



UCB announces first presentation of primary data from latest Phase 3 study evaluating *brivaracetam* as adjunctive treatment of partial-onset seizures in epilepsy

- Primary efficacy and safety data from the largest Phase 3 *brivaracetam* study involving 768 patients presented at the 68th Annual Meeting of the American Epilepsy Society
- For patients with uncontrolled partial-onset seizures *brivaracetam* showed statistically significant and clinically relevant reductions in seizure frequency, and the safety profile was consistent with previous studies^{1,4,5,6}
- Latest results represent important progress for UCB. Subject to regulatory filing and approval, *brivaracetam* would provide a new option for adult epilepsy patients with uncontrolled partial-onset seizures

Brussels (Belgium), 8th December 2014 – 0700 (CET) – Today UCB announced the primary efficacy and safety data from the latest Phase 3 study evaluating *brivaracetam* (fixed doses of 100 and 200 mg/day with no up-titration) as adjunctive treatment in adult epilepsy patients with partial-onset seizures.¹ This study with *brivaracetam* represents the largest Phase 3 study conducted in epilepsy patients with partial-onset seizures. *Brivaracetam* is an investigational antiepileptic drug (AED) and is not approved by any regulatory authority worldwide.

This study showed statistical significance for the two primary endpoints ($p < 0.001$ for *brivaracetam* 100 and 200 mg/day). The primary efficacy endpoint in the US was the percent reduction in partial-onset seizure frequency per 28 days over placebo. The primary efficacy endpoint in the EU was the responder rate, i.e., the proportion of patients showing a 50% or greater reduction in partial-onset seizure frequency. The most frequent treatment-emergent adverse events were somnolence, dizziness and fatigue. Data was presented at the 68th Annual Meeting of the American Epilepsy Society in Seattle, Wash. (5-9 December 2014).¹

“Improving the lives of people with epilepsy and addressing unmet medical needs is a priority for UCB. In our latest study, *brivaracetam* used as adjunctive therapy significantly reduced partial-onset seizure frequency for many patients. Over 80% of patients in this study had a history of taking two or more AEDs and almost half had a history of taking five or more AEDs,” said Professor Dr. Iris Loew-Friedrich, Chief Medical Officer and Executive Vice President UCB. “We are now focused on the next important step for *brivaracetam* with applications to US and EU regulatory authorities planned for early 2015.”

“This first presentation of primary study results from the latest Phase 3 *brivaracetam* study is anticipated by the epilepsy community. The two primary outcomes in this study evaluating adjunctive *brivaracetam* in the treatment of partial-onset seizures in adults with epilepsy were statistically significant and clinically relevant.” said Dr. Pavel Klein, Director, Mid-Atlantic Epilepsy and Sleep Center, Bethesda, MD.

Efficacy results¹

- Both *brivaracetam* doses (100 and 200 mg/day) demonstrated statistically significant percent reductions in partial-onset seizure frequency per 28 days over placebo (22.8% [n=252] and 23.2% [n=249] for 100 and 200 mg/day, respectively, $p < 0.001$)
- The 50% responder rate for *brivaracetam* 100 and 200 mg/day were 38.9% (98/252) and 37.8% (94/249), compared with 21.6% (56/259) for placebo, $p < 0.001$ for both dose arms. The odds ratios vs. placebo were 2.39 (95% Confidence Interval: 1.6,3.6) and 2.19 (95% Confidence Interval:1.5,3.3) for *brivaracetam* 100 and 200 mg/day, respectively

Safety results¹

- Treatment-emergent adverse events occurred in 68.4% (173/253) and 66.8% (167/250) of patients in the *brivaracetam* 100 and 200 mg/day groups, respectively, and in 59.4% (155/261) of patients in the placebo group
- The most commonly reported adverse events ($\geq 5\%$) for the combined *brivaracetam* groups (n=503) and the placebo group (n=261) were somnolence (18.1% vs. 7.7%), dizziness (12.3% vs. 5.0%), fatigue (9.5% vs. 3.8%) and headache (7.4% vs. 8.4%)
- Study-discontinuation rates (for any reason) were 11.4% and 10.4 % for *brivaracetam* 100 and 200 mg/day, respectively, vs. 6.5% for placebo

About the Phase 3 study¹

This Phase 3, multicentre, randomized, double-blind, placebo-controlled study enrolled adults (≥ 16 -80 years) with refractory partial-onset seizures whether or not secondary generalized, and not fully controlled despite treatment with one or two concomitant AEDs. In the study, 768 epilepsy patients with partial-onset seizures, were randomized (1:1:1) to adjunctive *brivaracetam* (100 or 200 mg/day) or placebo for a 12-week Treatment Period after having completed an 8-week prospective Baseline Period. Patients taking *levetiracetam*, either as concomitant antiepileptic drug or within 90 days prior to Visit 1 were excluded. The primary efficacy outcome in the US was the percent reduction over placebo in 28-day adjusted partial-onset seizure frequency. The primary endpoint in the EU was the 50% responder rate based on percent reduction in partial-onset seizure frequency from Baseline to end of the Treatment Period.

