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UCB presents latest data from generalized myasthenia gravis portfolio at AANEM meeting

- Results presented across UCB's generalized myasthenia gravis (gMG) development program builds the body of evidence around the complexities of gMG
- Presentations to include data from the Phase 3 MycarinG study of rozanolixizumab as well as the Phase 3 RAISE and RAISE-XT studies of zilucoplan

Brussels (Belgium), 22 September 2022 – 7:00 (CEST) – UCB, a global biopharmaceutical company, announced today it is presenting results from across its portfolio in generalized myasthenia gravis (gMG) at the American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) annual meeting featuring the Myasthenia Gravis Foundation of America (MGFA) Scientific Session, September 21 – 24. Presentations include study results for 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 gMG. In addition, the company is also presenting real-world findings into the burden of the disease for society and the potential role of a digital application in improving care.

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.

"Patients living with gMG experience high disease and treatment burden resulting in a significant impact on their daily lives. The data being presented at AANEM and the MG Scientific Session reinforce the potential of UCB's two investigational medicines with different mechanisms of action to provide targeted treatment options to patients," said Iris Loew-Friedrich, Executive Vice President and Chief Medical Officer at UCB. *"We are committed to meeting patients' needs, regardless of antibody profile, including those with MuSK Ab+ gMG who have particularly limited treatment options. With our gMG pipeline, we hope to address both drivers of disease pathology and which account for approximately 95% of patients living with gMG."*

Rozanolixizumab MycarinG Phase 3 Results

A subgroup analysis presented from the Phase 3 MycarinG study (Poster 16, MGFA Scientific Session) [1] analyzes the efficacy of rozanolixizumab in patients with muscle specific kinase antibody-positive (MuSK-Ab+)

gMG, which is often more severe and harder to treat than acetylcholine receptor antibody positive (AChR-Ab+) gMG.[2] In the analysis, rozanolixizumab demonstrated statistically significant and clinically meaningful improvements in MG-specific outcomes in patients with MuSK-Ab+ gMG, that were consistent with results in AChR-Ab+ gMG and the overall population. Improvements in Myasthenia Gravis-Activities of Daily Living (MG-ADL) score for the overall population (n=200), including MuSK-Ab+ patients, were -3.37 for 7mg/kg (n=66; 5 MuSK Ab+) and -3.40 for 10mg/kg (n=67) vs -0.78 (n=67) for placebo. 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).[1]

In a responder analysis from MycarinG (Poster 204, AANEM)[3], results presented demonstrated that rozanolixizumab significantly reduced MG-ADL from baseline to Day 43. In this primary endpoint, rozanolixizumab showed an LS mean difference vs placebo of 2.59 points at the 7mg/kg dose and 2.62 points at the 10mg/kg dose. Furthermore, a greater percentage of patients in the rozanolixizumab 7mg/kg and 10mg/kg arms than the placebo arm achieved a 2.0-point or greater improvement in MG-ADL, a 3.0-point or greater improvement in Quantitative Myasthenia Gravis (QMG) scores and a 3.0-point or greater improvement in Myasthenia Gravis Composite (MGC) scores. Rozanolixizumab had an acceptable safety profile and was generally well tolerated with similar occurrences of TEAEs between both doses.[3]

A further safety analysis of the MycarinG trial (Oral presentation, 'Clinical Trials 2' session, MGFA Scientific Session),[4] showed that rozanolixizumab was generally well tolerated, with the majority of treatment emergent adverse events (TEAEs) being mild to moderate in severity. 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) and were comparable between the rozanolixizumab groups. The most frequently reported TEAEs were headache, diarrhea, pyrexia and nausea. 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. There were no severe or serious infections in the rozanolixizumab groups. Treatment withdrawal due to TEAEs was low; the rate was similar in the rozanolixizumab 7 mg/kg and placebo groups and higher in the rozanolixizumab 10 mg/kg group.[4]

Zilucoplan Phase 3 RAISE and RAISE-XT Results

An interim analysis from RAISE-XT (data cut off 18 February 2022), a Phase 3, multicenter, open-label extension study (Poster 14, MGFA Scientific Session) is also being presented.[5] This ongoing study recruited patients with AChR-Ab+ gMG who participated in randomized Phase 2 (NCT03315130) and Phase 3 (NCT04115293) zilucoplan studies. Building on the data seen in the double-blind Phase 2 and Phase 3 studies, results demonstrated a favorable long-term safety profile for zilucoplan over 24 weeks with no major safety findings, with efficacy in patients who had previously received zilucoplan continuing to improve, and efficacy demonstrated as early as week 1 in patients who switched from placebo. At extension study Week 12, after 24 weeks, the zilucoplan group achieved an LS mean improvement in MG-ADL score from the double-blind study baseline of −6.30. MG-ADL improvement for the placebo-switch group, after 12 weeks of zilucoplan, was −6.32.

