UCB News

UCB announces European Commission approval of ZILBRYSQ®▼ (zilucoplan) for the treatment of adults with generalized Myasthenia Gravis

- European approval of ZILBRYSQ® (zilucoplan) granted 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]
- Zilucoplan is the first once-daily subcutaneous, targeted C5 complement inhibitor for gMG.[2]
- Approval supported by pivotal Phase 3 RAISE study in gMG[2] which demonstrated treatment with zilucoplan resulted in statistically significant improvements in MG-specific efficacy outcomes compared to placebo
- European approval for zilucoplan follows approvals in U.S. and Japan earlier in 2023[3,4]
- Alongside rozanolixizumab, which was recently approved in U.S. and Japan for the treatment of gMG,[4,5] and which has received a positive opinion from the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP),[6] zilucoplan is part of UCB's portfolio of two different medicines for gMG, each with a distinct mechanism of action and with potential to offer physicians new and additional treatment choices

Brussels (Belgium) 4 December 2023, 07:00: (CET) – UCB (Euronext Brussels: UCB), a global biopharmaceutical company, today announced that the European Commission (EC) has granted a marketing authorization for ZILBRYSQ® (zilucoplan) 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]

Zilucoplan is the first once-daily subcutaneous (SC), targeted peptide inhibitor of complement component 5 (C5) inhibitor for gMG, and the only C5 inhibitor approved for self-administration by adult patients with AChR antibody-positive gMG.[2]

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-injection can include reduced traveling time to and from hospitals, decreased interference with work obligations, and increased independence.[2]

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]

The EC approval of zilucoplan is supported by safety and efficacy data from the RAISE study (NCT04115293), published in The Lancet Neurology in May 2023.[2] The RAISE study was a multi-center, phase 3, randomized, double-blind, placebo-controlled study to assess 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 study demonstrated that zilucoplan delivered rapid, consistent, clinically meaningful and statistically significant improvements in different patient- and clinician-reported outcomes at week 12 in a broad population of adult patients with mild-to-severe anti-AChR antibody-positive gMG.[2]

As included within the zilucoplan EU Summary of Product Characteristics, the most frequently reported adverse reactions were injection site reactions (injection site bruising (13.9%) and injection site pain (7.0%))

GL-ZL-2300036 Date of preparation: December 2023

and upper respiratory tract infections (nasopharyngitis (5.2%), upper respiratory tract infection (3.5%) and sinusitis (3.5%)).[1]

European approval of zilucoplan follows approvals by the U.S. Food and Drug Administration (FDA) for the treatment of generalized myasthenia gravis (gMG) in adult patients who are AChR antibody-positive and by the Japanese Ministry of Health, Labour and Welfare (MHLW) for the treatment of gMG in adult patients who inadequately respond to steroids or other immunosuppressants.[3,4]

gMG is a rare, chronic, heterogeneous, unpredictable autoimmune disease characterized by dysfunction and damage at the neuromuscular junction (NMJ).[7,8,9] Several factors are understood to be drivers of gMG disease pathology, including the complement cascade, immune cells and pathogenic Immunoglobulin G (IgG) autoantibodies[10].

In AChR antibody-positive gMG, pathogenic AChR autoantibodies (IgG1 and IgG3) initiate the classical complement pathway, which, together with the alternative and lectin complement pathways, converge at C5, leading to MAC (membrane attack complex) deposition, damage to the NMJ, loss of AChRs and subsequent impaired synaptic transmission.[9,11] Preventing MAC formation reduces damage to the post-synaptic membrane, reduces disruption of ionic channel conductance and helps to preserve neuromuscular transmission.[11]

MG has a global prevalence of 100–350 cases per every 1 million people.[8]

Alongside approval of zilucoplan, UCB's neonatal Fc receptor (FcRn) blocker rozanolixizumab recently received a positive opinion from the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) as an add-on to standard therapy 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.[6] This follows approvals for rozanolixizumab in similar indications in the U.S. and Japan earlier this year,[4,5] further strengthening UCB's unique gMG portfolio and the company's commitment to addressing the gMG community's unmet needs.

"With the European Commission's approval of zilucoplan I'm very excited that UCB is taking another important step forward in delivering patient value to the gMG community, giving clinicians an opportunity to address complement activation in gMG with a once-daily, self-administered, subcutaneous treatment option. Alongside a positive CHMP opinion from European Medicines Agency for our FcRn blocker rozanolixizumab, and approvals for both zilucoplan and rozanolixizumab in the U.S. and Japan for the treatment of adults with gMG, our unique and differentiated portfolio of medicines reinforces our commitment to redefining treatment expectations for the gMG community," explained Jean-Christophe Tellier, CEO, UCB. *"We are extremely grateful to the patients, care partners, and investigators who participated in our clinical studies, and to our employees and collaborators, whose dedication and passion have made this significant achievement possible."*

The approval of zilucoplan from the EC is valid in all EU member states, as well as in the European Economic Area (EEA) countries Iceland, Liechtenstein, and Norway.

UCB is committed to making zilucoplan available to patients as quickly as possible and anticipates European availability will commence in the first quarter of 2024.

