UCB News

UCB announces European Commission approval of RYSTIGGO®▼ (rozanolixizumab) for the treatment of adults with generalized myasthenia gravis in Europe

- European approval of RYSTIGGO® (rozanolixizumab) 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) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive[1]
- Approval of this orphan medicinal product is based on pivotal Phase 3 MycarinG study in gMG,[2] which demonstrated that treatment with rozanolixizumab resulted in statistically significant and clinically meaningful improvements in gMG-specific outcomes compared to placebo,[2] including everyday activities such as breathing, talking, swallowing, and being able to rise from a chair[3]
- Rozanolixizumab is the first therapy approved in Europe for adults with AChR or MuSK antibody-positive gMG, the two most common subtypes of gMG
- The decision follows EC approval for UCB's ZILBRYSQ®▼ (zilucoplan) in Europe for the treatment of adult patients with gMG, alongside U.S. FDA and Japanese MHLW approvals of rozanolixizumab and zilucoplan for the treatment of gMG in adult patients in 2023.[4,5,6,7]
- UCB is the first and only company to offer a gMG-focused portfolio, that provides patients and clinicians the option of targeted therapies for both anti-AChR and anti-MuSK antibody-positive gMG

Brussels (Belgium) 08 January 2024, 07:00 CET – UCB (Euronext Brussels: UCB), a global biopharmaceutical company, today announced that the European Commission (EC) has granted a marketing authorization for RYSTIGGO® (rozanolixizumab) on 5th January 2024 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[1].

Rozanolixizumab 140 mg/ml solution for injection is a humanized IgG4 monoclonal antibody that binds to the neonatal Fc receptor (FcRn) resulting in the reduction of circulating IgG.[2] It is the first therapy approved in Europe for adults with anti-AChR or anti-MuSK antibody-positive gMG, the two most common subtypes of gMG.

In December 2023, the EC also granted a marketing authorization for UCB's ZILBRYSQ®▼(zilucoplan) as an add-on to standard therapy for the treatment of gMG in adult patients who are anti-AChR antibody-positive[4]. Zilucoplan is a once-daily subcutaneously (SC) injected, self-administered peptide inhibitor of complement component 5 (C5 inhibitor).[8]

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.

"With the European Commission approval of rozanolixizumab, alongside their recent approval of zilucoplan, I'm very excited that our gMG portfolio is now approved for use by healthcare professionals across Europe. This represents another important milestone in our ambition to deliver new and additional patient value to the gMG community and continues our launch trajectory", explained Jean-Christophe Tellier, CEO, UCB. *"We believe there is still a significant unmet need within the gMG community which can be addressed by bringing differentiated, generally well-tolerated, and effective treatment options to patients that address key aspects of gMG pathophysiology. We extend our gratitude to the patients, care partners, and investigators who participated in our clinical studies and who have shared their insights with us. I would also like to thank our employees and collaborators whose dedication, energy and passion have contributed to this significant achievement."*

GL-RZ-2300067 Date of preparation: December 2023

EC approval of rozanolixizumab is supported by safety and efficacy data from the pivotal Phase 3 MycarinG study (NCT03971422), published in *The Lancet Neurology* in May 2023.[2]**Error! Bookmark not defined.** The primary efficacy endpoint was the comparison of the change from baseline between treatment groups (approximately rozanolixizumab 7mg/kg and rozanolixizumab 10mg/kg) versus placebo in the MG-ADL score at Day 43. MG-ADL is a measurement tool that assesses the impact of gMG on daily functions of 8 items that are typically affected in gMG. These include activities such as breathing, talking, swallowing, and being able to rise from a chair.[3] Each item is assessed on a 4-point scale where a score of 0 represents normal function and a score of 3 represents loss of ability to perform that function. A total score ranges from 0 to 24, with the higher scores indicating more impairment. Reductions in MG-ADL score from baseline to Day 43 were greater in the approximately 7 mg/kg group (least-squares mean change −3.37 [SE 0.49]) and in the approximately 10 mg/kg group (−3.40 [0.49]) than with placebo (−0.78 [0.49]; for 7 mg/kg, least-squares mean difference −2.59 [95% CI −4.09 to −1.25], p<0.001; for 10 mg/kg, −2.62 [−3.99 to −1.16], p<0.001).[1]

Secondary efficacy endpoints included change from baseline to Day 43 in the Myasthenia Gravis Composite (MG-C) and the Quantitative Myasthenia Gravis (QMC) scores.

