



New Data Support Long-term Use of Antiepileptic Drug Vimpat® (Lacosamide) (C-V)

- Long-term data presented at American Epilepsy Society annual meeting demonstrate sustained efficacy and consistent tolerability profile
- Rates of cognitive adverse events similar to those associated with placebo
- Novel mechanism of action differs from traditional sodium channel agents
- Experts comment on Vimpat's role in treatment paradigm

Atlanta, December 7, 2009 – UCB today announced new findings on its antiepileptic drug (AED) Vimpat® that offer additional clinical evidence supporting the use of this AED as adjunctive therapy in adult patients with partial-onset seizures. Results of presented research demonstrate sustained efficacy in adult patients taking Vimpat® for up to three years, and a consistent long-term tolerability profile. A separate study reports that adverse events potentially related to cognition occurred at similar rates for Vimpat® and placebo. In pre-clinical studies, Vimpat® was shown to exert a novel effect on sodium channels. These and other Vimpat® data were presented at the 63rd annual meeting of the American Epilepsy Society (AES) in Boston.

Highlights include:

- Vimpat® was associated with sustained efficacy as measured by percent change in seizure frequency and responder rates (percent of patients reporting seizure reduction rates of 50 percent or greater) among patients on active treatment for 6, 12, 18, 24, 30, or 36 months.
- In an analysis of patients taking Vimpat® for a median of two years, no new types of treatment-emergent adverse events (TEAEs) occurred with long-term use, and rates of TEAEs were similar to those observed during the pivotal clinical trials.
- A preliminary retrospective analysis of Vimpat® phase II/III studies reported that rates of spontaneously reported adverse events potentially related to cognition among Vimpat® patients were dose-dependent and not significantly different from those observed in patients taking placebo.
- Experiments of the brain cells involved in epileptic seizures suggest that Vimpat® exerts a novel effect on sodium channels, different from traditional sodium channel AEDs.

“As a clinician, it is encouraging to know that the ongoing clinical program for Vimpat® has yielded safety and efficacy data totaling almost 3,000 patient years of exposure,” said Dr. Jacqueline French, Director of the Clinical Trials Consortium at the Comprehensive Epilepsy Center at New York University Langone Medical Center.

Vimpat® was launched in the U.S. in May 2009 as an add-on therapy for the treatment of partial-onset seizures in people with epilepsy who are 17 years and older, and is available as oral tablets and as an intravenous (IV) infusion to allow for consistent treatment in a hospital setting. In Europe, Vimpat® (film-coated tablets, syrup, and solution for infusion) is approved as adjunctive therapy for the treatment of partial-onset seizures with or without secondary generalization in patients with epilepsy, aged 16 years and older. Vimpat® has a novel mechanism of action that is different from all currently available AEDs, although the precise mechanism by which Vimpat® exerts its antiepileptic effect in humans is not yet clear.



Summary of Vimpat® Data Presented at 2009 AES Annual Meeting

Abstract: Long-term Efficacy of Lacosamide for Partial-Onset Seizures: An Interim Evaluation of Completer Cohorts Exposed to Lacosamide for up to 36 Months

This analysis of phase II/III open-label extension trials demonstrated that lacosamide produced long-term, sustained efficacy in patients with partial-onset seizures who completed 6, 12, 18, 24, 30, or 36 months of treatment. Researchers noted that given the study's "nested cohort" design, with each cohort including patients remaining from the shorter-duration cohort, the expected attrition of non-responders is accounted for, and efficacy findings reflect real-world use.

- The reduction in seizure frequency associated with lacosamide was sustained across all duration cohorts, as was the proportion of responders – patients who experienced a 50 or 75 percent or greater reduction in seizures compared to baseline:
 - The median percent reduction in seizure frequency for the first 3 months of treatment was 40.8 percent, 45.2 percent, 46.5 percent, 48.2 percent, 48.3 percent, and 46.5 percent for the 6, 12, 18, 24, 30, and 36 month cohort, respectively.
 - The median percent reduction for the last 3 months of treatment was 40.7 percent, 51.3 percent, 58.3 percent, 65.9 percent, 69.8 percent, and 59.7 percent for each cohort, respectively.
 - Responder rates were also sustained over time in each cohort:
 - Forty-one percent to 48 percent of patients reported a 50 percent or greater reduction in seizures during the first 3 months of treatment, compared with 42 percent to 70 percent for the last 3 months of treatment.
 - Seventeen percent to 24 percent of patients reported a 75 percent or greater reduction in seizures during the first 3 months of treatment, compared with 22 percent to 42 percent for the last 3 months.

