Publication in Neuropsychopharmacology Confirms CeNeRx's Novel RIMA Antidepressant TriRima & trade; Selectively and Reversibly Inhibits MAO-A

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The following news release was issued today by CeNeRx BioPharma, Inc., which funded a brain-imaging study conducted by Joanna Fowler at Brookhaven National Laboratory to assess the effects of a compound the company is developing as a possible treatment for depression.

Publication in Neuropsychopharmacology Confirms CeNeRx's Novel RIMA Antidepressant TriRima™ Selectively and Reversibly Inhibits MAO-A

Innovative PET Imaging Studies Confirm TriRima™ Demonstrates Reversible Inhibition of MAO-A in the Human Brain &mdash Represents First Validation in Humans of Mechanism of RIMA Antidepressants

December 7, 2009

RESEARCH TRIANGLE PARK, NC, December 7, 2009 -- CeNeRx BioPharma, Inc., a clinical stage company developing innovative treatments for diseases of the central nervous system, today announced that a newly published PET imaging study in human subjects confirms that CeNeRx's novel compound TriRima™ reversibly inhibits MAO-A (monoamine oxidase A), an enzyme in the brain that plays a key role in the regulation of mood. TriRima is a member of a new class of selective and reversible inhibitors of MAO-A known as RIMAs, and it is the first whose mechanism has been validated in human brain imaging studies.

In this Cooperative Research and Development Agreement (CRADA) study, funded by CeNeRx Biopharma, Inc., and published in the journal *Neuropsychopharmacology*[1], researchers led by Dr. Joanna Fowler of the Brookhaven National Laboratory used PET (positron emission tomography) imaging techniques to assess the degree and reversibility of TriRima's inhibition of brain MAO-A in 15 non-depressed men. TriRima blood plasma levels after oral administration were also measured.

The researchers reported that TriRima produced a robust dose-related inhibition of brain MAO-A at two hours after administration and that brain MAO-A recovered completely by 24 hours post-dosing, demonstrating TriRima's excellent reversibility. In addition, they found that the plasma concentration of TriRima was highly correlated with the degree of inhibition of brain MAO-A. These two findings make TriRima the first agent in the RIMA class with documented reversible inhibition of human brain MAO-A. In addition, because the degree of MAO-A inhibition was closely correlated with observed plasma levels, the authors concluded that the study validates the use of plasma TriRima concentrations as a surrogate marker for brain MAO-A inhibition and support the use of this relationship for modeling therapeutic dosing regimens of TriRima. Plasma concentrations of TriRima can be used without PET scan to model dosing regimens for future efficacy trials, optimize the therapeutic dose and determine the optimal degree of MAO-A inhibition required for clinical efficacy.

Lead study author Dr. Joanna Fowler, Director of the Radiotracer Chemistry, Instrumentation and Biological Imaging Program at the U.S. Department of Energy's Brookhaven National Laboratory and a recent winner of the President's National Medal of Science, commented, "The results of our study show that it is possible to employ powerful non-invasive technologies such as PET imaging to monitor the activity of potential therapeutic agents in the human brain. The current findings confirm earlier evidence that TriRima has a selective and reversible mechanism."

The depletion of the three neurotransmitters serotonin, norepinephrine and dopamine has long been thought to be associated with major depression, yet many current antidepressant drugs affect only one or two of these neurotransmitters. In contrast, TriRima's MAO-A inhibitor mechanism elevates the levels of all three. Conventional MAO inhibitors have shown good antidepressant efficacy as a result of this triple action effect, but their use has been limited by the potential for serious cardiovascular side effects if patients eat foods containing high amounts of the naturally-occurring substance tyramine. Because RIMA's are designed to act as selective and reversible inhibitors of MAO-A., they have potential to achieve the efficacy advantages of conventional MAO inhibitors while greatly reducing the risk of these cardiovascular effects. Thus, TriRima and the RIMA class may represent a potential new therapeutic option for the large segment of patients not adequately treated by current antidepressants, for whom the triple-action potential of a safe and effective MAO-A inhibitor might help relieve the disabling symptoms of depressive disease.

"This important publication confirms our belief that CeNeRx's RIMA compounds have the potential to bring the efficacy advantages of MAO-A inhibition to patients with major depression," said Dr. Daniel Burch, Vice President of R&D and Chief Medical Officer of CeNeRx. "Other neuroimaging studies[2] strongly suggest that elevated brain MAO-A is an important feature of major depression. The innovative work reported in this paper confirms that TriRima is able to effectively inhibit MAO-A in a predictable and reversible manner, significantly increasing the neurotransmitters that help treat the depression while ameliorating the risk of dietary-related cardiovascular effects associated with the older, irreversible MAO

inhibitors. The finding of a strong relationship between plasma levels of TriRima and MAO-A inhibition will continue to be of significant value as we advance the TriRima Phase II clinical program."

TriRima has been found to be safe and well-tolerated in several Phase I trials and is currently in Phase II development.

The article is currently available on-line at http://www.nature.com/npp/journal/vaop/ncurrent/abs/npp2009167a.html [3]

[1.] Neuropsychopharmacology advance online publication, November 4, 2009; doi: 10.1038/npp.2009.167. The article will be published in the December 2009 issue of *Neuropsychopharmacology*. Fowler JS, Logan J, Azzaro AJ, Fielding RM, Zhu W, Poshusta AK *et al* (2009). Reversible Inhibitors of Monoamine Oxidase-A (RIMAs): Robust, Reversible Inhibition of Human Brain MAO-A by CX157.

[2.] Meyer JH, Ginovart N, Boovariwala A, Sagrati S, Hussey D, Garcia A *et al* (2006). Elevated monoamine oxidase-A levels in the brain provides an explanation for the monoamine imbalance of major depression. *Arch Gen Psychiatry* 63: 1209–1216.

This study was carried out using the infrastructure of Brookhaven National Laboratory under contract DE-AC02- 98CH10886. Dr. Fowler's work is supported in part by a K award from the NIH (K05DA020001). An abstract of this study was presented at the 47th Annual Meeting of the American College of Neuropsychopharmacology, Scottsdale, Arizona, December 2008.

CeNeRx is a privately held clinical stage biopharmaceutical company developing and commercializing innovative treatments for diseases of the central nervous system. CeNeRx's most advanced compound, a reversible inhibitor of monoamine oxidase, or RIMA, is in Phase II development for the treatment of major depressive disorder. RIMAs may have efficacy advantages over current agents for depression and are expected to have a good safety profile. The company's CNS pipeline also includes CXB909, a small molecule, orally active agent for the prevention and treatment of neuropathies and neurodegenerative disorders; a series of novel compounds for anxiety and depression; and a series of selective cannabinoid compounds that have recently completed successful preclinical proof-of-concept studies for the treatment of pain, glaucoma and spasticity. More information about CeNeRx BioPharma can be found at www.cenerx.com [4].

Number: 09-1043 | BNL Media & Communications Office [5]

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