Serdaxin™: Anxiety and Depression Drug Candidate

SUMMARY
Serdaxin™ is an enhancer of both serotonin (5HT) and dopamine (DA) neurotransmitters, and has a non-SSRI mechanism. Its Phase II trials are planned for 2007. Serdaxin™'s differentiating characteristics derived from preclinical model studies and human experiences include:

- Unique mechanisms of simultaneous, increased availability of both 5HT and DA in the brain.
- Effectiveness for treating both anxiety and depression.
- Potential use in treatment of patients with both negative mood state and loss of positive mood state, and mixture of both mood states as well.
- Excellent safety profile with no motor impairment and cognition deficit of benzodiazepines, and no insomnia and sexual dysfunction of SSRIs – potentially resulting in improved patient compliance.

In-vivo efficacy. Preclinical studies demonstrated that Serdaxin™:

- Was very effective in controlling anxiety and depression in animal models (e.g., seed finding, elevated plus maze, light-dark box, etc)
- Was equipotent in preclinical models of anxiety and depression at a dose less than 1/10,000th of chlorodiazepoxide (e.g., Librium™) or fluoxetine (e.g., Prozac™).
- Has shown significant changes in the brain activity (e.g., fMRI)
- Significantly reduced aggressive behavior in the Resident/Intruder animal model.
- Improved cognitive function and did not disrupt learning and memory in the Morris water maze model.

MARKET OPPORTUNITY
Anxiety disorders affect about 40 million Americans (18%) in a given year, causing them to be filled with fearfulness and uncertainty.\(^1\) According to “The Economic Burden of Anxiety Disorders,” an article published in the Journal of Clinical Psychiatry, the cost of anxiety disorders in the US exceeds $42 billion annually.\(^2\) The market for anti-depressive drugs is the largest segment of the CNS sector with global sales of $16 billion in 2005.\(^3\)

Among currently available therapeutics, serotonin-based anti-depressants (e.g., SSRIs and SNRIs) appear effective, but in fact, are only partially effective in treating depression patients and have an estimated 50% response rate. Serotonin-based drugs are suggested to be effective in treating the negative mood state, but not effective for the diseases resulting from loss of mood state. Significant portions of patients have symptoms of a certain nature of both mood states, and thus show high relapse rate after the initial remission by SSRIs.

Unmet Needs for patients with anxiety or depression include:
- **Slow onset of action**: Most selective serotonin reuptake inhibitors (SSRIs) take six weeks or longer to show initial activity
- **Side effects**: Weight gain, insomnia, sexual dysfunction, cognitive deficit, motor impairment
- **Limited efficacy**: Only about 50% of patients taking SSRI drugs respond to the therapy
- **High relapse rate**: Up to 30% of depression patients
- **Low compliance rate**: Up to 30% of patients stop taking the medicine
Recent studies indicate that serotonin-based drugs may treat the negative mood state effectively, while the loss of positive mood state may respond well to dopamine-based drugs. The seemingly distinguishing effects of serotonin and dopamine toward the different mood states may provide advantages over current therapeutics that have limited efficacy and high relapse rate. The drug(s) with actions on both serotonin and dopamine would greatly resolve these issues.

Serdaxin™ can be an answer since the drug enhances availability of both serotonin and dopamine simultaneously in the brain, and thus may effectively treat both mood states. Further, Serdaxin™ has proven and well-established safety data in humans, and is devoid of the majority of side effects resulting from the current therapy. Serdaxin™ is thus expected to avoid medication non-compliance issues.

In summary, Serdaxin™ could establish a new standard of care and market leader position in treating anxiety and depression, and will be initially tested for Generalized Anxiety Disorder (GAD) and/or Major Depressive Disorder (MDD).

- **Generalized Anxiety Disorder (GAD):** GAD affects about 7 million US adults.
- **Major Depressive Disorder (MDD):** Estimated 45 million prevalent cases of MDD in US.

**Potential future applications.** Serdaxin™ may have utility in other CNS-based illnesses, such as the following areas:

- **Neuroprotection and Biodefense areas**
  - Serdaxin™ has shown near-complete protection of neuronal cells in the hippocampus from a neurotoxin (kainic acid) assault in animal models.
  - Under the collaborative agreement, the National Institute of Neurological Disorders and Stroke (NINDS) of NIH, is studying Serdaxin™ and its analogues for their potential utility in neurodegenerative diseases and biodefense.

- **Parkinson’s Disease (PD)**
  - PD has 2 phases: psychotic and motor events. Current PD drugs target only motor events.
  - Serdaxin™ could be the first drug to address both psychotic and motor events of PD, considering its effective control of anxiety-depression, as well as its near-complete protection of neurons from the neuro degeneration induced by a potent neurotoxin.

**INTELLECTUAL PROPERTY**

There are five US patents granted, and multiple ex-US patents filed under the PCTs covering behavioral disorders, sexual dysfunction, and neuroprotection.

**ALLIANCE OPPORTUNITIES**

Rexahn welcomes the opportunity to discuss strategic partnerships for Serdaxin™. Please contact:

Wendy Tsai  
Senior Director of Business Development  
Rexahn Pharmaceuticals  
9620 Medical Center Drive, Rockville MD 20850  
E-mail: tsaiw@rexahn.com

---


3 CNS Drug Discoveries, Espicom Business Intelligence, November 2006.