UCB announces NAYZILAM® (midazolam) nasal spray now approved by FDA to treat intermittent, stereotypic episodes of frequent seizure activity in people living with epilepsy in the U.S.

- **NAYZILAM® (midazolam) nasal spray* is a nasally administered benzodiazepine indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older.**
- **NAYZILAM allows for administration by a non-healthcare professional in patients actively seizing when and where a seizure cluster occurs.**
- **Approval of NAYZILAM adds to UCB's already existing anti-epilepsy drug portfolio, reinforcing the company's position as a global leader in epilepsy.**

Brussels (Belgium) & Atlanta, Georgia (U.S.) – 0700 CEST May 20 2019: UCB announced today that the U.S. Food and Drug Administration (FDA) has approved a New Drug Application for the company's newest anti-epileptic drug (AED) NAYZILAM® (midazolam) nasal spray CIV, a benzodiazepine indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older[1]. NAYZILAM now provides patients and caregivers with the first and only FDA-approved nasal option for treating seizure clusters.

** NAYZILAM® is Schedule IV Controlled Substance (CIV)*

It is estimated that more than 150,000 people in the U.S. with uncontrolled epilepsy also experience seizure clusters.[2] Rescue treatment of seizure clusters is critical because when left untreated, seizure clusters can increase the risk of physical injury, neurological damage, prolonged seizures, and status epilepticus.[3] Despite the impact of seizure clusters, many diagnosed patients may go untreated because currently available treatment options are not preferred.[4, 5, 6, 7]

NAYZILAM is a short-term treatment for seizure clusters in patients with epilepsy. The nasal spray is designed as a single-use treatment that can be carried with a patient. NAYZILAM allows for administration by a non-healthcare professional in patients actively seizing when and where a seizure cluster occurs. NAYZILAM can provide value to patients who are experiencing these disruptive seizures.

"As global leaders in epilepsy, the approval of NAYZILAM complements our already strong epilepsy portfolio, improving our ability to provide value to people living with poorly controlled seizures, and builds on our passion and expertise in this field. We are pleased to expand and diversify the solutions we can offer to the epilepsy community, providing an innovative and differentiated solution to help support management of seizure clusters," said Jean-Christophe Tellier, Chief Executive Officer, UCB.

NAYZILAM is the first new medication approved to treat seizure clusters in more than 20 years in the U.S. Its nasal delivery could provide significant value to patients who currently have limited treatment options.

"When a patient experiences seizure clusters, there is often significant impact on their overall quality of life, in addition to posing greater risks for increased emergency department related hospitalizations and more serious seizure emergencies," said Dr. Steven S. Chung, MD, Executive Director and Program Chair of the Neuroscience Institute and Director of the Epilepsy Program at Banner – University Medical Center. "Further, as a neurologist specializing in epilepsy, treating seizure clusters today presents a challenging barrier for many patients. The availability of a new treatment option, such as NAYZILAM, has potential to help improve the lives of patients and their families by providing another option for rescue care."

UCB acquired NAYZILAM from Proximagen LLC in June 2018. UCB looks forward to NAYZILAM launching in the U.S. To learn more, go to www.Nayzilam.com.

About NAYZILAM[1]

NAYZILAM® (midazolam) nasal spray CIV is a benzodiazepine indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older.

The effectiveness of NAYZILAM for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older was established in a randomized, double-blind, placebo-controlled trial (Study 1; NCT01390220)[8]. Study 1 enrolled patients with epilepsy on a stable regimen of antiepileptic drugs who were identified by their physicians as having intermittent, stereotypic episodes of frequent seizure activity that were distinct from the patient's usual seizure pattern.

Study 1 was conducted in two phases: an open-label Test Dose Phase followed by a randomized, double-blind, placebo-controlled, Comparative Phase. In the Test Dose Phase, tolerability was assessed in 292 patients who, in the absence of a seizure, received two 5 mg doses of NAYZILAM (10 mg total dosage) separated by 10 minutes. Patients were excluded from participation in the Comparative Phase if they failed to meet pre-defined blood pressure, heart rate, sedation, electrocardiogram, and peripheral oxygen saturation criteria.

