UCB News

UCB presents efficacy and safety results for zilucoplan and rozanolixizumab in generalized myasthenia gravis

- Phase 3 RAISE and MycarinG studies in generalized myasthenia gravis (gMG) show zilucoplan and rozanolixizumab improve gMG-specific outcomes with consistent statistical significance and clinical relevance
- Regulatory submissions for zilucoplan and rozanolixizumab are planned for later this year
- Findings from a real-world smartphone data collection study reaffirm UCB's commitment to delivering pioneering, tailored care solutions for individuals living with gMG

Brussels (Belgium), 10 May 2022 – 7:00 (CEST) – UCB, a global biopharmaceutical company, today announced results from two Phase 3 studies evaluating its investigational treatments, zilucoplan, a self-administered, subcutaneous (SC) peptide inhibitor of complement component 5 (C5 inhibitor) and rozanolixizumab, an SC-infused monoclonal antibody targeting the neonatal Fc receptor (FcRn) in adults with generalized myasthenia gravis (gMG).

These results will be presented as posters at the 14th Myasthenia Gravis Foundation of America (MGFA) International Conference on Myasthenia and Related Disorders, taking place from May 10-12, 2022.

Phase 3 RAISE results

Data from the Phase 3 RAISE trial (NCT04115293) (poster 26)[1] demonstrated treatment with zilucoplan (0.3 mg/kg daily) resulted in clinically meaningful and statistically significant improvements in key gMG-specific outcomes compared with placebo in patients with acetylcholine receptor autoantibody positive (AChR+) gMG.

The study met its primary endpoint with zilucoplan showing a placebo-corrected mean improvement of 2.12 points in the Myasthenia Gravis Activities of Daily Living (MG-ADL) score at week 12 ($p<0.001$). Significant improvement in the MG-ADL was observed from Week 1.

All key secondary endpoints were also met, including statistically significant improvements in the Quantitative Myasthenia Gravis (QMG) score, Myasthenia Gravis Composite (MGC) and Myasthenia Gravis Quality of Life 15-Item revised (MG-QoL15r), again with significant improvement observed from Week 1. The proportion of patients on zilucoplan who responded to treatment by at least a 3-point reduction on MG-ADL and at least a 5-point reduction in QMG were also significantly higher than placebo.

A favorable safety profile and good tolerability was observed, consistent with prior data, showing a similar rate of treatment-emergent adverse events (TEAEs) between zilucoplan (76.7%) and placebo (70.5%). The most common TEAEs were injection site bruising, headache, diarrhea, and MG worsening.

In the RAISE study, 174 patients were randomised to Placebo (N=88) and Zilucoplan 0.3 mg/kg (N=86). Patient demographics and baseline disease characteristics were generally balanced between treatment arms.

"*The results from the RAISE study are an exciting development in the gMG treatment paradigm and reinforce the critical role that complement inhibition could play for physicians treating patients with this debilitating illness. By targeting the underlying mechanisms of gMG at the neuromuscular junction, complement inhibitors like zilucoplan have the potential to provide rapid, consistent disease control earlier in the disease course. These findings are an encouraging sign that we may be able to meet patients' needs effectively, with treatments that are minimally invasive and well tolerated,"* 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.

Phase 3 MycarinG results

Results from the Phase 3 MycarinG study (NCT03971422) (poster 25)[2] demonstrated that rozanolixizumab significantly reduced MG-ADL from baseline to Day 43 at ~7 mg/kg and ~10 mg/kg doses compared with placebo in patients with AChR or muscle-specific tyrosine kinase (MuSK) autoantibody positive gMG. Rozanolixizumab demonstrated a placebo-corrected mean improvement of 2.586 points at the ~7 mg/kg dose and 2.619 points in the MG-ADL at the ~10 mg/kg dose compared with placebo (both doses at $p<0.001$).

Rozanolixizumab treatment reduced mean maximum total IgG levels by more than 70% (71 % for 7 mg/kg and 78% for 10 mg/kg) and anti-AChR autoantibody levels decreased over the treatment period in line with the total IgG reduction. Rozanolixizumab was generally well tolerated, with the majority of TEAEs being mild to moderate in intensity. A higher proportion of TEAEs occurred in the active treatment arms versus placebo (81.3% for ~7 mg/kg, 82.6% for ~10 mg/kg and 67.2% for placebo). The most frequently reported TEAE was headache, most of which were mild to moderate, with severe headaches managed with over-the-counter analgesic medications. The other most common TEAEs were diarrhea, pyrexia and nausea.

Due to the fluctuating and unpredictable nature of gMG and the subjectivity of symptoms, patient reported outcomes (PROs) help provide greater insight into disease impact and more granular detail on the effect of treatments than traditional endpoints. Within the MycarinG study, the MG Symptoms PRO measure, which was developed by UCB with patients, was used to assess a series of quality-of-life measures, including muscle weakness fatigability, physical fatigue and bulbar muscle weakness, throughout the treatment and observation periods (poster 64)[3]. All three MG Symptoms PRO scales or subdomains showed significant improvement from baseline with rozanolixizumab ~7 mg/kg and ~10 mg/kg doses compared with placebo at Day 43, indicating treatment with rozanolixizumab improves patients' symptoms and their ability to undertake daily activities. Further evaluation of the MG Symptoms PRO measure is ongoing.

In the MycarinG study, a total of 66 patients were randomized to rozanolixizumab 7 mg/kg, 67 to rozanolixizumab 10 mg/kg and 67 to placebo. Baseline characteristics were generally balanced between treatment groups.

"*The one constant in gMG is unpredictability. People living with this disease experience symptoms that are nebulous, fluctuating, and which vary from one day to the next. For this reason, there is an urgent need for more effective, targeted, and convenient treatments that reduce the burden of disease on patients' daily lives. The results from the MycarinG study are extremely encouraging, and demonstrate the potential of rozanolixizumab as a new, effective and flexible treatment option to help ease the day-to-day burden of this*

challenging disease and improve treatment outcomes for patients," said 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.

"Every person living with gMG is unique, so a one-size-fits-all treatment approach will never be appropriate. This is why at UCB we are investigating two medicines with different MOAs. This unique approach means we may be able to offer physicians and patients a range of treatment options to meet the individual needs of many different patients, and therefore leave no one behind in our ambition to improve outcomes in gMG," said Iris Loew-Friedrich, Executive Vice-President and Chief Medical Officer at UCB.

UCB anticipates filing regulatory submissions for both zilucoplan and rozanolixizumab later this year.

Digital innovation for patients living with myasthenia gravis

Findings from a three-month observational study carried out by UCB in collaboration with digital health company Sharecare, to collect real-world data from gMG patients using smartphones, were also presented at the conference (poster 84)[4]. Beyond demonstrating that decentralized, smartphone-based methods to collect real-world data from gMG patients are feasible and may provide enhanced visibility into the burden of the disease, the study also identified unique clusters of exacerbation subtypes with specific symptom representation. This requires further validation but suggests that digital phenotyping holds promise for furthering understanding of exacerbations. This analysis forms part of UCB's holistic approach to delivering differentiated patient experiences, combining patient insights, pioneering research and artificial intelligence to deliver tailored support for individuals living with gMG.

"*Our gMG pipeline is supported by a holistic and integrated platform of support services and digital innovation that aims to deliver broad access to seamless and flexible services across the gMG care continuum,"* continued Charl van Zyl, Executive Vice President Neurology & Head of Europe/International Markets at UCB *"Our ultimate goal is to transform the lives of people living with this challenging disease by putting patients at the center of our world and advancing scientific solutions that meet their complex and varying needs."*

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About Generalized Myasthenia Gravis (gMG)
Myasthenia gravis is a rare disease impacting almost 200,000 patients in the U.S., EU and Japan.[5,6] People living with gMG can

experience a variety of symptoms, including drooping eyelids, double vision and difficulty swallowing, chewing and talking, as well as severe muscular weakness that can result in life threatening weakness of the muscles of respiration.[7]

gMG is a chronic and unpredictable auto-immune disease in which pathogenic autoantibodies can inhibit synaptic transmission at the neuro-muscular junction by targeting specific proteins on the post-synaptic membrane. This disrupts the ability of the nerves to stimulate the muscle and results in a weaker contraction[8]. gMG can occur at any age and in any race, although previous studies have shown that women are more often impacted than men.[8] Most patients with gMG have pathogenic IgG antibodies that disrupt the transmission of nerve impulses to muscles in the NMJ and some activate the complement cascade. Complement-mediated destruction via MAC formation is a key mechanism causing damage at the NMJ and is the key driver of disease in AChR Ab+ gMG.

About the zilucoplan RAISE study[9]
The RAISE study (NCT04115293) is a multi-center, Phase 3, randomized, double-blind, placebo-controlled study to confirm the efficacy, safety, and tolerability of zilucoplan in patients with gMG. Patients will be randomized in a 1:1 ratio to receive daily subcutaneous (SC) doses of zilucoplan or placebo for 12 weeks.