▼ *This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.*

GL-ZL-2300036 Date of preparation: December 2023

About zilucoplan

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

In September 2023 the Japanese MHLW approved zilucoplan for the treatment of gMG in adult patients who inadequately respond to steroids or other immunosuppressants.[4] In October 2023 the U.S. FDA approved zilucoplan for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody-positive.[3]

Zilucoplan is currently under review by the Australian Therapeutic Goods Administration (TGA) and Health Canada for the treatment of adults with gMG. Responses from regulatory agencies to these submissions are expected between H2 2023 and H2 2024. Orphan designation for zilucoplan was granted by the FDA in 2019 for the treatment of myasthenia gravis.[12]

About Generalized Myasthenia Gravis (gMG)

gMG is a rare autoimmune disease with a global prevalence of 100–350 cases per every 1 million people.[8] 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.[7,13]

In MG, pathogenic autoantibodies can impair synaptic transmission at the neuromuscular junction (NMJ) by targeting specific proteins on the post-synaptic membrane.[14] This disrupts the ability of the nerves to stimulate the muscle and results in a weaker contraction. gMG can occur in any race, gender or age.[7,13]

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.[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.[2]

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. Safety was assessed by the incidence of treatment-emergent adverse events (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.

About Rozanolixizumab

Rozanolixizumab is a humanized IgG4 monoclonal antibody that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG.[15] It has been designed to block the interaction of FcRn and Immunoglobulin G (IgG), accelerating the catabolism of antibodies and reducing the concentration of pathogenic IgG autoantibodies.[15]

In June 2023, rozanolixizumab-noli was approved by the FDA, for the treatment of gMG in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody-positive, having been granted Priority Review for its Biologic License Application (BLA).[16]

In September 2023 rozanolixizumab was approved by, the Japanese Ministry of Health, Labour and Welfare (MHLW) for the treatment of gMG in adult patients who inadequately respond to steroids or other immunosuppressants.[4]

In November 2023 rozanolixizumab received a positive opinion from the European Medicines Agency CHMP as an add-on to standard therapy 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.[6] Feedback from the EC on this recommendation is anticipated during Q1 2024.

Rozanolixizumab is also currently under review by the Center of Drug Evaluation of the China National Medical Products Administration, the Australian Therapeutic Goods Administration (TGA), Health Canada and Switzerland (Swissmedic) for the treatment of adults with gMG. Responses from regulatory agencies to these submissions are expected during H2 2023 and H1 2024.

▼ZILBRYSQ® (zilucoplan) EU/EEA* Important Safety Information

▼ *This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.* The most frequently reported adverse reactions were injection site reactions (injection site bruising (13.9%) and injection site pain (7.0%)) and upper respiratory tract infections (nasopharyngitis (5.2%), upper respiratory tract infection (3.5%) and sinusitis (3.5%)). The adverse reactions from the pooled placebo-controlled (n=115) and open-label extension (n=213) studies in gMG are as follows: Very common adverse reactions: (≥ 1/10): Upper respiratory tract infections and Injection site reactions; Common adverse reactions (≥ 1/100 to < 1/10) Diarrhoea, Lipase increased, Amylase increased and Morphoea; Uncommon adverse reaction ((≥ 1/1000 to < 1/100) blood eosinophils increased. Zilucoplan is contra-indicated in patients with hypersensitivity to the active substance or to any of the excipients, in patients who are not currently vaccinated against *Neisseria meningitidis* and in patients with unresolved *Neisseria meningitidis* infection. Due to its mechanism of action, the use of zilucoplan may increase the patient's susceptibility to infections with *Neisseria meningitidis*. As a precautionary measure, all patients must be vaccinated against meningococcal infections, at least 2 weeks prior to the start of treatment. If treatment needs to start less than 2 weeks after vaccination against meningococcal infections, the patient must receive appropriate prophylactic antibiotic treatment until 2 weeks after the first vaccination dose. Meningococcal vaccines reduce but do not completely eliminate the risk of meningococcal infections. Vaccines against serogroups A, C, Y, W, and where available, serogroup B, are recommended for preventing the commonly pathogenic meningococcal serogroups. Vaccination and prophylactic antibiotic treatment should occur according to most current relevant guidelines. During treatment, patients should be monitored for signs and symptoms of meningococcal infection and evaluated immediately if infection is suspected. In case of a suspected meningococcal infection, appropriate measures such as treatment with antibiotics and discontinuation of treatment, should be taken until the meningococcal infection can be ruled out. Patients should be instructed to seek immediate medical advice if

GL-ZL-2300036 Date of preparation: December 2023

signs or symptoms of meningococcal infections occur. Prescribers should be familiar with the educational materials for the management of meningococcal infections and provide a patient alert card and patient/carer guide to patients treated with zilucoplan. In addition to Neisseria meningitidis, patients treated with zilucoplan may also be susceptible to infections with other Neisseria species, such as gonococcal infections. Patients should be informed on the importance of gonorrhea prevention and treatment. Prior to initiating zilucoplan therapy, it is recommended that patients initiate immunizations according to current immunization guidelines. *Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. https://ema.europa.en/en. EC Date of approval 01 Dec 2023.*

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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

GL-ZL-2300036 Date of preparation: December 2023

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GL-ZL-2300036 Date of preparation: December 2023

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GL-ZL-2300036 Date of preparation: December 2023