**METHOD:** Patients 10-17 years with bipolar I depression were randomized to 6 weeks of double-blind (DB) treatment with lurasidone or placebo. Patients who completed the study were eligible to enroll in a 2-year, open-label (OL) extension study in which patients were continued on flexibly-dosed lurasidone (20-80 mg/d; LUR-LUR) or switched from placebo to lurasidone (PBO-LUR). The primary efficacy measure was the Children's Depression Rating Scale, Revised (CDRS-R); response was defined as ≥50% reduction from DB baseline in the CDRS-R total score.

**RESULTS:** A total of 306 patients completed the 6-week DB study and entered the extension study; 195 (63.7%) completed 52 weeks, and 168 (54.9%) completed 104 weeks of treatment. Mean CDRS-R total score at DB baseline was 59.4 in patients treated with lurasidone, and 58.7 in patients treated with placebo; and mean CDRS-R total score at OL baseline (after 6 weeks of DB treatment) was 36.6 in the LUR-LUR group and 41.9 in the PBO-LUR group. For the total sample of patients in the OL study, mean change (from OL baseline) in the CDRS-R score was -13.4 at week 52 and -16.4 at week 104; and responder rates were 51.0% at OL baseline (64.5% for LUR-LUR; 36.9% for PBO-LUR), 88.4% at week 52, and 91.1% at week 104. During OL treatment with lurasidone, 31 patients (10.1%) discontinued due to an adverse event. The most commonly reported events were headache (23.9%), nausea (16.4%), and somnolence (9.8%). OL treatment with lurasidone was associated with few effects on metabolic parameters or prolactin. Mean change from DB baseline in weight was +4.25 kg at week 52 (vs. an expected weight gain of 3.76 kg based on CDC normative data), and +6.75 kg at week 104 (vs. CDC expected weight gain of 6.67 kg).

**CONCLUSION:** Two years of treatment with lurasidone in children and adolescents with bipolar depression was generally well-tolerated, with relatively low rates of study discontinuation. Lurasidone treatment was associated with few effects on weight, metabolic parameters, and prolactin. Patients also continued to experience improvement in depressive symptoms during long-term treatment with lurasidone.

Clinicaltrials.gov identifier: NCT01914393

Funding Acknowledgements: Supported by funding from Sunovion Pharmaceuticals Inc.

## 160

## Lurasidone and Metabolic Syndrome: Results from Short- and Long-Term Clinical Studies in Patients with Bipolar Depression

*Michael Tocco, PhD[1]; John W. Newcomer, MD[2]; Yongcai Mao, PhD[1]; and Andrei Pikalov, MD, PhD[1]*

[1] Sunovion Pharmaceuticals Inc., Fort Lee, NJ and Marlborough, MA
[2] Thriving Mind South Florida, Miami, FL and Washington University School of Medicine, St. Louis, MO

**ABSTRACT:** Background: Among patients with depressive disorders, the prevalence of metabolic syndrome (MetS) is estimated to range from 35-40% and has been associated with increased mortality rates. The aim of this post-hoc analysis was to assess the effect of treatment with lurasidone on the prevalence of MetS in patients with bipolar depression.

**METHOD:** Lurasidone data (dose range, 20-120 mg/d) used in the current analyses consisted of 3 double-blind (DB), placebo-controlled, 6-week studies in adults with bipolar I depression (total N=1,192), consisting of 1 monotherapy, and 2 adjunctive therapy trials with lithium or valproate. Patients who completed the short-term trials continued into a 6-month open-label (OL) extension study, with 6-month (LOCF-endpoint) data available on 274 patients treated with lurasidone monotherapy, and 436 patients treated with lurasidone adjunctive therapy. Also analyzed was a recurrence prevention study in stabilized bipolar patients who completed up to 20 weeks of OL adjunctive treatment with lurasidone, and then were randomized to 28 weeks of DB adjunctive therapy with lurasidone or placebo (N=497). MetS was defined based on NCEP ATP III criteria (2005 revision).

**RESULTS:** In the short-term monotherapy and adjunctive therapy studies, the proportion of patients at baseline meeting NCEP III criteria for MetS were 27.6% and 23.6%, respectively, for lurasidone, and 23.8% and 25.1%, respectively, for placebo; and at week 6 (LOCF) the proportion with MetS was 27.5% and 26.6%, respectively, for lurasidone and 29.9% and 20.2%, respectively, for placebo. The proportion of patients who did not meet MetS criteria at baseline but developed MetS at week 6 (LOCF) was similar for lurasidone vs. placebo in the monotherapy study (9.9% vs. 11.6%); and in the two adjunctive therapy studies (10.3% vs. 8.3%). During the 6-month OL extension study, the proportion of patients treated with lurasidone monotherapy and adjunctive therapy who did not meet MetS criteria at OL baseline but developed MetS at month 6 (LOCF) was 11.7% and 11.9%, respectively. Conversely, the proportion of patients who met MetS criteria at OL baseline, but no longer met criteria at month 6 (LOCF) was 9.5% and 7.7%, respectively. In the 20-week, OL phase of the recurrence prevention study, the proportion of patients treated with adjunctive lurasidone who did not meet MetS criteria at OL baseline but developed MetS at endpoint was 11.5% (LOCF). After up to 28 weeks of DB treatment,

https://doi.org/10.1017/S1092852920000760 Published online by Cambridge University Press

the proportion of patients who did not meet MetS criteria at DB baseline but developed MetS at endpoint was 9.0% in the adjunctive lurasidone group, and 10.5% in the adjunctive placebo group (LOCF).