Poster Session 2, Sunday, December 6, 5:00 pm – 6:00 pm, Hall D, Level 2 (Abstract 2.227)

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Abstract: Long-term Safety and Tolerability of Lacosamide for Partial-Onset Seizures: An Interim Evaluation of Patients Exposed to Lacosamide in Double-Blind and Open-Label Trials

This analysis of 1,327 patients exposed to lacosamide during double-blind or open-label extension trials demonstrated that the incidence of adverse events, as well as vital signs and clinical laboratory and ECG findings, among patients taking lacosamide for a median duration of 700 days, or almost 2 years (minimum duration: 1 day; maximum duration: 2,437 days, or 6.7 years), were similar to those reported with short-term use. The dose most commonly used for the longest period of time was 400 mg/day.

- There were no new types of TEAEs judged by researchers to be related to the drug that emerged with long-term use.
- The most common TEAEs (greater than or equal to 10 percent) reported at any time during the double-blind and open-label extension trials were dizziness (45.6 percent), headache (20.6 percent), diplopia (18.5 percent), nausea (15.3 percent), nasopharyngitis (14.3 percent), vomiting (14.1 percent), fatigue (13.8 percent), abnormal coordination (12.5 percent), blurred



vision (12.0 percent), tremor (11.5 percent), somnolence (11.5 percent), convulsion (11.4 percent), and contusion (10.4 percent).

- Long-term lacosamide treatment was not associated with any clinically relevant changes in median or mean measurements for body weight, hematology, clinical chemistry, or vital signs. A small increase in mean PR interval was observed. There were no reports of higher-degree heart block (i.e., second or third-degree).

Poster Session 2, Sunday, December 6, 4:00 pm – 5:00 pm, Hall D, Level 2 (Abstract 2.231)

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Abstract: Preliminary Evaluation of the Risk of Cognitive Adverse Events in Lacosamide Clinical Trials for Adjunctive Treatment of Partial Onset Seizures

This preliminary analysis of spontaneously reported TEAEs potentially related to cognitive function showed that rates of these TEAEs among patients taking therapeutic doses of Vimpat[®] were dose-dependent. Researchers noted that these findings are preliminary, and should be confirmed with formal neuropsychological testing.

- A retrospective analysis of pooled safety data from three lacosamide double-blind phase II/III studies was conducted to calculate the rates of spontaneously reported TEAEs potentially related to cognition
 - The analysis encompassed all treatment groups, i.e., patients taking lacosamide 200 mg/day to 600 mg/day; a total of 1,308 patients were included. (In the U.S. and Europe, doses above 400 mg/day are not approved doses.)
- The incidence of cognition-related TEAEs among the combined 200 mg/day and 400 mg/day groups was 6.1 percent versus 4.7 percent for placebo (OR 1.3; 95 percent CI 0.7-2.3); the incidence rate for all lacosamide treatment groups was 7.7 percent (OR 1.6; 95 percent CI: 0.9-2.7).
- The incidence of TEAEs potentially related to cognition appeared dose-related, occurring at 1.9 percent for the lacosamide 200 mg/day group (OR 0.4; 95 percent CI: 0.1-1.3), 8.5 percent for lacosamide 400 mg/day (OR 1.7; 95 percent CI: 1.0-3.2), and 13.8 percent at the unapproved 600 mg/day dose (OR 2.8; 95 percent CI 1.3-5.7).
- The only individual TEAE potentially related to cognition occurring at an incidence of 2 percent or greater at approved doses was cognitive disorder (2.1 percent for lacosamide 400 mg/day versus 0.4 percent for lacosamide 200 mg/day and 0.3 percent for placebo); other spontaneously reported TEAEs included:
 - Memory impairment (1.5 percent for lacosamide 400 mg/day, 1.1 percent for lacosamide 200 mg/day and 1.6 percent for placebo).
 - Confusional state (1.5 percent, 0.0 percent and 0.8 percent, respectively).
 - Disturbance in attention (1.1 percent, 0.0 percent and 0.5 percent, respectively).

