Two Drugs Approved for Major Depressive Disorder

Summertime was a hot season for new therapies in the treatment of major depressive disorder (MDD), with U.S. Food and Drug Administration (FDA) approval of two new pharmaceutical agents.

Fetzima™ (levomilnacipran extended-release capsules) is a once-daily serotonin and norepinephrine reuptake inhibitor (SNRI) agent. In the placebo-controlled, pivotal Phase III studies of adult patients with MDD, statistically significant and clinically meaningful improvement in depressive symptoms (primary endpoint) was demonstrated across three Fetzima dosage strengths of 40, 80, and 120 mg once daily compared with placebo as measured by the Montgomery Asberg Depression Rating Scale total score (primary endpoint). Fetzima also demonstrated superiority over placebo as measured by improvement in the Sheehan Disability Scale functional impairment total score (secondary endpoint).

Forest Laboratories Inc. expects Fetzima to be available to wholesalers in the fourth quarter of 2013.

The second approval was for Khedezla™ (desvenlafaxine) extended-release tablets containing the SNRI desvenlafaxine, which is also contained in Pristiq®. Pristiq was approved by the FDA in 2008 and contains desvenlafaxine as the succinate salt.

Khedezla will be available in 50-mg and 100-mg strengths for once daily administration.


Investigational NMDA Receptor Modulator Enters Phase I Trial

Naurex Inc., a clinical-stage company developing treatments to address unmet needs in psychiatry and neurology, announced that it has begun

FDA OKs Additional Bipolar-Related Indications for Latuda

The U.S. Food and Drug Administration recently approved two new indications for the use of Latuda® (lurasidone HCl) as (a) monotherapy and (b) adjunctive therapy with either lithium or valproate, both to treat adult patients with major depressive episodes associated with bipolar I disorder.

Two positive double-blind, randomized, placebo-controlled, 6-week clinical trials supported the two new indications. In both studies, the pre-specified primary endpoint was reduction in depressive symptoms, as measured by change from baseline in the Montgomery Asberg Depression Rating Scale (MADRS) total score at Week 6. The key secondary endpoint (i.e., adjusted for multiple comparisons) was change from baseline in the Clinical Global Impression-Bipolar Version-Severity of Illness (CGI-BP-S) score at Week 6. Other secondary endpoints included changes from baseline at Week 6 in responder rates; rates of remission; Hamilton Anxiety Rating Scale; Sheehan Disability Scale; Quick Inventory of Depressive Symptomatology-Self-Report; and Quality of Life, Enjoyment and Satisfaction Questionnaire-Short Form.

Both studies showed that treatment with Latuda resulted in statistically significant reductions in MADRS scores at study endpoint compared to placebo, with significant separation from placebo observed as early as Week 2 of treatment. Additionally, across both studies, patients receiving Latuda demonstrated statistically significant improvements versus placebo at Week 6 on secondary endpoints, including CGI-BP-S, responder rates, rates of remission, anxiety symptoms, self-assessment of depression, as well as measures of functionality and quality and enjoyment of life.

patient dosing in a Phase I trial of its novel, orally active agent NRX-1074. NRX-1074 is a follow-on to Naurex’s first-generation compound GLYX-13, which has demonstrated good safety, robust efficacy, and rapid onset of effect within hours of a single dose in a Phase IIa trial. NRX-1074 and GLYX-13 are N-methyl-D-aspartate (NMDA) receptor functional partial agonists, a new class of central nervous system (CNS)-active compounds identified by Naurex scientists, who have generated multiple series of novel drug candidates based on these discoveries.

The Phase I trial is a randomized, placebo-controlled, ascending dose study that will assess the safety and pharmacokinetics of NRX-1074 in normal volunteers.

NRX-1074 is several thousand times more potent than GLYX-13, and preclinical studies have shown that it is active when administered orally. NRX-1074 has in vivo mechanistic activity similar to GLYX-13, including a ketamine-like efficacy signature with rapid onset and long-acting duration of antidepressant-like effect. Similar to GLYX-13, in animal studies NRX-1074 has demonstrated good safety with no signs of CNS-related side effects. Naurex’s initial development focus for this fast-acting, potent, orally available compound is in major depression.

In the Phase IIa trial, a single administration of GLYX-13 produced statistically significant reductions in depression scores in participants who had failed treatment with current antidepressant agents. The reductions were evident within 24 hours and persisted for an average of 7 days. A measure of the antidepressant efficacy of GLYX-13 observed at 24 hours and at 7 days was nearly double that seen with most antidepressant agents after 4 to 6 weeks of repeated dosing. In this study, GLYX-13 was also well tolerated. Reported side effects were mild to moderate and were consistent with those observed in participants receiving placebo. GLYX-13 did not produce any of the schizophrenia-like psychotomimetic effects associated with other drugs that modulate the NMDA receptor.