**CONCLUSION:** This post-hoc analysis found that short- and long-term treatment with lurasidone was associated with a relatively low risk for the development of metabolic syndrome in patients with bipolar I disorder. These findings are consistent with similar analyses in patients with schizophrenia.

Funding Acknowledgements: Supported by funding from Sunovion Pharmaceuticals Inc.

## 161
## The NeuroStar Outcomes Registry

*Miriam Mina[1]; Todd Hutton, MD[2]; and Karen Heart[3]*

[1] Associate Director of Clinical Applications, Neuronetics, Inc., Malvern, PA
[2] Medical Director, Southern California TMS Center, USC Keck School of Medicine, Pasadena, CA
[3] Director Medical Operations, Neuronetics, Inc., Malvern, PA

**ABSTRACT:** Objective: NeuroStar® Advanced Therapy System is an effective acute treatment for patients with major depressive disorder (MDD). To further understand the efficacy of the NeuroStar in a clinical setting, Neuronetics has established the largest patient treatment and outcomes registry for Major Depressive Disorder (MDD) to collect and analyze the efficacy of transcranial magnetic stimulation (TMS) on patients receiving NeuroStar treatment.

**METHODS:** Individual NeuroStar providers are invited to participate in the registry and over 100 clinical practice sites have agreed to provide their de-identified patient treatment data. An integrated electronic data management system (TrakStar) allows for large-scale data collection to be automated. The data collected for the registry include Demographic Elements (age, gender), Treatment Parameters, and Clinical Ratings. Clinical assessments performed at baseline and the end of acute treatment are the Patient Health Questionnaire 9-item (PHQ-9) and the Clinician Global Impression - Severity of Illness (CGI-S). De-identified patient data is uploaded to a Registry server; an independent statistical service then creates final data reports.

**RESULTS:** Over 3300 evaluable patients have entered the NeuroStar Outcomes Registry since September 2016. The population is 64% female with a mean patient age of 47.8 (SD±16.9); Mean baseline PHQ-9 is 19.0 (SD ±5.0). Response & remission rate on PHQ-9 is 63% & 33%, and on CGI-S was 76% & 54%, respectively.

**CONCLUSIONS:** For the over 3300 patients in the Outcomes Registry, approximately 2/3 patients achieve response and 1/3 patients achieve remission with an acute course of NeuroStar TMS. These treatment outcomes are consistent with previous open-label study data (Carpenter et al., 2012) using the NeuroStar system. The NeuroStar Outcomes Registry is ongoing and has surpassed Star*D dataset (Rush et al., 2006) with over 3300 evaluable patients from more than 100 clinical sites in 3 years.

Funding Acknowledgements: Funding: Neuronetics, Inc.

## 162
## Post-lithium Delirious Mania in Patients with Bipolar Disorder

*Muhammad Zaidi, MD[1]; Michael Champ, MD[2]; Aquanette Brown, MD[3]; and Tzvetelina Dimitrova, MD[3]*

[1] Saint Elizabeths Hospital, DC
[2] Medstar Georgetown University Hospital, DC
[3] Veterans Affairs Medical Centre, DC

**ABSTRACT:** Delirious mania is a life-threatening condition, presenting with symptoms of acute delirium and psychotic mania as a complication of medical or psychiatric condition. It is not recognized as a diagnosis in DSM-V and is under recognized in clinical practice. It was first described by Calmeil (Calmeil, 1832). In 1849 Luther Bell described 40 cases with an associated 75% mortality rate. More recently, Jacobowski et al (2013) compiled a comprehensive review of clinical characteristics, diagnostic work up, and treatment recommendations for delirious mania. In addition to acute onset, clinical course is frequently worsened by psychosis and catatonia. Delirium leads to disequilibrium of neurotransmitters, particularly depletion of acetylcholine and elevation of dopamine.

Lithium has been used for the treatment of mania for many decades. Suppes et al performed a meta-analysis of 14 studies including 257 patients with Bipolar I disorder and concluded that patients relapsed 28 times more when stopping lithium compared to those who continued this medication. Baldessarini et al (1999) completed analysis of 227 patients with Bipolar I and II disorders, dividing the sample into "abrupt" (1-14 days) and "gradual" (15-30 days) discontinuation groups and concluded that the frequency of relapse following "abrupt" cessation was four times higher compared to following "gradual" cessation. In a study of 450 bipolar patients, Baldessarini et al (2003) reviewed the long-term treatment of lithium as monotherapy (86 % of the study's population) in the context of lithium maintenance population morbidity. Greater pretreatment morbidity lead to larger relative reduction in morbidity as a result of treatment with lithium. A subgroup of bipolar patients with "abrupt"

https://doi.org/10.1017/S1092852920000760 Published online by Cambridge University Press