UCB News

For media

• Twitter (@UCB News)	• For media: #UCB announces priority review designation of BLA for the treatment of adults with generalized myasthenia gravis (gMG) filed with U.S. FDA. MAA also recently filed with EMA.

UCB announces rozanolixizumab BLA for the treatment of generalized myasthenia gravis filed with U.S. FDA and designated for Priority Review

- Biologic License Application (BLA) designated Priority Review by FDA and seeks approval for rozanolixizumab for the treatment of adults with generalized myasthenia gravis (gMG) who are anti-acetycholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive
- Rozanolixizumab FDA Priority Review follows recent European Medicines Agency (EMA) validation of the Marketing Authorization Application (MAA) for rozanolixizumab in adults with gMG
- FDA and EMA submissions based on pivotal Phase 3 MycarinG study in gMG which demonstrated treatment with rozanolixizumab resulted in clinically meaningful and statistically significant improvements in MG specific outcomes
- UCB expects to receive feedback from the agencies in Q2 of 2023

Brussels (Belgium) 6 Jan 2023 – 7:00AM (CET) – UCB, a global biopharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) has accepted the company's filing to review a Biologic License Application (BLA) for its investigational treatment rozanolixizumab, and that the Agency has granted Priority Review.[1] Rozanolixizumab is a subcutaneous (SC) monoclonal antibody targeting the neonatal Fc receptor (FcRn) for the treatment of adults with generalized myasthenia gravis (gMG) who are anti-acetycholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive[2].

A FDA Priority Review designation is typically granted by the Agency to a medicine which, if approved, could deliver significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications[3]. Priority Review designation means the FDA's goal is to take action on an application within 6 months, compared to 10 months under standard review[3]. In 2019, the U.S. FDA granted orphan drug designation to rozanolixizumab for the treatment of MG.[4]

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

The FDA Priority Review designation follows the recent European Medicines Agency (EMA) validation of the Marketing Authorization Application (MAA) for rozanolixizumab for the treatment of adults with AChR or MuSK antibody positive gMG who require treatment in addition to steroids or non-steroidal immunosuppressants. Validation confirms that the application is complete and the formal review process by the EMA's Committee for Medicinal Products for Human Use (CHMP) can begin. Orphan designation was granted by the European Commission in April 2020 to rozanolixizumab for the treatment of myasthenia gravis.[5]

UCB expects to receive feedback from both the FDA and EMA during the second quarter of 2023.

"People living with MG suffer from unpredictable, fluctuating, and debilitating symptoms that have a huge impact on their lives, and there is a clear need for additional targeted treatments. We are firmly committed to supporting the gMG community by providing solutions to help improve outcomes for patients and reduce the day-to-day burden of the disease," said Charl van Zyl, Executive Vice President Neurology Solutions & Head of EU/International Markets, UCB. "*The FDA's decision to assess rozanolixizumab via their priority review process, as well as the recent filing of the MAA in Europe, brings us important steps further on our journey towards approvals for rozanolixizumab. We look forward to working with the FDA and EMA to help bring this new treatment option to patients."*

gMG is a chronic and unpredictable auto-immune disease in which pathogenic autoantibodies can impair synaptic transmission at the neuromuscular 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.[6] 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.[6,7] In the U.S. the prevalence of MG is estimated at 14 to 20 per 100,000 population; approximately 36,000 to 60,000 cases.[6] In Europe, the prevalence is estimated at 10 per 100,000 population.[8]

Data from the MycarinG study

The Priority Review BLA and the MAA are based on data from the pivotal Phase 3 MycarinG study (NCT03971422), in which rozanolixizumab demonstrated statistically significant and clinically meaningful improvements in MG-specific outcomes in patients with AChR MuSK antibody positive MG. In the primary endpoint, rozanolixizumab significantly reduced MG-ADL from baseline to Day 43. Rozanolixizumab showed an LS mean difference vs placebo (95% CI) of -2.59 points at the 7mg/kg dose and -2.62 points at the 10mg/kg dose.[9]

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 ($p<0.001$) 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[9], demonstrating clinically meaningful reductions in these assessments.

