News

For the attention of accredited medical writers only

Long-term use of antiepileptic drug Vimpat® (lacosamide) effectively reduced partial-onset seizure frequency and improved health-related quality of life

Data presented at the 64th Annual Meeting of the American Epilepsy Society

- First presentation of the effects of long-term Vimpat® treatment on patients' self-reported seizure severity, health-related quality of life and health status found improvements in all administered scales
- In an open-label extension trial lasting five years, adjunctive treatment with Vimpat® demonstrated significant reduction in partial-onset seizure frequency
- Long-term, open-label, adjunctive treatment with Vimpat® was generally well-tolerated with a safety profile consistent with that of other Vimpat® clinical trials

Brussels (Belgium), 6th December 2010, 1800 CET – UCB today announced new findings for Vimpat® (lacosamide) that offer additional support regarding the long-term benefits of the antiepileptic drug (AED) as an adjunctive therapy for adults with uncontrolled partial-onset seizures.

"These data add to the growing body of support showing that Vimpat® reduces seizure frequency and improves patient-reported quality of life measures on a long-term basis," said Aatif Husain, MD, lead author of one of the studies and Director, Clinical Neurophysiology Training Program, Duke University Medical Center. "These results, combined with the consistent long-term tolerability profile, are important milestones for this AED."

An open-label extension study analyzed patient-reported outcomes and found that, after a year of treatment with Vimpat®, patients reported significant improvements in all aspects of seizure severity and across almost all health-related quality of life (HRQoL) assessments, including social functioning and emotional well-being.

Results of this open-label extension study demonstrated sustained efficacy in adults taking Vimpat® as adjunctive therapy up to five years, and a long-term tolerability profile consistent with that of previous Vimpat® trials. These and other Vimpat® data were presented at the 64th annual meeting of the American Epilepsy Society (AES) in San Antonio, Texas.

Vimpat® tablets and injection were launched in the US in May 2009 as an add-on therapy for the treatment of partial-onset seizures in people with epilepsy who are aged 17 years and older. Vimpat® injection is a short-term replacement when oral administration is not feasible in these patients. Vimpat® oral solution was launched in June 2010. The availability of the oral tablets, oral solution, and intravenous (IV) injection allows for consistent treatment in a hospital setting. The most common adverse reactions occurring in greater than or equal to 10 percent of Vimpat®-treated patients, and greater than placebo, were dizziness, headache, nausea, and diplopia. Additional important safety information for Vimpat® is available at the end of the press release.

In the European Union, 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® solution for infusion may be used when oral administration is temporarily not feasible.

The maximum recommended daily dose for Vimpat® in the European Union and the U.S. is 400 mg/day.

Summary of Vimpat® Data Presented at 2010 AES Annual Meeting:

***Abstract 1.262*: Improved Seizure Severity, Health-Related Quality of Life (HRQoL), and Health Status Reported by Patients During Long-Term Treatment with Lacosamide**

This phase III open-label extension trial examined the effects of long-term lacosamide treatment on patients' self-reported seizure severity, HRQoL and health status. Analyses were based on scores from the following assessments:

- Quality of Life in Epilepsy scale (QOLIE-31), an epilepsy-specific assessment with 31 questions that ask patients to measure their health-related quality of life. (*Note: At the 2009 AES annual meeting, data were presented that identified the clinically meaningful values that should be considered when analyzing and interpreting QOLIE-31 score changes.)*
- Seizure Severity Questionnaire (SSQ), which allows patients to review various aspects of their seizures, such as altered consciousness and cognitive, emotional, and physical effects.
- Patient Global Impression of Change (PGIC), a scale that allows patients to rank how much they think their condition has improved during the treatment period of the trial.

Phase III open-label extension trial results presented at the 2010 AES annual meeting showed:

- For QOLIE-31:
  - Patients reported improvement on all QOLIE-31 subscales, with the exception of medication effects. It should be noted that, within QOLIE-31 subscales, "medication effects" are defined as side effects.

- Approximately half the patients reported improvements in seizure worry—which means patients reported being less worried or fearful about having another seizure—and social functioning, indicating the efficacy of lacosamide for both seizures and health-related outcomes.
- Significant improvements were also found for quality of life and emotional well-being. For quality of life scores, patients were asked to rank how they felt about the state of their lives (i.e., from "best possible" to "worst possible"). For emotional well-being, patients were asked to rank their energy level, nervousness, mood, and other feelings or emotions.
- On average, scores showed additional improvement after the first year of treatment.

- For SSQ:
  - At one year, patients reported a significant mean improvement on all SSQ subscales, including cognitive, emotional and physical effects during and after seizures.
- For PGIC:
  - At week 16, 79.5 percent of patients (n=283) reported overall improvement, with 53.0 percent of patients in the "very much" or "much improved" category.
  - At one year, 79.1 percent of patients (n=244) reported overall improvement, with 64.3 percent of those patients in the "very much" or "much improved" category.

