



UCB's Rozanolixizumab and Zilucoplan Phase 3 Generalized Myasthenia Gravis studies published in prestigious *The Lancet Neurology Journal*

- **MycarinG** study publication reports the clinically meaningful and statistically significant effects of rozanolixizumab across key endpoints in adult patients with acetylcholine receptor autoantibody positive (AChR-Ab+) or muscle-specific tyrosine kinase (MuSK-Ab+) autoantibody positive gMG, in the largest study in patients with gMG to date.
- **RAISE** publication describes clinically meaningful and statistically significant improvements in MG-specific efficacy outcomes, as well as a favorable safety profile, for zilucoplan, the first C5 complement inhibitor to be self-administered at home by adult patients with AChR-Ab+ gMG.
- **Rozanolixizumab and zilucoplan are investigational therapies** currently under regulatory review in the U.S., Europe and Japan.

Brussels (Belgium) 13 April 2023 – 07:00 AM (CET) – UCB, a global biopharmaceutical company, today announced that *The Lancet Neurology* has published data from the Phase 3 MycarinG study evaluating the efficacy and safety of rozanolixizumab in adult patients with acetylcholine receptor autoantibody-positive (AChR-Ab+) or muscle-specific tyrosine kinase autoantibody-positive (MuSK-Ab+) generalized myasthenia gravis (gMG) and the Phase 3 RAISE study evaluating the efficacy and safety of zilucoplan in adult patients with mild to severe AChR-Ab+ gMG.^{1,2}

UCB is investigating both therapies as part of a broad offering to treat adult patients living with gMG throughout their treatment journey; each has an individual mechanism of action targeting the underlying disease pathology that causes gMG.

The safety and efficacy of rozanolixizumab and zilucoplan have not been established and neither treatment is approved for use in any indication by any regulatory authority worldwide.

"There is an ongoing need for well-tolerated, targeted treatment options to improve the quality of life of people living with gMG. Many of the current treatment options only offer symptomatic relief which results in a treatment burden in addition to the already substantial disease burden," said Iris Loew-Friedrich, Executive Vice-President and Chief Medical Officer at UCB. *"These papers published in The Lancet Neurology further reinforce the potential of rozanolixizumab and zilucoplan – with their different MOAs – to provide targeted treatment options to patients to help them manage fluctuating and unpredictable symptoms both at home and in a healthcare setting."*





In the **MycarinG study¹ (n=200)** - the largest gMG population Phase 3 study published to date – in adult patients with AChR-Ab+ or MuSK-Ab+ gMG, rozanolixizumab demonstrated statistically significant and clinically meaningful improvements in MG-specific outcomes in patients with MuSK-Ab+ or AChR-Ab+ gMG, that were consistent with prior published results. Reductions in MG-ADL score from baseline to day 43 were greater in the rozanolixizumab 7 mg/kg group (least-squares mean change -3.37 [SE 0.49]) and in the rozanolixizumab 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], $p < 0.0001$; for 10 mg/kg, -2.62 [-3.99 to -1.16], $p < 0.0001$). In the MuSK-Ab+ specific subgroup, improvement in MG-ADL was -7.28 (7mg/kg; n=5), -4.16 (10mg/kg; n=8), and 2.28 (placebo; n=8). In the AChR-Ab+ specific subgroup, improvement in MG-ADL was -3.03 (7mg/kg; n=60), -3.36 , (10mg/kg; n=60), and -1.10 (placebo; n=59).

Both rozanolixizumab doses were generally well tolerated with similar occurrences of TEAEs between both doses. The most frequently reported TEAEs were headache, diarrhea, and pyrexia. A higher incidence of headache was reported in the rozanolixizumab groups versus placebo, with most cases mild to moderate and severe cases generally managed with non-opioid analgesics. Treatment discontinuation rates due to TEAEs were low.

Importantly, the MycarinG study included Patient-Reported Outcomes (PROs) measures as secondary endpoints. The novel Myasthenia Gravis Symptoms PRO (MGS-PRO) – a measure used to assess symptom severity and impact of MG on patient lives, including physical fatigue which is not covered in other MG clinical outcome assessments – demonstrated statistically significant results vs placebo.

