



## GLOBAL PRESS RELEASE

# UCB Pharma\* announces unique mode of action for Keppra®

## Novel binding site for epilepsy drug provides new platform for drug discovery

**24 June 2004** – A major advance in understanding the mode of action of the novel anti-epilepsy drug, Keppra (levetiracetam), appears to confirm it as the first of a new class of central nervous system (CNS) drugs.<sup>1</sup>

UCB Pharma CNS scientists have identified the binding site for Keppra (levetiracetam) in the brain as a synaptic vesicle protein called SV2A. This protein appears to play a substantial role in the release of neurotransmitters that are essential for normal neuronal activity in the brain and spinal cord.

The identification of SV2A as the binding site for Keppra – announced this week in the leading scientific journal *Proceedings of the National Academy of Sciences*<sup>1</sup> – has two immediate repercussions. It provides an innovative and unique drug discovery platform to identify new drugs with improved characteristics at UCB Pharma – one of Europe's leading speciality pharmaceutical companies – and provides molecular evidence that Keppra is different from all other anti-epileptic and CNS drugs. No other known anti-epileptic drugs bind to SV2A.

“By showing that Keppra works in a different way from other treatments, this important discovery helps to explain why Keppra is making such a difference to the lives of people with epilepsy. It also underlines our assessment that Keppra has the potential to be the first blockbuster drug in epilepsy,” commented Roch Doliveux, CEO of UCB Pharma.

In 2003, global sales of Keppra rose by 36% to €314 million. In the USA, Keppra prescriptions are up 58% compared to last year (MAT March/2004 vs MAT March/2003).

With 20.3% market share in value Keppra currently occupies second place in its specific field of treatment.<sup>2</sup>

UCB Pharma CNS scientists have shown that Keppra and related compounds bind to SV2A in brain from mice with normal levels of the protein. No binding has been observed in brain from genetically-modified mice lacking SV2A.<sup>1</sup>

While the precise role of the SV2A protein is not known, studies have shown that Keppra and other related UCB Pharma compounds display a high correlation between the binding affinity to SV2A and their anti-epileptic activity.<sup>1</sup>

Keppra is indicated as adjunctive, or add-on, therapy in the treatment of partial onset seizures with or without secondary generalised seizures in patients with epilepsy over the age of 16 years.<sup>3</sup> UCB Pharma has conducted a pivotal trial of Keppra in children under 16, and will file for marketing authorisation for Keppra as add-on therapy in children with partial seizures in Q4 2004.

Monotherapy studies are ongoing for Keppra, and preliminary results show that the drug is a well-tolerated, effective and rational choice for the treatment of partial seizures.<sup>4,5</sup> UCB Pharma hopes to gain a monotherapy indication for Keppra in Q2 2006.

### **Future research**

SV2A, the binding site for levetiracetam, also provides a novel target for future drug discovery at UCB Pharma. The company has filed two patent applications related to the discovery and has two drug candidates in clinical development for several CNS diseases. These both possess improved interaction with SV2A protein compared with Keppra.<sup>6,7,8,9</sup>

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Keppra® is a registered trademark of the UCB Group. Please consult your national product information as the trademark, as well as the prescribing information, may differ from one country to the other.

#### **\*About UCB Pharma**

UCB Pharma is part of the UCB Group of companies, a pharmaceutical and specialty chemical company with headquarters in Brussels, Belgium which operates on a global scale. UCB Pharma is one of Europe's leading specialty pharmaceutical companies, specialising in the fields of allergy and respiratory disease and in treatments for disorders of the central nervous system. Among products developed by UCB Pharma are Keppra® (levetiracetam), a novel adjunctive treatment for partial onset seizures associated with epilepsy, Nootropil® (piracetam) a cerebral function regulator, Xyzal® (levocetirizine) a fast acting antihistamine for intermittent and persistent allergic rhinitis and chronic idiopathic urticaria in adults and children, and Zyrtec® (cetirizine), the world's most widely used second generation antihistamine<sup>10</sup>. With over 6,500 employees operating in over 100 countries, in 2003 UCB Pharma achieved a consolidated turnover of €1,463 billion.

#### **About the UCB Group**

UCB is committed to pharmaceuticals as well as to technically innovative products for surface applications. It employs 12,000 people around the world. UCB, listed on Euronext Brussels, posted sales of €3 billion and net result of €340 million in 2003.

#### **References**

1. Lynch BA, Lambeng N, Nocka K et al. The synaptic vesicle protein SV2A is the binding site for the antiepileptic drug levetiracetam. PNAS 2004;101(26): 9861-9866.
2. IMS MAT Q4 2003. Epilepsy only. Value market share among new AEDs; US; France: UK Germany Spain; Italy.
3. SmPC
4. Ben-Menachem E, Falter U. Efficacy and tolerability of levetiracetam 3000 mg/d in patients with refractory partial seizures: a multicenter, double-blind, responder-selected study evaluating monotherapy. European Levetiracetam Study Group. Epilepsia. 2000;41(10):1276-83.

5. Ben-Menachem E, Da Silva S. Preliminary efficacy of levetiracetam in long-term monotherapy. Poster presentation at the 6th European Congress on Epileptology, Vienna, June 2004.
6. Matagne A, Kenda B, Michel P and Klitgaard H. ucb 34714, a new pyrrolidone derivative: comparison with levetiracetam in animal models of chronic epilepsy in vivo. *Epilepsia* 2003; 44(Suppl. 9):260.
7. Lamberty Y, Ardid D, Eschaliere A et al. ucb 34714, a new pyrrolidone derivative, is effective in two models of human neuropathy in the rat: comparison to gabapentin. Program No.586.8. 2003 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.
8. De Ryck M, Matagne A, Kenda B et al. ucb 34714, a new pyrrolidone derivative, antagonizes harmaline-induced tremor in rats: comparison to drugs for essential tremor and anti-epileptic drugs. Program No.634.20. 2003 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.
9. Data on file (RRLE03A2101)
10. IMS MIDAS December 2003

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