The primary endpoint for RAISE study is change from baseline to Week 12 in the Myasthenia Gravis-Activities of Daily Living (MG-ADL) score. Secondary endpoints include change in the Quantitative Myasthenia Gravis (QMG) score, the Myasthenia Gravis Composite (MGC) and the Myasthenia Gravis Quality of Life 15 revised (MG-QoL15r) from baseline to Week 12, the proportion requiring rescue therapy, the proportion with minimum symptom expression (MSE) (defined as MG-ADL of 0 or 1), 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. The majority of patients taking part in the RAISE trial opted to enroll in any future 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/NCT04115293.

About the rozanolixizumab MycarinG study[10]
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.

The primary endpoint for the MycarinG study is change in the Myasthenia Gravis-Activities of Daily Living Profile (MG-ADL) score, an eight-item patient-reported scale developed to assess MG symptoms and their effects on daily activities. Additional endpoints include response rates, changes in the Myasthenia Gravis composite (MGC) score, the Quantitative MG (QMG) score, patient-reported outcomes and adverse events (AEs). The majority of patients taking part in the MycarinG study opted to enroll in any future 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.

About Zilucoplan
Zilucoplan is a once-daily self-administered SC peptide inhibitor of complement component 5 (C5 inhibitor) under clinical development by UCB in gMG. Results from the RAISE study, a multi-center, Phase 3, randomized, double-blind, placebo-controlled study demonstrate the efficacy, safety, and tolerability of zilucoplan in patients with gMG, and regulatory submissions are planned in 2022.

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 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.[11,12]

Rozanolixizumab is under clinical development with the aim of improving the lives of people with pathogenic IgG-autoantibody-driven autoimmune diseases.

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 UCB in Rare Diseases
At UCB, we don't just see patients or population sizes, we see people in need. Through decades of serving the neurology and immunology communities, we have improved lives with impactful medicines and by enhancing the social and emotional well-being of patients. As a continuation of our heritage, we are now expanding our efforts to tackle rare neurological and immunological diseases where current options offer little hope..

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 8,500 people in approximately 40 countries, UCB generated revenue of €5.8 billion in 2021. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

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[1] Outcomes from RAISE: A randomized, placebo-controlled, double-blind, Phase 3 trial of zilucoplan in generalized myasthenia gravis. Howard JF et al. Data presented at MGFA International Conference 2022. Poster 26.
[2] Efficacy and safety of rozanolixizumab in patients with generalized myasthenia gravis: A randomized, multicenter, double-blind, placebo-controlled, Phase 3 study (MycarinG). Bril V et al. Data presented at MGFA International Conference 2022. Poster 25
[3] Patient-reported and quality-of-life outcomes from MycarinG, a randomized, placebo-controlled, double-blind, Phase 3 trial of rozanolixizumab in generalized myasthenia gravis. Habib A et al. Data presented at MGFA International Conference 2022. Poster 64
[4] A decentralized, prospective, observational study to collect real-world data from patients with myasthenia gravis using smartphones. Steyaert S et al. Data presented at MGFA International Conference 2022. Poster 84.
[5] Chen J, et al. Incidence, mortality, and economic burden of myasthenia gravis in China: A nationwide population-based study. Lancet Reg Health West Pac.2020;5:10063.
[6] Gilhus N. Myasthenia Gravis. N Engl J Med. 2016;375:2570-2581.
[7] Hansen JS, et al. Mortality in myasthenia gravis: A nationwide population-based follow-up study in Denmark. Muscle Nerve. 2016;53:73-77.
[8] Myasthenia Gravis Foundation of America. Clinical Overview of MG. https://myasthenia.org/Professionals/Clinical-Overview-of-MG. Accessed May 2022.
[9] Clinical Trials.gov 'Safety, Tolerability, and Efficacy of Zilucoplan in Subjects With Generalized Myasthenia Gravis (RAISE)': https://clinicaltrials.gov/ct2/show/NCT04115293. Accessed May 2022.
[10] Clinical Trials.gov 'A Study to Test Efficacy and Safety of Rozanolixizumab in Adult Patients With Generalized Myasthenia Gravis': https://clinicaltrials.gov/ct2/show/NCT03971422. Accessed May 2022.
[11] Kiessling P, et al. The FcRn inhibitor rozanolixizumab reduces human serum IgG concentration: A randomized phase 1 study. Sci Transl Med. 2017;9(414).
[12] Smith B, et al. Generation and characterization of a high affinity anti-human FcRn antibody, rozanolixizumab, and the effects of different molecular formats on the reduction of plasma IgG concentration. MAbs.2018;10:1111-30.