In the Comparative Phase, 201 patients treated a single seizure cluster episode in an outpatient setting with either a blinded dose of NAYZILAM 5 mg (134 patients) or placebo (67 patients). If the seizure activity persisted or recurred, patients in both groups had the option to receive a subsequent unblinded dose of NAYZILAM 5 mg to be used between 10 minutes and 6 hours after administration of the initial blinded dose of study drug.

The primary efficacy endpoint for Study 1 was treatment success, defined as the termination of seizures within 10 minutes after the initial blinded dose of study drug and the absence of a recurrence of seizures within 6 hours of the initial blinded dose of study drug. A statistically significantly higher percentage of NAYZILAM-treated patients met the primary efficacy endpoint.

Numerical differences in favor of NAYZILAM were observed on each of the components of the treatment success responder definition; termination of seizure(s) within 10 minutes after initial dose of study drug (80.6 versus 70.1%) and the absence of seizure recurrence between 10 minutes and 6 hours after the initial dose of study drug (58.2 versus 37.3%). The most common adverse reactions (≥5% in any NAYZILAM treatment group) were somnolence, headache, nasal discomfort, throat irritation, and rhinorrhea.

Study 1 also evaluated the occurrence and time to next seizure after the initial blinded dose of study drug. A smaller proportion of NAYZILAM-treated patients experienced the next seizure within 24 hours after the initial blinded dose of study drug (37.3% versus 46.3%). NAYZILAM-treated patients experienced a statistically longer time-to-next-seizure than the placebo group.

About Epilepsy[9, 10, 11. 12]

Epilepsy is a chronic neurological disorder of the brain. It is the fourth most common neurological condition worldwide and affects approximately 65 million people. In the U.S. more than 3.4 million people have epilepsy. Anyone can develop epilepsy; it occurs across all ages, races and genders, and is defined as one or more unprovoked seizures with a risk of further seizures. Around one third of patients with epilepsy currently live with uncontrolled seizures.

About Seizure Clusters

Of the one third of patients living with uncontrolled epilepsy, it is estimated that more than 150,000 people in the U.S. with refractory epilepsy also experience seizure clusters.[2] Seizure clusters are broadly defined as acute episodes of consecutive seizures that occur within a short period of time with a patient regaining consciousness during the interictal period. These clusters are also distinguishable from a person's typical seizure pattern.[2, 13, 14, 15, 16] Other names for seizure clusters include acute-repetitive seizures (ARS), serial seizures, crescendo seizures, and seizure flurries, which highlight the repetitive nature of the seizures.[17] Seizure clusters are a form of seizure emergency that can evolve into prolonged seizures or status epilepticus.[3]

About UCB in Epilepsy

UCB has a rich heritage in epilepsy with over 20 years of experience in the research and development of anti-epileptic drugs. As a company with a long-term commitment to epilepsy research, our goal is to address unmet medical needs. Our scientists are proud to contribute to advances in the understanding of epilepsy and its treatment. We partner and create super-

networks with world-leading scientists and clinicians in academic institutions, pharmaceutical companies, and other organizations who share our goals. At UCB, we are inspired by patients, and driven by science in our commitment to support patients with epilepsy.

Important Safety Information for NAYZILAM[1]

NAYZILAM is indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older.

CONTRAINDICATIONS

NAYZILAM is contraindicated in patients with acute narrow-angle glaucoma.

RISKS FROM CONCOMITANT USE WITH OPIOIDS

Concomitant use of benzodiazepines, including NAYZILAM, and opioids may result in profound sedation, respiratory depression, coma, and death.

- **Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.**
- **Limit dosages and durations to the minimum required.**
- **Follow patients for signs and symptoms of respiratory depression and sedation.**

RISKS OF CARDIORESPIRATORY ADVERSE REACTIONS

Serious cardiorespiratory adverse reactions have occurred after administration of midazolam. Warn patients and caregivers about the risks of respiratory depression, cardiac and respiratory arrest.

Respiratory depression was observed with the administration of NAYZILAM during clinical trials. Cardiac or respiratory arrest caused by NAYZILAM was not reported during clinical trials.