Poster Session 2, Sunday, December 6, 5:00 pm – 6:00 pm; Hall D, Level 2 (Abstract 2.228)

D. Hebert¹, C. Helmstaedter², A. M. Kanner³, J. Isojarvi¹, A. Eggert⁴, P. Doty¹

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Abstract: Effect of the New Anticonvulsant Drug Lacosamide on Persistent Na⁺-Current and Firing Behavior of Hippocampal Pyramidal Cells

This animal study examined the neurological impact of lacosamide on persistent sodium currents ($I_{Na,P}$) in the brain cells that regulate excitation – hippocampal CA1 pyramidal neurons. Findings suggest that lacosamide blocks persistent sodium currents in a manner that differs from that of carbamazepine, which acts on the sodium channel in a manner shared by traditional sodium channel agents.

- Intact hippocampal CA1 neurons of mice were monitored for sodium current activity.
- Lacosamide was shown to block $I_{Na,P}$ in a dose-dependent manner ($IC_{50} = 81\mu M$) and at a concentration range that is close to the mean plasma concentration (9.35 $\mu g/ml$; $\sim 38\mu M$) observed in patients after 12 weeks of treatment with lacosamide 400 mg/day.
- In addition, lacosamide was not shown to affect the voltage-dependence of activation of $I_{Na,P}$; this preferential action is in contrast to carbamazepine, for which a slight but significant hyperpolarizing shift of the voltage-dependence of activation has been observed.

Poster Session 2, Sunday, December 6, 4:00 pm – 5:00 pm; Hall D, Level 2 (Abstract 2.203)

Mischa Uebachs¹, Thoralf Opitz¹, Thomas Stoehr², Isabelle Niespodziany³, Christian Wolff³, Heinz Beck¹

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Additional UCB-supported Vimpat[®] studies to be presented at the AES meeting include:

- Efficacy of Adjunctive Lacosamide in Patients with Partial-onset Seizures and Prior Surgical Interventions for Epilepsy
Poster Session 2, Sunday, December 6, 5:00 pm – 6:00 pm, Hall D, Level 2 (Abstract 2.233)
S. Benbadis¹, C. Elger², D. Hebert³, J. Isojarvi³
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- Minimally Important Change in QOLIE-31 Scores: Estimates from Three Placebo-Controlled Lacosamide Trials in Patients with Partial Onset Seizures
Poster Session 2, Sunday, December 6, 4:00 pm – 5:00 pm, Hall D, Level 2 (Abstract 2.224)
Christine de La Loge¹, Simon Borghs², Knut Mueller³, Joyce Cramer⁴
¹UCB Pharma, Brussels, Belgium; ²Business & Decision Life Sciences, Brussels, Belgium; ³UCB Pharma, Monheim, Germany; ⁴Yale University, Orange, CT, USA
- Pharmacokinetic Evaluation of Intravenous Lacosamide as Short-Term Replacement for Oral Lacosamide in Partial-Onset Seizures
Poster Session 2, Sunday, December 6, 4:00 pm – 5:00 pm, Hall D, Level 2 (Abstract 2.223)
Willi Cawello, PhD¹, Gregory Krauss, MD², Melissa Brock, PharmD³, Andrea Eggert PharmD, BCPP⁴
¹SCHWARZ BIOSCIENCES, GmbH, A Member of the UCB Group of Companies, Monheim, Germany; ²Department of Neurology, Johns Hopkins Epilepsy Center, Baltimore, Maryland, United States, 21287; ³SCHWARZ BIOSCIENCES, Inc., RTP, NC, United States; ⁴UCB, Inc., Atlanta, GA, United States



- A Multicenter, Open-Label Trial to Assess the Safety And Tolerability of a Single Intravenous Loading Dose of Lacosamide Followed by Oral Maintenance as Adjunctive Therapy in Subjects with Partial-Onset Seizures: An Interim Report
Poster Session 2, Sunday, December 6, 4:00 pm – 5:00 pm, Hall D, Level 2 (Abstract 2.222)
Nathan B. Fountain¹, Gregory Krauss², Jouko Isojarvi³, Deanne Dilley³, Pamela Doty³
¹University of Virginia, Charlottesville, Virginia; ²John Hopkins University, Baltimore, Maryland; ³Schwarz Biosciences (a member of the UCB Group), Raleigh, North Carolina
- Outcome of Infants with Prenatal Exposure to Lacosamide During the Clinical Development Program
Poster Session 2, Sunday, December 6, 5:00 pm – 6:00 pm, Hall D, Level 2 (Abstract 2.235)
Jouko Isojarvi¹, Christina Williams¹, Pamela Doty¹
¹SCHWARZ BIOSCIENCES (a member of the UCB Group), Raleigh, North Carolina

Important safety information about Vimpat® in the U.S.