NOTES TO EDITORS

About *brivaracetam* and the clinical development program

Discovered and developed by UCB, *brivaracetam* is a selective synaptic vesicle protein 2A ligand.^{2,3} The phase 3 clinical development plan for *brivaracetam* consisted of the following studies:

N01252: an evaluation of the efficacy and safety/tolerability of adjunctive *brivaracetam* 20, 50, and 100 mg/day compared with placebo over 12 weeks, in 399 randomized patients (≥ 16 to 70 years) with partial-onset seizures not fully controlled despite treatment with 1-2 concomitant AEDs.⁴

N01253: an evaluation of the efficacy and safety/tolerability of adjunctive *brivaracetam* at doses of 5, 20, and 50 mg/day compared with placebo over 12 weeks, in 400 randomized patients (≥ 16 to 70 years) with partial-onset seizures, not fully controlled despite treatment with 1-2 concomitant AEDs.⁵

N01254: an evaluation of the safety and tolerability of adjunctive *brivaracetam* given at individualized tailored doses between 20 and 150 mg/day, compared with placebo over 16 weeks, in 480 randomized patients (≥ 16 to 70 years) with uncontrolled epilepsy (up to 20% could be patients with generalized epilepsy), not fully controlled despite treatment with 1-3 concomitant AEDs.⁶

N01358: an evaluation of the efficacy and safety of adjunctive *brivaracetam* 100 and 200 mg/day compared with placebo over 12 weeks in 768 randomized patients (≥ 16 to 80 years) with partial-onset seizures, not fully controlled despite treatment with 1-2 concomitant AEDs.¹

About Epilepsy⁷⁻⁹

Epilepsy is a chronic neurological disorder affecting approximately 65 million people worldwide and more than 2 million people in the US. It is the fourth most common neurological disorder in the US. Although epilepsy may be linked to factors such as health conditions, race and age, it can develop in anyone at any age. In the US, approximately 1 in 26 people will develop epilepsy in their lifetime.

It is considered to be a disease of the brain defined by any of the following conditions: (1) at least two unprovoked (or reflex) seizures occurring >24 hours apart; (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; (3) diagnosis of an epilepsy syndrome.

About UCB in Epilepsy

UCB has a rich heritage in epilepsy with over 20 years of experience in the research and development of antiepileptic drugs. As a company with a long-term commitment to epilepsy research our goal is to address unmet medical needs. Our scientists are proud to contribute to advances in the understanding of epilepsy and its treatment. We partner and create super-networks with world-leading scientists and clinicians in academic institutions, pharmaceutical companies and other organizations who share our goals. At UCB, we are inspired by patients and driven by science in our commitment to support patients with epilepsy.

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References

1. Klein P., *et al.* A Randomized, Double-blind, Placebo-controlled, Multicenter, Parallel-group Study to Evaluate the Efficacy and Safety of Brivaracetam in Adult Patients with Partial Onset Seizures. Presented at AES 2014
2. Kenda, B.M., *et al.*, Discovery of 4-Substituted Pyrrolidone Butanamides as New Agents with Significant Antiepileptic Activity. *Journal of Medicinal Chemistry*, 2004. 47(3): 530-549.
3. Gillard, M., *et al.*, Binding characteristics of brivaracetam, a selective, high affinity SV2A ligand in rat, mouse and human brain: relationship to anti-convulsant properties. *Eur J Pharmacol*, 2011. 664(1-3): 36-44
4. Ryvlin, P., *et al.*, Adjunctive brivaracetam in adults with uncontrolled focal epilepsy: results from a double-blind, randomized, placebo-controlled trial. *Epilepsia*, 2014. 55(1):47-56
5. Biton, V., *et al.*, Brivaracetam as adjunctive treatment for uncontrolled partial epilepsy in adults: a phase III randomized, double-blind, placebo-controlled trial. *Epilepsia*, 2014. 55(1): 57-66
6. Kw an, P., *et al.*, Adjunctive brivaracetam for uncontrolled focal and generalized epilepsies: results of a phase III, double-blind, randomized, placebo-controlled, flexible-dose trial. *Epilepsia*, 2014. 55(1):38-46
7. Fisher, R.S., *et al.*, ILAE Official Report: A practical clinical definition of epilepsy. *Epilepsia*, 2014. 55(4): 475-482
8. Institute of Medicine. *Epilepsy Across the Spectrum. Promoting Health and Understanding*, Washington, DC: The National Academic Press, 2012 brief report. Accessed 29th October 2014 from http://www.iom.edu/-/media/Files/Report%20Files/2012/Epilepsy/epilepsy_rb.pdf
9. The Epilepsy Foundation of America. Who gets epilepsy? Accessed 29th October 2014 from <http://www.epilepsy.com/learn/epilepsy-101/who-gets-epilepsy>

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 8500 people in approximately 40 countries, the company generated revenue of €3.4 billion in 2013. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

Forward looking statements

This press release contains forward-looking statements based on current plans, estimates and beliefs of management. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, political, regulatory or clinical results and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and assumptions which could cause actual results to differ materially 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, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms, costs associated with research and development, changes in the prospects for products in the pipeline or under development by UCB, effects of future judicial decisions or governmental investigations, product liability claims, challenges to patent protection for products or product candidates, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in tax laws or the administration of such laws and hiring and retention of its employees. UCB is providing this information as of the date of this press release and expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report a change in its expectations.

There is no guarantee that new product candidates in the pipeline will progress to product approval or that new indications for existing products will be developed and approved. Products or potential products which are the subject of partnerships, joint ventures or licensing collaborations may be subject to differences between the partners. Also, UCB or others could discover safety, side effects or manufacturing problems with its products after they are marketed.

Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement.