUTICS

Concluding Remarks

Herriot Tabuteau, MD

Chief Executive Officer
Axsome Therapeutics, Inc.

AXS-05:
Clinical Programs in Psychiatry

	Clinical Program				
	ASCEND	**GEMINI**	**STRIDE-1**	**AXS-05 / OL**	**ADVANCE-1**
Indication	MDD	MDD	TRD	MDD/TRD	AD Agitation
Phase	Pivotal Phase 2	Pivotal Phase 3	Pivotal Phase 3	Open-label Phase 3	Pivotal Phase 2/3
Objectives	Efficacy of AXS-05 vs. BUP	Efficacy of AXS-05 vs. PBO	Efficacy of AXS-05 vs. BUP	Long-term safety of AXS-05	Efficacy of AXS-05 vs. BUP and PBO
Status	Completed	Completed	Completed	Ongoing	Dosing Complete
Subjects Dosed	96	326	310	876	>360

Abbreviations: BUP = bupropion; MDD = Major Depressive Disorder; OL = Open-label; PBO = placebo; TRD = Treatment Resistant Depression

- NDA filing of AXS-05 in the treatment of MDD, based on positive results from GEMINI and ASCEND trials on track for 4Q 2020
- FDA Breakthrough Therapy designation granted in MDD, Fast Track designation in TRD and AD agitation

Our CNS Candidates and Pipeline

- Five differentiated clinical-stage CNS assets targeting significant and growing markets
- Patent protection to 2034-2036, worldwide rights for most product candidates

Product Candidate	Phase 1	Phase 2	Phase 3	NDA
AXS-05 (DM + BUP)	Major Depressive Disorder: Breakthrough Therapy Designation			
	Treatment Resistant Depression: Fast Track Designation			
	Agitation in Alzheimer's Disease: Fast Track Designation			
	Smoking Cessation			
AXS-07 (MoSEIC™ Mx + Riz)	Migraine			
AXS-12 (Reboxetine)	Narcolepsy: U.S. Orphan Designation			
AXS-14 (Esreboxetine)	Fibromyalgia			
AXS-09 (DM + *S*-BUP)	CNS Disorders			

Abbreviations: BUP = Bupropion; CNS = Central Nervous System; DM = Dextromethorphan; Mx = Meloxicam; Riz = Rizatriptan; *S*-BUP = Esbupropion.

Our Clinical and Regulatory Milestones

Product Candidate	Indication	2020
AXS-05 (DM + BUP)	MDD	• NDA submission (4Q)
	TRD	• STRIDE-1 topline results
	AD Agitation	✓ ADVANCE-1 Phase 2/3 topline results (early 2Q)
	Smoking Cessation	• FDA meeting (2020)
AXS-07 (MoSEIC™ Mx + Riz)	Migraine	• INTERCEPT Phase 3 topline results (imminent) • NDA submission (4Q)
AXS-12 (Reboxetine)	Narcolepsy	• Phase 3 trial start (2020)
AXS-14 (Esreboxetine)	Fibromyalgia	• FDA meeting (2020)

Abbreviations: AD = Alzheimer's Disease; BUP = Bupropion; DM = Dextromethorphan; MDD = Major Depressive Disorder; Mx = Meloxicam; Riz = Rizatriptan; TRD = Treatment Resistant Depression.
✓ Accomplished milestone.
• Upcoming milestone.

AXSOME

THERAPEUTICS

Thank you.

For more information, please contact

Mark Jacobson
Chief Operating Officer
212-332-3243
mjacobson@axsome.com

axsome.com