Vimpat® (lacosamide) is a medicine that is used with other medicines to treat partial-onset seizures in patients 17 years of age and older with epilepsy. Vimpat® is generally well-tolerated, but may not be for everyone. Patients should discuss with their doctor if Vimpat® is right for them.

The most common side effects with Vimpat® are dizziness, headache, nausea and double vision. Vimpat® may also cause problems with coordination and balance. Patients should not drive, operate machinery or do other dangerous activities until they know how Vimpat® affects them. Patients should not stop taking Vimpat® without first talking to their doctor. Stopping Vimpat® suddenly can cause serious problems. Vimpat® could make patients feel faint. Patients should tell their doctor if they have a heart condition or if they are taking other medicines that affect the heart. In rare cases, Vimpat® may cause reactions that could affect the heart, liver or kidney. The patient should contact their doctor immediately if they are tired, have jaundice (yellowing of skin or eyes), and have dark urine. Antiepileptic drugs, including Vimpat®, may cause suicidal thoughts or actions in a very small number of people, about 1 in 500. Patients should call their healthcare provider right away if they have new or worsening symptoms of depression, any unusual changes in mood or behavior, or suicidal thoughts, behavior, or thoughts about self harm that they have never had before or may be worse than before. To report SUSPECTED ADVERSE REACTIONS, contact UCB, Inc. at 1-866-822-0068 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full prescribing information at <http://www.vimpat.com/pdfs/PI.pdf>.

Important safety information about Vimpat® in Europe

Vimpat® is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy aged 16 years and older. Vimpat® solution for infusion is an alternative for patients when oral administration is temporarily not feasible.

Contraindications: Hypersensitivity to the active substance or to peanuts or soya or to any of the excipients; known second- or third-degree atrioventricular (AV) block. Special warnings and precautions for use: Treatment with lacosamide has been associated with dizziness which could increase the occurrence of accidental injury or falls. Therefore, patients should be advised to exercise caution until they are familiar with the potential effects of the medicine. Prolongations in PR interval with lacosamide have been observed in clinical studies. Lacosamide should be used with caution in patients with known



conduction problems or severe cardiac disease such as a history of myocardial infarction or heart failure. Caution should especially be exerted when treating elderly patients as they may be at an increased risk of cardiac disorders or when lacosamide is used in combination with products known to be associated with PR prolongation. Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents. Therefore patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge. Undesirable effects: The most common adverse reactions (greater than 10 percent) are dizziness, headache, diplopia, and nausea. Other common adverse reactions (1–10 percent) are depression, balance disorder, coordination abnormal, memory impairment, cognitive disorder, somnolence, tremor, nystagmus, vision blurred, vertigo, vomiting, constipation, flatulence, pruritus, gait disturbance, asthenia, fatigue, fall, and skin laceration. Refer to the European Summary of Product Characteristics for full prescribing information. <http://www.emea.europa.eu/humandocs/PDFs/EPAR/vimpat/emea-combined-h863en.pdf> (Accessed 02.03.09)

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**About UCB**

UCB, Brussels, Belgium (www.ucb.com) is a biopharmaceutical company dedicated to the research, development and commercialization of innovative medicines with a focus on the fields of central nervous system and immunology disorders. Employing approximately 10,000 people in over 40 countries, UCB generated revenue of EUR 3.6 billion in 2008. UCB is listed on Euronext Brussels (symbol: UCB).

Forward-looking statements

This press release contains forward-looking statements based on current plans, estimates and beliefs of management. Such statements are subject to risks and uncertainties that may cause actual results to be materially different from those that may be implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: changes in general economic, business and competitive conditions, effects of future judicial decisions, changes in regulation, exchange rate fluctuations and hiring and retention of its employees.

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