The MG-C is a 10-item instrument that measures the symptoms and signs of MG based on physician examination and patient history. Items are related to ptosis, double vision, eye closure, talking, chewing, swallowing, breathing, neck flexion, shoulder abduction, and hip flexion. Each item is scored on an ordinal scale with four possible categories and weighted. The total score ranges from 0 to 50, with higher scores indicating more severe impairments. The MG-C is composed of items originating from other scales (i.e., QMG, MMT, MG-ADL). A statistically significant difference favoring rozanolixizumab compared to placebo was observed in the MG-C score change from baseline to Day 43 [least squares mean difference] -3.90 (95% CI (−6.63 to −1.25), p<0.001 for rozanolixizumab approximately 7mg/kg; least-squares mean difference −5.53 (95% CI −8.30 to −2.97), p<0.001 for rozanolixizumab approximately 10mg/kg.[1]

The QMG is a 13-item categorical grading system that assesses muscle weakness. Each item is assessed on a 4-point scale where a score of 0 represents no weakness and a score of 3 represents severe weakness. A total possible score ranges from 0 to 39, where higher scores indicate more severe impairment.[9] A statistically significant difference favoring rozanolixizumab compared to placebo was observed in the QMG total score change from baseline to Day 43 [least squares mean difference -3.48 (95% CI (−5.61 to −1.58), p<0.001 for rozanolixizumab approximately 7mg/kg; least-squares mean difference −4.76 (95% CI −6.82 to −2.86), p<0.001 for rozanolixizumab approximately 10mg/kg.[1]

As included within the rozanolixizumab EU Summary of Product Characteristics, the most commonly reported adverse reactions were headache (48.4 %), diarrhoea (25.0 %) and pyrexia (12.5 %)[1].

gMG is a rare, chronic, heterogeneous, unpredictable autoimmune disease characterized by dysfunction and damage at the neuromuscular junction (NMJ).[10,11,12] gMG has a global prevalence of 100–350 cases per every 1 million people.[11]

This announcement follows approvals of rozanolixizumab and zilucoplan by the Japanese Ministry of Health, Labour and Welfare (MHLW) for treatment of gMG in adult patients (only for patients who inadequately respond to steroids or other immunosuppressants), approval of rozanolixizumab by the U.S. Food and Drug Administration (FDA) for the treatment of gMG in adult patients who are anti-AChR or anti-MuSK antibody positive , and approval of zilucoplan by the FDA for the treatment of gMG in adult patients who are AChR antibody-positive. [7,5,6]

Orphan designation was granted by the European Commission in 2020 to rozanolixizumab for the treatment of myasthenia gravis and maintained after having received the positive CHMP Opinion.[13]

The approval of rozanolixizumab 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 rozanolixizumab available to patients as quickly as possible and anticipates European availability will commence in the first quarter of 2024.

GL-RZ-2300067 Date of preparation: December 2023

▼ *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.*

About rozanolixizumab

- Rozanolixizumab 140 mg/ml solution for injection is a subcutaneously administered, humanized monoclonal antibody that specifically binds to human neonatal Fc receptor (FcRn). 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.[2]
- 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).[5]
- In September 2023, rozanolixizumab was granted approval by the Japanese Ministry of Health, Labour and Welfare (MHLW) for the treatment of generalized myasthenia gravis (gMG) in adult patients (only for patients who inadequately respond to steroids or other immunosuppressants).[7]
- Rozanolixizumab is currently under review by the Center of Drug Evaluation of the China National Medical Products Administration, the Australian Therapeutic Goods Administration (TGA), Canada (Health Canada), the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) and Switzerland (Swissmedic) for the treatment of adults with gMG. Questions from regulatory agencies to these submissions are expected during H1 2024.