"The findings from the MycarinG study support the mechanism of action of neonatal Fc receptor inhibition and the potential for rozanolixizumab in adult patients with acetylcholine receptor autoantibody positive (AChR-Ab+) or muscle-specific tyrosine kinase (MuSK-Ab+) autoantibody positive generalized myasthenia gravis," explained Professor Vera Bril, Professor of Medicine (Neurology), University of Toronto, Director of the Neuromuscular Section, Division of Neurology, University of Toronto and University Health Network, Toronto, and lead investigator of the MycarinG study. *"Rozanolixizumab showed clinically meaningful improvements in patient-reported and investigator-assessed outcomes for both 7 mg/kg and 10 mg/kg doses. Both doses were generally well tolerated. If approved in the future, rozanolixizumab represents a potential additional treatment option for adult patients with generalized myasthenia gravis."*

In the **RAISE study² (n=174)**, in adult patients with mild to severe AChR-Ab+ gMG, zilucoplan demonstrated rapid efficacy, with consistent, sustained, clinically meaningful and statistically significant improvements versus placebo from baseline to week 12 in both patient and clinician-reported endpoints, including MG-ADL, which was the primary efficacy endpoint, and QMG, MGC and MGQoL15, which were secondary efficacy endpoints (the threshold for clinically meaningful MG-QoL15r has not yet been established).² At Week 12, more patients receiving zilucoplan, achieved a ≥ 3 -point reduction in MG-ADL score without rescue therapy, compared with those receiving placebo (73% and 46%, respectively; odds ratio [95% CI] = 3.18 [1.66 , 6.10]; $p = 0.0005$). Additionally, more patients receiving zilucoplan, compared with those receiving placebo, (58% and 33%, respectively) achieved a ≥ 5 -point reduction in QMG score without rescue therapy at Week 12 (odds ratio [95% CI] = 2.87 [1.52 , 5.40]; $p = 0.0012$).





Zilucoplan was generally well tolerated with a favorable safety profile. The most frequently reported TEAEs in the zilucoplan group were injection site bruising, headache, diarrhea, and (worsening of) MG.² Incidences of serious TEAEs and serious infections were similar in both groups. All patients who completed the 12-week treatment period (n=166) chose to enroll in RAISE-XT, the ongoing open label extension study.² If approved, zilucoplan would be the first C5 complement inhibitor in gMG that patients can self-administer at home.

"In the RAISE study, zilucoplan showed rapid and clinically meaningful improvements in myasthenia gravis-specific efficacy outcomes, had a favorable safety profile, and was generally well tolerated, with no major safety findings," said James F. Howard, MD, Distinguished Professor of Neuromuscular Disease, Professor of Neurology, Medicine and Allied Health, The University of North Carolina at Chapel Hill School of Medicine and lead investigator in the RAISE trial. *"These results suggest that, if approved in the future, zilucoplan could present a potential new treatment option for a broad population of adult patients with AChR-Ab+ generalized myasthenia gravis."*

Earlier this year, the US Food and Drug Administration (FDA) accepted UCB's filing to review a Biologic License Application (BLA) for rozanolixizumab for the treatment of gMG in adult patients. The BLA was designated for Priority Review, with a response from the agency anticipated in Q2 2023. This BLA followed the European Medicines Agency's (EMA) validation of the Marketing Authorization Application (MAA) for rozanolixizumab, and the FDA's acceptance of a New Drug Application (NDA) and the EMA's validation of the MAA for zilucoplan in the same indication. Regulatory applications for rozanolixizumab and zilucoplan for the treatment of gMG have also been filed in Japan. Responses from regulatory agencies to these submissions are expected in H2 2023.