Rozanolixizumab demonstrated an acceptable safety and tolerability profile with similar occurrences of TEAEs between both doses. 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.Treatment discontinuation rates due to TEAEs were low.[9]

In the MycarinG study, 200 patients were randomised 1:1:1 to receive weekly rozanolixizumab 7 mg/kg (N=66), 10 mg/kg (N=67) or placebo (N=67) for 6 weeks, which was followed by an 8-week observation period.[6]

"Patients living with MG may experience high disease and treatment burden resulting in a significant impact on their daily lives. If approved, rozanolixizumab has the potential to address unmet needs of gMG patients," said Iris Loew-Friedrich, Executive Vice-President and Chief Medical Officer at UCB. *"Through rozanolixizumab and zilucoplan, we intend to bring two medicines with different mechanisms of action that have the potential to provide targeted treatment options to patients. With our gMG pipeline, we hope to address both drivers of disease pathology and which account for approximately 95% of people living with gMG. Priority Review Designation by the FDA for rozanolixizumab reflects the extent to which our science speaks for itself in potentially addressing the significant unmet needs still faced by the gMG community."*

UCB is currently investigating two potential therapies with different modes of action for the treatment of gMG. Alongside rozanolixizumab, a NDA for zilucoplan – a subcutaneous self-administered peptide inhibitor of complement component 5 (C5 inhibitor) has recently been filed with the U.S. FDA for the treatment of adults with AChR antibody positive gMG. Additionally, zilucoplan received MAA validation from the EMA for the treatment of adults with AChR antibody positive gMG and who require treatment in addition to steroids or non-steroidal immunosuppressants.[10,11,12]

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About Generalized Myasthenia Gravis (gMG)

Myasthenia gravis is a rare disease impacting more than 700,000 people worldwide.[13] People living with gMG can experience a variety of symptoms, including drooping eyelids, double vision, difficulty swallowing, chewing

and talking, as well as severe muscular weakness that can result in life threatening weakness of the muscles of respiration.[6, 4]

gMG is a chronic and unpredictable auto-immune disease in which pathogenic autoantibodies can impair synaptic transmission at the neuromuscular junction (NMJ) 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.[6, 14] gMG can occur in any race, although previous studies have shown that women are more often impacted than men.[15,16] 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.[2] Complement-mediated destruction via MAC formation is a key mechanism causing damage at the NMJ and is the key driver of disease in AChR antibody positive gMG gMG.

About the rozanolixizumab MycarinG study [17]

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 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. 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 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. [2, 18]

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.[4] Orphan designation was granted in 2020 by the European Commission for rozanolixizumab to the treatment of myasthenia gravis.[5]

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 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.[10] In 2019, the US FDA granted orphan drug designation to zilucoplan for the treatment of myasthenia gravis.[11] Orphan designation was granted in 2022 by the European Commission to zilucoplan for the treatment of myasthenia gravis.[12]

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 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, myelin oligodendrocyte glycoprotein antibody-associated disease (MOG-AD) and autoimmune encephalitis (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 approximately 8,600 people in approximately 40 countries, the company generated revenue of €5.8 billion in 2021. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news.

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 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 with a product similar to one of UCB's products that implicate an entire class of products may have a material adverse effect on sales of the entire class of affected products. Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment, including pricing pressure, political and public scrutiny, customer and prescriber patterns or practices, and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement activities and outcomes. Finally, a breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of UCB's data and systems.
Given these uncertainties, you should not place undue reliance on any of such forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labelling in any market, or at any particular time, nor can there be any guarantee that such products will be or will continue to be commercially successful in the future.

UCB is providing this information, including forward-looking statements, only as of the date of this press release and it does not reflect any potential impact from the evolving COVID-19 pandemic, unless indicated otherwise. UCB is following the worldwide developments diligently to assess the financial significance of this pandemic to UCB. UCB expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report or reflect any change in its forward-looking statements with regard thereto or any change in events, conditions or circumstances on which any such statement is based, unless such statement is required pursuant to applicable laws and regulations.

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