UCB News

UCB receives CHMP positive opinion of zilucoplan for the treatment of adults with generalized myasthenia gravis in Europe

- The Committee for Medicinal Products for Human Use (CHMP) positive opinion[1] is based on the pivotal Phase 3 RAISE study in generalized myasthenia gravis (gMG) in adult patients which demonstrated that treatment with zilucoplan resulted in statistically significant and clinically meaningful improvements in gMG-specific efficacy outcomes[2]
- If approved by the European Commission zilucoplan will be the first once-daily subcutaneous (SC) targeted peptide inhibitor of complement component 5 (C5 inhibitor) and the only gMG-targeted therapy for self-administration by adult patients with AChR antibody positive gMG
- CHMP positive opinion in Europe follows recent FDA approval of rozanolixizumab-noli for the treatment of generalized myasthenia gravis (gMG) in adult patients in the U.S. who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive[3]
- UCB's two different medicines for gMG, each with a distinct mechanism of action, aim to offer a unique portfolio of treatments that embody our commitment to addressing the gMG community's unmet needs

Brussels (Belgium) Friday 15 September 2023 – UCB (Euronext Brussels: UCB), a global biopharmaceutical company, today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a positive opinion recommending granting marketing authorization for zilucoplan in the European Union (EU) as an add-on to standard therapy for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.[1]

The CHMP's positive opinion is now being reviewed by the European Commission, which grants centralized marketing authorizations for medicinal products in the EU. Feedback from the commission is anticipated before the end of the year.

Following approval, zilucoplan will be the first once-daily subcutaneous (SC), targeted peptide inhibitor of complement component 5 (C5 inhibitor) and the only self-administered gMG therapy for use by adult patients with AChR antibody positive gMG.

As a C5 inhibitor, zilucoplan inhibits complement-mediated damage to the neuromuscular junction through its targeted dual mechanism of action.[2] Benefits of SC self-administration can include reduced traveling time to and from hospitals, decreased interference with work obligations, and increased independence. Unlike monoclonal antibody C5 inhibitors, as a peptide, zilucoplan can be used concomitantly with intravenous immunoglobulin and plasma exchange, without the need for supplemental dosing.[2]

UCB's RAISE study[2], published earlier this year in the *Lancet Neurology* journal, demonstrated that zilucoplan delivered rapid, consistent, statistically significant and clinically meaningful benefits in different patient-and-clinician-reported outcomes - Myasthenia Gravis-Activities of Daily Living (MG-ADL) score, Quantitative Myasthenia Gravis (QMG) score, Myasthenia Gravis Composite (MGC) score and Myasthenia Gravis Quality of Life 15-item scale (MG-QoL15r)* - at week 12 in a broad population of mild to severe adult patients with AChR antibody positive gMG. Additionally, rapid improvements in fatigue were observed as an exploratory endpoint.

"Until now, people living with gMG have only had access to C5 therapy intravenously, which can be inconvenient and time-consuming. This positive CHMP opinion for zilucoplan is a significant step towards our

goal of delivering a treatment to address the unmet needs of people living with gMG", said Iris Loew-Friedrich, Executive Vice-President and Chief Medical Officer at UCB. *"If approved, we hope zilucoplan, a self-administered, once daily, subcutaneous targeted C5 inhibitor, will be able to help a broad population of mild to severe adult patients with AChR-antibody positive gMG. We would like to extend our thanks to the patients, care partners, and investigators who participated in the RAISE study, and to our employees and collaborators, whose dedication and commitment to the gMG community made this important milestone possible."*

gMG is a rare, chronic, heterogeneous, unpredictable autoimmune disease characterized by dysfunction and damage at the neuromuscular junction (NMJ).[4,5,6] gMG has a global prevalence of 100–350 cases per every 1 million people.[5]

The CHMP positive opinion recommending the approval of zilucoplan is supported by safety and efficacy data from the Phase 3 RAISE study (NCT04115293), published in *The Lancet Neurology* in May 2023.[2] The primary endpoint for the RAISE study was change from baseline to Week 12 in the Myasthenia Gravis-Activities of Daily Living (MG-ADL) score. A statistically significant and clinically meaningful difference favoring zilucoplan in comparison to placebo was observed in the MG-ADL total score change from baseline: least squares mean change −4·39 [95% CI −5·28 to −3·50] vs −2·30 [−3·17 to −1·43], least squares mean difference −2·09 [−3·24 to −0·95]; p=0·0004. Secondary endpoints included change from baseline to Week 12 in QMG, MGC and MG-QoL15r. A statistically significant and clinically meaningful difference favoring zilucoplan compared to placebo was observed in the QMG total score change from baseline to Week 12 (p<0.0001), least squares mean change −6.19 [95% CI −7.29 to −5.08] vs −3.25 [−4.32 to −2.17]. Change from baseline to Week 12 in MGC in comparison to placebo was clinically meaningful and statistically significant. MG-QoL 15r change from baseline to Week 12 compared to placebo was also statistically significant.[2] Change from baseline to week 12 in the Neuro-QoL short-form fatigue scale was an exploratory end point, therefore, p value was nominal, not multiplicity controlled.

The most common adverse events (reported in at least 10% of patients treated with zilucoplan) were injection-site bruising, headache, diarrhea and MG worsening.[2]

"With this CHMP positive opinion of zilucoplan, we are very proud and excited to expand our support to the gMG community. Following the FDA approval and strong momentum with our FcRn blocker rozanolixizumab-noli in the U.S., and with our tailored patient support services and commitment to widespread access, I am confident that UCB will be the only company able to deliver a portfolio of two targeted therapies with different mechanisms of action and the experience to provide truly individualized transformational patient value to people living with this often-debilitating rare disease." said Jean-Christophe Tellier, CEO, UCB.