"Our ultimate goal is to provide targeted treatment options that can help reduce the ongoing daily burden of gMG, giving patients additional flexible treatment options that work alongside their daily life," said Charl van Zyl, Executive Vice President Neurology Solutions & Head of EU/International Markets, UCB. *"With measures such as MGS-PRO in the MycarinG study, we have been able to see the positive impact rozanolixizumab has had on patient experience, while results from the RAISE study demonstrated the potential of zilucoplan as an effective and generally well-tolerated treatment that can be self-administered at home, giving people greater independence. These results bring us one step forward towards offering tailored options to meet individual patient needs."*

gMG is a rare, chronic, heterogeneous (phenotypic and pathogenic), and unpredictable auto-immune disease characterized by dysfunction and damage at the neuromuscular junction.³ Several factors are understood to be drivers of gMG disease pathology, including complement, immune cells and pathogenic IgG autoantibodies.⁴

People living with gMG can experience a variety of symptoms, including drooping eyelids, double vision, and difficulty in swallowing, chewing and talking, as well as severe muscle weakness that can result in life-threatening weakness of the muscles of respiration.^{5,6} MG is a rare disease with a global prevalence of 100–350 cases per every 1 million people.⁷





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About the rozanolixizumab MycarinG study⁸

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.¹ The primary endpoint for the MycarinG study is change from baseline to day 43 in the Myasthenia Gravis-Activities of Daily Living (MG-ADL) score, an eight-item patient-reported scale developed to assess MG symptoms and their effects on daily activities.¹ Additional secondary endpoints include response rates, changes in the Myasthenia Gravis Composite (MGC) score, the Quantitative MG (QMG) score, patient-reported outcomes and treatment-emergent adverse events (TEAEs) from baseline to day 43.¹ The majority of patients taking part in the MycarinG study opted to enroll in the open-label extensions to this clinical trial. As a result, UCB is exploring the potential for further extension studies into this treatment.⁹

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

About rozanolixizumab

Rozanolixizumab is a SC administered, humanized monoclonal antibody that specifically binds, with high affinity, 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.^{10,11}

Rozanolixizumab is under clinical development with the aim of improving the lives of people with pathogenic IgG-autoantibody-driven autoimmune disease. In 2019, the US FDA granted orphan drug designation to rozanolixizumab for the treatment of myasthenia gravis.¹² Orphan designation was granted in 2020 by the European Commission to rozanolixizumab for the treatment of myasthenia gravis.¹³

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





About the zilucoplan RAISE study¹⁴

The RAISE study (NCT04115293) was a multi-center, Phase 3, randomized, double-blind, placebo-controlled study to confirm the efficacy, safety, and tolerability of zilucoplan in adult patients with AChR-Ab+ gMG. Patients were randomized in a 1:1 ratio to receive daily subcutaneous (SC) doses 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 and the proportion with a ≥ 5 -point reduction in QMG, all measured at Week 12. 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>

About zilucoplan

Zilucoplan is a once-daily SC, self-administered peptide inhibitor of complement component 5 (C5 inhibitor) under clinical development by UCB in gMG. As a C5 inhibitor, zilucoplan inhibits complement-mediated damage to the neuromuscular junction through its targeted dual mechanism of action.² In 2019, the US FDA granted orphan drug designation to zilucoplan for the treatment of myasthenia gravis.¹⁵ Orphan designation was granted in 2022 by the European Commission to zilucoplan for the treatment of myasthenia gravis.¹⁶

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 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 the central nervous system. With approximately 8 700 people in approximately 40 countries, the company generated revenue of € 5.5 billion in 2022. UCB is listed on Euronext Brussels (symbol: UCB).

Forward looking statements

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





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which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of such jurisdiction.

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⁸ ClinicalTrials.gov 'A Study to Test Efficacy and Safety of Rozanolixizumab in Adult Patients With Generalized Myasthenia Gravis': <https://clinicaltrials.gov/ct2/show/NCT03971422>. Accessed February 2023.

⁹ ClinicalTrials.gov 'A Study to Evaluate Rozanolixizumab in Study Participants With Generalized Myasthenia Gravis'. <https://clinicaltrials.gov/ct2/show/NCT04650854?term=Rozanolixizumab&draw=2&rank=3>

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¹³ European Medicines Agency. <https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu3202272>. Accessed March 2023

¹⁴ ClinicalTrials.gov 'Safety, Tolerability, and Efficacy of Zilucoplan in Subjects With Generalized Myasthenia Gravis (RAISE)': <https://clinicaltrials.gov/ct2/show/NCT04115293>. Accessed March 2023.

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