Borghs S.,[1, 2] De Backer M.,[2] Mueller K.,[3] Doty P.,[4] Cramer J.[5]
[1] Business & Decision Life Sciences, Brussels, Belgium; [2]UCB Pharma S.A., Brussels, Belgium; [3] UCB Pharma, Monheim, Germany; [4]SCHWARZ BIOSCIENCES (a member of the UCB Group), Raleigh, North Carolina,[5]Yale University, Houston, TX, USA

***Abstract 1.263*: Long-Term Efficacy of Lacosamide as Adjunctive Therapy in Patients with Uncontrolled POS: Results from a Phase III Open-Label Extension Trial**

A multicenter phase III open-label extension trial lasting five years demonstrated that adjunctive therapy with lacosamide reduced the frequency of partial onset seizures in adults with epilepsy. The median modal dose of lacosamide (i.e., the dose that patients used most often during the trial) was 500mg/day over a median treatment duration of 1,075 days, or nearly three years. The maximum recommended daily dose for lacosamide in the U.S. and European Union is 400 mg/day.

- A total of 308 patients were exposed to lacosamide in this trial and, of those, 307 had post-baseline efficacy data available. For the entire treatment period, which began from baseline of the phase III double-blind clinical trial:
  - 48 percent of patients reported a 50 percent or greater reduction in seizures.
  - 24 percent of patients reported a 75 percent of greater reduction in seizures.
- Of the 193 patients who were treated with lacosamide for at least 2 years, 3.1 percent of patients remained seizure free (n=6) from the first dose of open-label treatment with lacosamide through at least 2 years of the study.

- A majority (82%) of patients were receiving 2-3 concomitant AEDs at baseline of the previous trial and 50% had tried seven or more lifetime AEDs.

E. Faught[1], S. Chung[2], A. Husain[3], J. Isojarvi[4], C. McShea[4], and P. Doty[4]
[1]Emory University, Atlanta, GA; [2]Barrow Neurological Institute, Phoenix, Arizona; [3]Duke University, Durham, North Carolina; [4]SCHWARZ BIOSCIENCES (a member of the UCB Group), Raleigh, North Carolina

***Abstract 1.265*: Long-Term Safety of Lacosamide as Adjunctive Therapy in Patients with Uncontrolled Partial-Onset Seizures: Results from a Phase III Open-Label Extension Trial**

This analysis of a multicenter phase III open-label extension trial demonstrated that long-term adjunctive treatment with lacosamide up to 800 mg/day was generally well tolerated in patients with partial onset seizures. The maximum recommended daily dose for lacosamide in the U.S. and European Union is 400 mg/day.

- A total of 308 patients were exposed to lacosamide over the trial period and, of those, 138 patients remained at trial closure. Of the patients remaining at trial closure, 93 percent continued lacosamide as part of their post-trial treatment regimen.
- There were no meaningful changes from baseline of the previous trial in hematology, blood chemistry, urinalysis, ECG parameters, vital signs, body weight, or physical/neurological exam findings with long-term lacosamide treatment.
- The safety profile was consistent with that of other clinical trials with lacosamide.
- The most common treatment-emergent adverse events (greater than or equal to 15 percent) occurring at anytime over the duration of the trial included dizziness (50.0%), headache (21.8 percent), contusion (18.5 percent), nausea (18.5 percent), convulsion (17.2 percent), nasopharyngitis (17.2 percent), fall (15.9 percent), vomiting (15.9 percent), and diplopia (15.3 percent).

A. Husain[1], E. Faught[2], S. Chung[3], J. Isojarvi[4], C. McShea[4], P. Doty[4]
[1]Duke University Medical Center, Durham, NC; [2]Emory University, Atlanta, GA; [3]Barrow Neurological Institute, Phoenix, Arizona; [4]SCHWARZ BIOSCIENCES (a member of the UCB Group), Raleigh, NC

Additional UCB-supported Vimpat® studies presented at the AES meeting, included:

- ***Abstract 1.247*: Investigation of Lacosamide Binding to Collapsin Response Mediator Protein-2 (CRMP-2)**
  Christian Wolff[1], Bruce Carrington[2], Christy Van der Perren[1], Anne Vandendriessche[1], Michel Famelart[1], Michel Varrin-Doyer[3], Michel Gillard[1], Patrik Foerch[1], Véronique Rogemond[3] Jerôme Honnorat[3], Alastair Lawson[2], Karen Miller[1]
  [1]UCB Pharma S.A., CNS Research, Braine l'Alleud, Belgium; [2]UCB Pharma S.A., Structural Biology, Slough, UK; [3]Université Claude Bernard Lyon 1, UMR_S INSERM 842, Lyon, France

- ***Abstract 1.284*: Safety of Lacosamide Monotherapy in Migraine Prophylaxis, Fibromyalgia, and Osteoarthritis: Placebo-controlled Evaluations**

T. Daniels, S. Lu, P. Verdru, G.D. Rudd
Schwarz Biosciences (a member of the UCB Group), Raleigh, North Carolina

- ***Abstract 2.191:*** **Lacosamide Does Not Alter Bone Densitometry Parameters in Juvenile Dogs**
  *M. Cornet, D. Tytgat and M. Léonard**
  UCB Pharma SA, Non-Clinical Development, Braine-l'Alleud, Belgium
  **Present address: Novartis Pharma AG, Basel, Switzerland*

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

Warnings and Precautions
AEDs increase the risk of suicidal behavior and ideation. Patients taking Vimpat® should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

Patients should be advised that Vimpat® may cause dizziness, ataxia, and syncope. Caution is advised for patients with known cardiac conduction problems, who are taking drugs known to induce PR interval prolongation, or with severe cardiac disease. In patients with seizure disorders, Vimpat® should be gradually withdrawn to minimize the potential of increased seizure frequency. Multiorgan hypersensitivity reactions have been reported with AEDs. If this reaction is suspected, treatment with Vimpat® should be discontinued.

For full prescribing information on Vimpat®, visit http://www.vimpat.com/prescribing-information.aspx, and for more information on Vimpat®, visit Vimpat.com or contact UCB at (800) 477-7877.

Vimpat® is a Schedule V controlled substance.

Important safety information about Vimpat® in the EU and EEA
Vimpat® is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization 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 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. Cases with second and third degree AV block associated with lacosamide treatment have been reported in post-marketing experience. 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 behavior have been reported in patients treated with anti-epileptic agents. Therefore patients should be monitored for signs of suicidal ideation and behaviors and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behavior emerge. Lacosamide syrup contains sodium methylhydroxybenzoate (E219), which may cause allergic reaction (possibly delayed). Patients with rare hereditary problems of fructose intolerance should not take this medicine. The syrup contains aspartame (E951), a source of phenylalanine, which may be harmful for people with phenylketonuria. Both the syrup and solution for infusion contain sodium. To be taken into consideration for patients on a controlled sodium diet. Effects on ability to drive and use machines: Lacosamide may have minor to moderate influence on the ability to drive and use machines. Lacosamide treatment has been associated with dizziness and blurred vision. Accordingly patients should be advised not to drive a car or to operate other potentially hazardous machinery until they are familiar with the effects of lacosamide on their ability to perform such activities. Laboratory abnormalities: Abnormalities in liver function tests have been observed in controlled trials with lacosamide in adult patients with partial-onset seizures who were taking 1-3 concomitant

antiepileptic drugs. Elevations of ALT to ≥3XULN occurred in 0.7% (7/935) of lacosamide patients and 0% (0/356) of placebo patients. Multiorgan Hypersensitivity Reactions: Multiorgan hypersensitivity reactions have been reported in patients treated with some antiepileptic agents. These reactions are variable in expression but typically present with fever and rash and can be associated with involvement of different organ systems. Potential cases have been reported rarely with lacosamide and if multiorgan hypersensitivity reaction is suspected, lacosamide should be discontinued. Undesirable effects: The most common adverse reactions (≥10 %) are dizziness, headache, diplopia, and nausea. Other common adverse reactions (1–<10 %) are depression, confusional state, balance disorder, coordination abnormal, memory impairment, cognitive disorder, somnolence, tremor, nystagmus, hypoesthesia, dysarthria, disturbance in attention, vision blurred, vertigo, tinnitus, vomiting, constipation, flatulence, dyspepsia, dry mouth, pruritus, rash, muscle spasms, gait disturbance, asthenia, fatigue, irritability, injection site pain or discomfort (specific to solution for infusion), irritation (specific to solution for infusion), fall, and skin laceration. Refer to the European Summary of Product Characteristics for other adverse reactions and full prescribing information. Date of revision 25th October 2010

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000863/WC500050338.pdf (Accessed 27th October 2010)

About epilepsy
Epilepsy is a chronic neurological disorder affecting approximately 40 million people worldwide and three million people in the U.S.—making it as common as breast cancer. Anyone can develop epilepsy; it occurs across all ages, races and genders. Uncontrolled seizures and medication side effects pose challenges to independent living, learning and employment, so the goal of epilepsy treatment is seizure freedom with minimal side effects. However, only half of people diagnosed will achieve seizure freedom with the first medication they try and more than one million people in the U.S. continue to experience seizures despite trying two or more antiepileptic drugs. New medications and treatments give hope to those living with uncontrolled seizures.

For further information
Nancy Nackaerts, External Communications, UCB
T +32.473.864.414, nancy.nackaerts@ucb.com

Andrea Levin / Public Relations Manager, CNS, UCB, Inc.
Office: 770.970.8352 / Mobile: 404.483.7329 / Email: andrea.levin@ucb.com

Eimear O Brien, Associate Director, Global CNS Communications
T +32 2 559 9271, eimear.obrien@ucb.com

About UCB
UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With more than 8,000 people in about 40 countries, the company generated revenue of EUR 3.1 billion in 2009. 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.