CENTRAL NERVOUS SYSTEM DEPRESSION FROM CONCOMITANT USE WITH OTHER CENTRAL NERVOUS SYSTEM DEPRESSANTS, OR MODERATE OR STRONG CYP3A4 INHIBITORS

Drug products containing midazolam, including NAYZILAM, have a central nervous system (CNS) depressant effect.

Risks from Concomitant Use with Other CNS Depressants

NAYZILAM may cause an increased CNS-depressant effect when used with alcohol or other CNS depressants (e.g., opioids). Warn patients and caregivers that the use of NAYZILAM in combination with alcohol or other CNS depressant drugs may increase the risk of hypoventilation, airway obstruction, desaturation, or apnea and may contribute to profound and/or prolonged drug effect.

Risks from Concomitant Use with Moderate or Strong CYP3A4 Inhibitors

Concomitant use of NAYZILAM with moderate or strong CYP3A4 enzyme inhibitors may result in prolonged sedation because of a decrease in plasma clearance of midazolam. Caution patients against engaging in hazardous occupations requiring mental alertness, such as operating machinery, driving a motor vehicle or riding a bicycle until they have completely returned to their level of baseline functioning.

SUICIDAL BEHAVIOR AND IDEATION

Antiepileptic drugs (AEDs), including NAYZILAM, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Monitor patients treated with NAYZILAM for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Advise patients and caregivers to be alert for these behavioral changes and to immediately report them to the healthcare provider.

IMPAIRED COGNITIVE FUNCTION

Midazolam, including NAYZILAM, is associated with a high incidence of partial or complete impairment of recall for several hours following an administered dose. Counsel patients on when they can engage in activities requiring complete mental alertness, operate hazardous machinery, or drive a motor vehicle after taking NAYZILAM.

GLAUCOMA

Benzodiazepines, including NAYZILAM, can increase intraocular pressure in patients with glaucoma. NAYZILAM may be used in patients with open-angle glaucoma only if they are receiving appropriate therapy. NAYZILAM is contraindicated in patients with narrow-angle glaucoma.

ADVERSE REACTIONS

In the randomized, double-blind, placebo-controlled trial, the most common adverse reactions (⩾ 5% in any NAYZILAM treatment group) were somnolence, headache, nasal discomfort, throat irritation, and rhinorrhea.

NAYZILAM is a Schedule IV controlled substance.

Please refer to the full Prescribing Information at www.Nayzilam.com.

For additional medical information about NAYZILAM, patient assistance, or any other information please visit our website or call ucbCARES at 1-844-599-2273.

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For further information:

Corporate Communications

France Nivelle
Global Communications, UCB
T+32.2.559.9178,
France.nivelle@ucb.com

Jim Baxter
Neurology Communications, UCB
T+32.2.473.78.85.01,
jim.baxter@ucb.com

Laurent Schots
Media Relations, UCB
T+32.2.559.92.64,
laurent.schots@ucb.com

Investor Relations

Antje Witte,
Investor Relations, UCB
T+32.2.559.94.14,
antje.witte@ucb.com

Isabelle Ghellynck,
Investor Relations, UCB
T +32.2.559.9588,
isabelle.ghellynck@ucb.com

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 in immunology or neurology. With around 7 500 people,

operating in 40 countries, the company generated revenue of € 4.6 billion in 2018. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCBUSA

Forward looking statements
This press release contains forward-looking statements based on current plans, estimates and beliefs of management. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, political, regulatory or clinical results and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and assumptions which could cause actual results to differ materially from those that may be implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: changes in general economic, business and competitive conditions, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms, 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, product liability claims, challenges to patent protection for products or product candidates, 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.

Additionally, information contained in this document shall not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any offer, solicitation or sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of such jurisdiction. UCB is providing this information as of the date of this document and expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report a change in its expectations.

There is no guarantee that new product candidates in the pipeline will progress to product approval or that new indications for existing products will be developed and approved. Products or potential products which are the subject of partnerships, joint ventures or licensing collaborations may be subject to differences between the partners. Also, UCB or others could discover safety, side effects or manufacturing problems with its products after they are marketed.

Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement.

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