readmission among youths with BD. Randomized trial of family-focused therapy was used to determine early interventions for symptomatic teenagers at risk for BD.

Keywords: interventions, adolescents, compliance, bipolar, decrease in hospitalization

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Open-label Study of Pimavanserin Patients with Comorbid Parkinson's Disease and Depression

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ABSTRACT: Study Objectives: Depression occurs in ~50% of Parkinson's disease (PD) patients, increases in severity and duration as the disease progresses, and is associated with increased morbidity. Improvement of depression in PD patients is correlated with reduced physical disability and improved quality of life. We are assessing use of pimavanserin (PIM) for treatment of depression in adults with PD.

METHOD: A Phase-2, 8-week, open-label, single-arm study is being conducted to evaluate the safety and efficacy of PIM as an adjunct to SSRI/SNRI or as monotherapy in adults with both PD and symptoms of depression (baseline Hamilton Depression Scale [17-items] total score [HAMD-17] ≥15). The primary endpoint of the study is change from Baseline to Week 8 in the HAMD-17. Secondary measures included the Clinical Global Impression (CGI) scales (improvement and severity) and Scales of Outcomes in PD-Sleep (SCOPA).

RESULTS: Interim results based on the first 34 of 40 planned patients have been evaluated: 55.9% of patients were male, and average age was 68.1 years, with 19 patients on adjunctive therapy and 15 on monotherapy. At baseline, patients had a mean (SE) HAMD-17 of 19.8(0.6). Change from Baseline to Week 8 (least squares mean [LSM] [SE]) in the HAMD-17 was –10.7(1.0) (95% CI; –12.7,–8.7; P<0.001), with significant improvement seen as early as Week 2 (–8.4[1.0]; 95% CI; –10.5,–6.4; P<0.001). Significant improvement was seen for both adjunctive treatment and monotherapy: 45.2% of patients responded to treatment (≥50% improvement on the HAMD-17) at Week 8, and 35.5% reached remission (HAMD-17 ≤7). On the Clinical Global Impressions–Improvement scale, 54.8% were much/very much improved at Week 8. Significant improvement was seen in change from Baseline to Week 8 SCOPA–Global Sleep Quality, –Nighttime Sleep, and –Daytime Sleepiness: –1.0 (0.4) (95% CI; –1.7,–0.3; P=0.010), –2.1(0.7) (95% CI; –3.6,–0.6; P=0.008), –2.1(0.4) (95% CI; –3.0,–1.2; P<0.001) respectively. Twenty-one of the 34 enrolled patients have completed the study to date, and another 7 are still continuing. Thirteen patients reported adverse events, the most common being falls, UTI, diarrhea, and nausea.

CONCLUSIONS: These interim data suggest that PIM as adjunctive treatment or monotherapy is associated with early improvement of depressive symptoms in patients with PD and is well tolerated. This is consistent with recently reported data of PIM in major depressive disorder. Final data will be shared at the time of this presentation. However, additional placebo-controlled data will be needed to determine fully the efficacy of PIM in patients with comorbid PD and depression.
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Safety and Efficacy of Lurasidone in Children and Adolescents with Bipolar Depression: Results from a 2-Year Open-label Extension Study

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ABSTRACT: Background: Bipolar I disorder frequently has an early onset, with an estimated prevalence rate of 1.8% in pediatric populations. Early onset is associated with a high degree of chronicity; however, limited data are available on the long-term efficacy of drug therapies in pediatric populations. The aim of the current study was to evaluate the long-term safety and efficacy of lurasidone in children and adolescents with bipolar depression.

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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.

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

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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,

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