Zilucoplan is also currently under review by the Japanese Pharmaceuticals and Medical Devices Agency (PMDA), the U.S. Food and Drug Administration (FDA), the Australian Therapeutic Goods Administration (TGA) and Health Canada for the treatment of adults with gMG. Responses from the PMDA and FDA are expected by the end of Q4 2023. Responses from the TGA and Health Canada are expected by H1 2024. Orphan designation was granted by the European Commission in 2022 to zilucoplan for the treatment of myasthenia gravis.[7]

The CHMP positive opinion of zilucoplan follows the recent FDA approval in the U.S. of rozanolixizumab-noli for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive[3]. Rozanolixizumab-noli is currently only approved in the U.S. and is under review by the Japanese Pharmaceuticals and Medical Devices Agency

(PMDA) and the European Medicines Agency (EMA) for the treatment of adults with gMG. Responses from regulatory agencies to these submissions are expected during H2 2023 and H1 2024.

In progressing a portfolio of medicines for the treatment of gMG, with the aim of providing HCPs the option of addressing either complement activation or pathogenic antibodies for appropriate patients, UCB hopes to offer a comprehensive portfolio of targeted therapeutics, embodying a commitment to addressing the gMG community's unmet needs.

About zilucoplan

Zilucoplan is a once-daily SC, self-administered peptide inhibitor of complement component 5 (C5 inhibitor). As a C5 inhibitor, zilucoplan inhibits complement-mediated damage to the neuromuscular junction through its targeted dual mechanism of action.[2]

The safety and efficacy of zilucoplan have not been established and it is not currently approved for use in any indication by any regulatory authority worldwide.

About Generalized Myasthenia Gravis (gMG)

gMG is a rare autoimmune disease with a global prevalence of 100–350 cases per every 1 million people.[5] People living with gMG can experience a variety of symptoms, including severe muscular weakness that can result in double vision, drooping eyelids, difficulty with swallowing, chewing and talking, as well as life-threatening weakness of the muscles of respiration.[4,8]

In gMG, pathogenic autoantibodies can impair synaptic transmission at the neuromuscular junction (NMJ) by targeting specific proteins on the post-synaptic membrane.[9] This disrupts the ability of the nerves to stimulate the skeletal muscle and results in a weaker contraction. gMG can occur in any race, gender or age.[4,8]

About the RAISE study[2]

The RAISE study (NCT04115293) was a multi-center, Phase 3, randomized, double-blind, placebo-controlled study to confirm the efficacy, safety profile, and tolerability of zilucoplan in adult patients with anti-acetylcholine receptor (AChR) antibody positive gMG. Patients were randomized in a 1:1 ratio to receive daily subcutaneous (SC) injections of 0.3 mg/kg zilucoplan or placebo for 12 Weeks.

The primary endpoint for the RAISE study was change from baseline to Week 12 in the Myasthenia Gravis-Activities of Daily Living (MG-ADL) score. Secondary endpoints included change from baseline in the Quantitative Myasthenia Gravis (QMG) score, the Myasthenia Gravis Composite (MGC) and the Myasthenia Gravis Quality of Life 15 revised (MG-QoL15r) score from baseline to Week 12, time to first rescue therapy, the proportion of patients with minimal symptom expression (MSE) (defined as MG-ADL of 0 or 1 without rescue therapy), the proportion with a ≥3-point reduction in MG-ADL without rescue therapy and the proportion with a ≥5-point reduction in QMG without rescue therapy, all measured at Week 12. The secondary safety endpoint was incidence of TEAEs. Patients who completed the RAISE trial had the possibility to enter the open-label extension study, RAISE-XT (NCT04225871).[2]

For more information about the trial visit https://clinicaltrials.gov/ct2/show/NCT04115293.

* The threshold for clinical meaningfulness for MG-QoL 15r has not be established

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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 approximately 8,600 people in approximately 40 countries, the company generated revenue of €5.5 billion in 2022. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news.

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This press release may contain forward-looking statements including, without limitation, statements containing the words "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will", "continue" and similar expressions. These forward-looking statements are based on current plans, estimates and beliefs of management. All statements, other than statements of historical facts, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, arbitration, political, regulatory or clinical results or practices and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to known and unknown risks, uncertainties and assumptions which might cause the actual results, financial condition, performance or achievements of UCB, or industry results, to differ materially from those that may be expressed or implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: the global spread and impact of COVID-19, changes in general economic, business and competitive conditions, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms or within expected timing, 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, safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, product liability claims, challenges to patent protection for products or product candidates, competition from other products including biosimilars, 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. There is no guarantee that new product candidates will be

discovered or identified in the pipeline, will progress to product approval or that new indications for existing products will be developed and approved. Movement from concept to commercial product is uncertain; preclinical results do not guarantee safety and efficacy of product candidates in humans. So far, the complexity of the human body cannot be reproduced in computer models, cell culture systems or animal models. The length of the timing to complete clinical trials and to get regulatory approval for product marketing has varied in the past and UCB expects similar unpredictability going forward. Products or potential products, which are the subject of partnerships, joint ventures or licensing collaborations may be subject to differences disputes between the partners or may prove to be not as safe, effective or commercially successful as UCB may have believed at the start of such partnership. UCB's efforts to acquire other products or companies and to integrate the operations of such acquired companies may not be as successful as UCB may have believed at the moment of acquisition. Also, UCB or others could discover safety, side effects or manufacturing problems with its products and/or devices after they are marketed. The discovery of significant problems with a product similar to one of UCB's products that implicate an entire class of products may have a material adverse effect on sales of the entire class of affected products. Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment, including pricing pressure, political and public scrutiny, customer and prescriber patterns or practices, and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement activities and outcomes. Finally, a breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of UCB's data and systems.
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