April 27, 2020

Axsome advances in agitation, but confirmatory study is still needed

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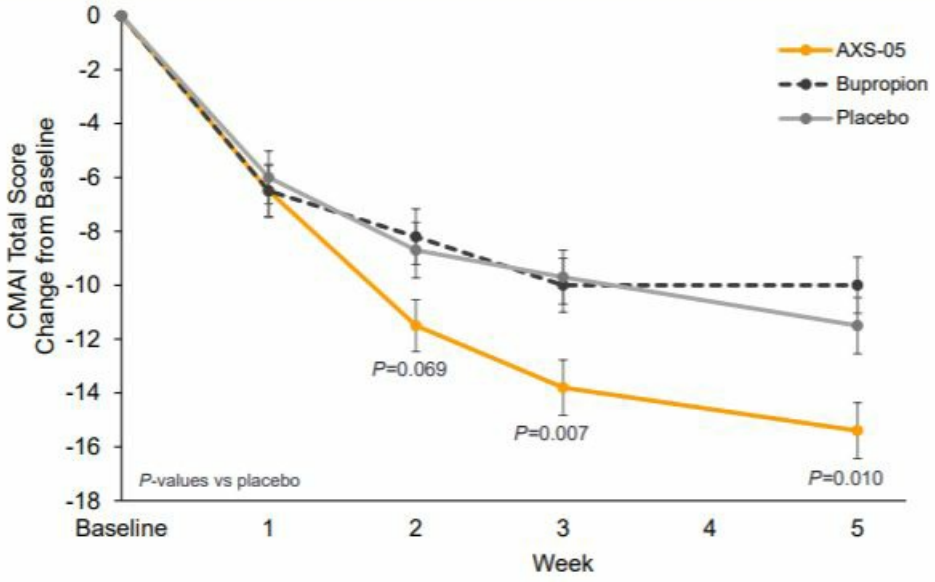
Despite a strong placebo response, not untypical for neuropsychiatry studies, Axsome bagged a win in Alzheimer's disease agitation today. The pivotal phase II/III Advance-1 study pitted AXS-05 against placebo or bupropion, one of AXS-05's components. AXS-05 met the primary endpoint, change from baseline in CMAI total score, a 29-item scale to assess agitation − a relief after last month's failure with the same project in treatment-resistant depression. The clinical need in Alzheimer's disease agitation is dire; antipsychotics are often used off-label, but come with black box warnings of an increased risk of mortality in elderly patients with dementia. AXS-05 showed an encouraging safety profile, and investors were obviously impressed − Axsome shares surged 30% at market open. However, a second trial will be needed for filing, Axsome said on a call today, and this is often where neurology projects are scuppered by marked placebo responses. An example of this is Avanir's AVP-786. This asset is mechanistically similar to AXS-05, and showed mixed results in two phase III studies in Alzheimer's disease agitation. A third trial is ongoing.

ADVANCE-1

Improvement in Agitation Symptoms:
Change in Cohen-Mansfield Agitation Inventory (CMAI)



	AXS-05 (n = 152)	Bupropion (n = 49)	Placebo (n = 156)
Primary Endpoint: Change in CMAI total score at Week 5	-15.4	-10.0	-11.5
P-value vs. AXS-05		<0.001	0.010

Notes: P-values calculated from LSMean. Abbreviations: BID = twice daily; CMAI = Cohen-Mansfield Agitation Index

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13

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