A presentation on the quality-of-life (QoL) outcomes with zilucoplan from the Phase 3 RAISE study (NCT04115293) (Oral presentation, 'Clinical Trials 2' session, MGFA Scientific Session)[6] demonstrated that zilucoplan clinically meaningfully and highly statistically significantly improved MG-ADL at week 12 (LS mean difference v placebo –2.09; p<0.001) and showed consistently greater improvement in fatigue vs placebo (LS mean difference vs placebo at Week 12, –3.06; nominal p=0.0069). An overall Work Impairment due to

problem score with zilucoplan vs placebo (LS mean difference vs placebo –12.83; p=0.0912) was also observed. Zilucoplan demonstrated a favorable safety profile, with a similar rate of TEAEs between zilucoplan (76.7%) and placebo (70.5%), and good tolerability. The most common TEAEs were injection-site reactions (26.7% zilucoplan vs 14.8% placebo); all were non-serious, and mild in severity, except for one instance of injection-site pain of moderate severity in the zilucoplan group and no patients discontinued due to an injection-site reaction. All patients in the zilucoplan arm who completed the 12-week treatment period have entered the ongoing RAISE-XT extension study (NCT04225871).

Additionally, in a detailed responder analysis from Phase 3 RAISE trial being presented (Poster 200, AANEM)[7] significantly higher proportions of patients receiving zilucoplan achieved ≥3-point and ≥5-point improvements in MG-ADL and QMG without rescue therapy vs placebo, respectively Zilucoplan demonstrated a clinically meaningful placebo-corrected mean improvement of 2.09 points (p<0.001) in MG-ADL, with 73.1% (p<0.001) of patients receiving zilucoplan achieving a 3.0-point or greater reduction in MG-ADL compared to placebo (46.1%) and 58% (p=0.0012) of patients receiving zilucoplan achieving a 5.0-point or greater reduction in QMG compared to placebo (33.3%). Zilucoplan had a favorable safety profile with no major safety findings and good tolerability.[7]

Real-world costs of gMG and digital application supporting patients

Data from a study exploring the health care utilization and societal costs of MG in Norway (Poster 9, MGFA Scientific Session)[8] highlighted the burden on both patients and society. It showed that societal costs such as lost life years, QoL, and productivity are significant and greater than direct treatment-related costs (estimated to be only 11.5% of societal costs).

A further study on the real-world assessment of patient perceptions on an MG symptom-tracking application[9] showed the potential of the smartphone application to equip patients with information that would allow them to better communicate their individual disease experience to their healthcare professional while also making behavioral changes to better manage their disease. Further assessment of this application is underway. (Oral presentation, 'Outcomes' session, MGFA Scientific Session).

"We are proudly and firmly committed to supporting the gMG community by increasing knowledge and understanding of the true burden of this disease to help improve outcomes," said Charl van Zyl, Executive Vice President Neurology & Head of Europe/International Markets at UCB. *"By focusing on patients and reinforcing our gMG pipeline with a platform of support services and digital innovations, we aim to transform the lives of people living with this disease."*

UCB anticipates filing regulatory submissions in the European Union, Japan and the U.S. for both zilucoplan and rozanolixizumab later this year.

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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.[10,11] 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.[12]

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.[13] gMG can occur at any age and in any race, although previous studies have shown that women are more often impacted than men.[13] 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[14]
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 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 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) score from baseline to Week 12, time to rescue therapy, the proportion with minimal 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. Secondary safety endpoint is incidence of TEAEs. Patients who completed the RAISE trial had the possibility to enter the open label extension study, RAISE-XT (NCT04225871).

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

About the rozanolixizumab MycarinG study[15]
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 (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 the open label 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 demonstrated the efficacy, safety, and tolerability of zilucoplan in patients with gMG, and regulatory submissions are planned in 2022. In 2019, the US FDA granted orphan drug designation to zilucoplan for the treatment of myasthenia gravis.[16] Orphan designation was granted in 2022 by the European Commission to zilucoplan for the treatment of myasthenia gravis.[17]

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 an 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.[18,19]

Rozanolixizumab is under clinical development with the aim of improving the lives of people with pathogenic IgG-autoantibody-driven autoimmune diseases. In 2019, the US FDA granted orphan drug designation to rozanolixizumab for the treatment of myasthenia

gravis.[20] Orphan designation was granted in 2020[21] by the European Commission for rozanolixizumab for the treatment of myasthenia gravis.

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, including investigational treatments for gMG, MOG-AD and AIE.

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 7,600 people in approximately 40 countries, UCB generated revenue of €5.3 billion in 2020. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

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