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.[8]
- In September 2023, the Japanese Ministry of Health, Labour and Welfare (MHLW) approved zilucoplan for the treatment of gMG in adult patients (only for patients who inadequately respond to steroids or other immunosuppressants).[7]
- In October 2023, zilucoplan was approved by the U.S. Food and Drug Administration (FDA) for the treatment of gMG in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.[6]
- In December 2023, the European Commission granted zilucoplan approval 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[4]
- Zilucoplan is currently under review by the Australian Therapeutic Goods Administration (TGA), the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA), Canada (Health Canada), South Korea (Ministry of Food and Drug Safety) and Switzerland (Swissmedic) for the treatment of adults with gMG. Questions from regulatory agencies to these submissions are expected during H2 2023 and H1 2024.
- Orphan designation was granted by the FDA in 2019 to zilucoplan for the treatment of myasthenia gravis.[14]

About generalized Myasthenia Gravis (gMG)

gMG is a rare autoimmune disease with a global prevalence of 100–350 cases per every 1 million people.[11] 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.[10,15]

In gMG, pathogenic autoantibodies can impair synaptic transmission at the neuromuscular junction (NMJ) by targeting specific proteins on the post-synaptic membrane.[16] 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.[10,15]

About the MycarinG study[2]

The MycarinG study (NCT03971422) is a multi-center, Phase 3, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of rozanolixizumab in adult patients with gMG, with an open-label extension.

GL-RZ-2300067 Date of preparation: December 2023

The primary endpoint for the MycarinG study is change in the Myasthenia Gravis-Activities of Daily Living (MG-ADL) score at Day 43, an eight-item patient-reported scale developed to assess MG symptoms and their effects on daily activities. Additional endpoints include changes in the Myasthenia Gravis composite (MG-C) score, the Quantitative MG (QMG) score, patient-reported outcomes at Day 43 and adverse events (AEs). The majority of patients taking part in the MycarinG study opted to enroll in the extensions to this clinical trial. As a result, UCB is exploring the potential for further extension studies into this treatment.

For more information about the trial, visit https://clinicaltrials.gov/ct2/show/NCT03971422.

RYSTIGGO®▼ (rozanolixizumab) 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 commonly reported adverse reactions were headache (48.4 %), diarrhoea (25.0 %) and pyrexia (12.5 %). The adverse reactions from the placebo-controlled study in gMG are as follow : Very common (≥ 1/10) headache, diarrhoea and pyrexia; Common (≥ 1/100 to < 1/10) rash, angioedema, arthralgia and injection site reactions. Headache was the most common reaction reported in 31 (48.4 %) and 13 (19.4 %) of the patients treated with rozanolixizumab and placebo, respectively. All headaches, except 1 (1.6 %) severe headache, were either mild (28.1 % [n=18]) or moderate (18.8 % [n=12]) and there was no increase in incidences of headache with repeated cyclic treatment.

Rozanolixizumab is contra-indicated in patients with hypersensitivity to the active substance or to any of the excipients.

Treatment with rozanolixizumab in patients with impending or manifest myasthenic crisis has not been studied. The sequence of therapy initiation between established therapies for MG crisis and rozanolixizumab, and their potential interactions, should be considered.

Aseptic meningitis (drug induced aseptic meningitis) has been reported following rozanolixizumab treatment at a higher dose with subsequent recovery without sequelae after discontinuation. If symptoms consistent with aseptic meningitis occur, diagnostic workup and treatment should be initiated as per standard of care.

Due to its mechanism of action, the use of rozanolixizumab may increase the patient's susceptibility to infections. Treatment with rozanolixizumab should not be initiated in patients with a clinically importantactive infection until the infection is resolved or is adequately treated. During treatment with rozanolixizumab, clinical signs and symptoms of infections should be monitored. If a clinically important active infection occurs, withholding rozanolixizumab until the infection has resolved should be considered.

Hypersensitivity reactions including mild to moderate rash or angioedema were observed in patients treated with rozanolixizumab. Patients should be monitored during treatment with rozanolixizumab and for 15 minutes after the administration is complete for clinical signs and symptoms of hypersensitivity reactions. If a hypersensitivity reaction occurs during administration, rozanolixizumab infusion should be discontinued and appropriate measures should be initiated if needed. Once resolved, administration may be resumed

Immunisation with vaccines during rozanolixizumab therapy has not been studied. The safety of immunisation with live or live-attenuated vaccines and the response to immunisation with vaccines are unknown. All vaccines should be administered according to immunisation guidelines and at least 4 weeks before initiation of treatment. For patients that are on treatment, vaccination with live or live-attenuated vaccines is not recommended. For all other vaccines, they should take place at least 2 weeks after the last infusion of a treatment cycle and 4 weeks before initiating the next cycle.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. *https://www.ema.europa.eu/en*.

GL-RZ-2300067 Date of preparation: December 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 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

GL-RZ-2300067 Date of preparation: December 2023

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GL-RZ-2300067 Date of preparation: December 2023