UCB News

For media

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UCB announces U.S. FDA acceptance of new drug application and EMA MAA validation for zilucoplan for the treatment of generalized myasthenia gravis in adult patients

- New drug application (NDA) for zilucoplan seeks approval for the treatment of generalized myasthenia gravis (gMG) in adult patients who are acetylcholine receptor antibody positive (AChR-Ab+)
- Acceptance by U.S. Food and Drug Administration (FDA) follows the recent European Medicines Agency (EMA) validation of Marketing Authorization Application (MAA) for treatment of adult patients with AChR-Ab+ gMG and who require treatment in addition to steroids or non-steroidal immunosuppressants
- Both NDA and MAA are based on pivotal Phase 3 RAISE study in gMG, which demonstrated treatment with zilucoplan resulted in clinically meaningful and statistically significant improvements in key MG-specific outcomes compared to placebo
- UCB expects to receive feedback from the agencies in Q4 of 2023

Brussels (Belgium), 14 November 2022 – 7:00 (CEST) – UCB, a global biopharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) has accepted for review the New Drug Application (NDA) for its investigational treatment, zilucoplan.

Zilucoplan is a subcutaneous (SC), self-administered peptide inhibitor of complement component 5 (C5 inhibitor) for the treatment of adult patients with acetylcholine receptor antibody positive (AChR-Ab+) generalized myasthenia gravis (gMG).

In 2019, the U.S. FDA granted orphan drug designation to zilucoplan for the treatment of MG.[1] 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.

This acceptance follows the recent European Medicines Agency (EMA) validation of the Marketing Authorization Application (MAA) for zilucoplan for the treatment of adult patients with AChR-Ab+ gMG and 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 in 2022 by the European Commission to zilucoplan for the treatment of myasthenia gravis.[2]

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.[4] People living with MG 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.[3] 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.[4] In Europe, the prevalence is estimated at 10 per 100,000 population.[5]

"People living with gMG experience high treatment burden, on top of the debilitating impact of the condition, and there is a clear need for additional targeted treatments to support the gMG community. Our goal is to provide a solution that can help meet these needs and transform lives," said Charl van Zyl, Executive Vice President Neurology Solutions & Head of EU/International Markets, UCB. *"The acceptance of the NDA by the FDA as well as the acceptance of the MAA by the EMA, brings us one step further on our journey towards approval for this medicine. We look forward to working with the FDA and EMA to help bring this important new treatment option to patients."*

The NDA and MAA are based on data from the pivotal Phase 3 RAISE study (NCT04115293), which demonstrated at week 12 that 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 AChR-Ab+ gMG. The study met its primary endpoint with zilucoplan showing a placebo-corrected mean improvement of 2.09 points in the Myasthenia Gravis Activities of Daily Living (MG-ADL) score at week 12 ($p<0.001$).[6]

Zilucoplan demonstrated a favorable safety and tolerability profile, 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, and diarrhea. Rates of treatment discontinuation due to a TEAE were low and all patients who completed the 12-week treatment period have entered the ongoing RAISE-XT open-label extension study (NCT04225871).[6,7]

In the RAISE study, 174 adult patients were randomised to receive daily SC, self-administered doses of placebo (N=88) or zilucoplan 0.3 mg/kg (N=86). Patient demographics and baseline disease characteristics were generally balanced between treatment arms.[6]

As a complement C5 inhibitor, zilucoplan is a targeted therapy that inhibits key components in the underlying pathophysiology of gMG, addressing the underlying mechanism of neuromuscular junction damage.[8,9]

"We are deeply committed to improving outcomes for the gMG community. People who live with gMG suffer unpredictable, fluctuating, and debilitating symptoms, which have a huge impact on their lives. We want to help reduce the day-to-day burden of this challenging disease," said Iris Loew-Friedrich, Executive Vice-President and Chief Medical Officer at UCB. *"If approved, zilucoplan has the potential to address the unmet*

need for people with gMG by providing targeted improvements in signs and symptoms of gMG disease activity and severity. A benefit of targeted treatment is that it may help reduce the adverse events that can be associated with non-specific immunosuppressive treatment of gMG."

UCB anticipates making regulatory filings for zilucoplan in gMG in Great Britain, Japan, and rest of the world from Q3 2022 onwards.

Alongside zilucoplan, UCB is also investigating rozanolixizumab, a SC-administered, humanized monoclonal antibody that specifically binds, with high affinity, to human neonatal Fc receptor (FcRn), as a potential treatment for gMG. UCB anticipates filing regulatory submissions for rozanolixizumab later this year.[10]

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About Generalized Myasthenia Gravis (gMG)

Myasthenia gravis is a rare disease impacting more than 700,000 people worldwide.[11] 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.[3, 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.[4, 12] gMG can occur in any race, although previous studies have shown that women are more often impacted than men.[13,14] 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.[15] 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 [6,7]

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 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 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 without rescue therapy, all measured at Week 12. The secondary safety endpoint is incidence of TEAEs. Patients who completed the 12 week RAISE trial had the possibility to enter the open label extension study, RAISE-XT.

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.9 In 2019, the US FDA granted orphan drug designation to zilucoplan for the treatment of myasthenia gravis.[1] Orphan designation was granted in 2022 by the European Commission to zilucoplan for the treatment of myasthenia gravis.[2]

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.[16,15]

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.[17] Orphan designation was granted in 2020[18] by the European Commission for rozanolixizumab to 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, myelin oligodendrocyte glycoprotein antibody-associated disease (MOG-AD) and autoimmune enteropathy (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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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' 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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