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News Release

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Bayer starts Phase II study NIRVANA to evaluate elinzanetant in women with sleep disturbances associated with menopause

- New Phase II study NIRVANA aims to explore efficacy and safety of investigational compound elinzanetant as a non-hormonal treatment for sleep disturbances associated with menopause (SDM)
- SDM may have an impact on women's quality of life, work productivity as well as their physical and mental wellbeing
- The new Phase II study expands upon the ongoing clinical development program of elinzanetant, an investigational first dual neurokinin-1,3 (NK-1, 3) receptor antagonist

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Berlin, January 8, 2024 – Bayer, a global leader in women's healthcare, announced today the expansion of the clinical development program for the investigational compound elinzanetant. The first study participants were recently enrolled into NIRVANA, an exploratory Phase II study to evaluate the efficacy and safety of elinzanetant in women with sleep disturbances associated with menopause (SDM).

Together with vasomotor symptoms (also known as VMS or hot flashes) and mood symptoms, sleep disturbances belong to the most frequent and disruptive symptoms associated with menopause.[1] Approximately 40% to 60% of women experience sleep disturbances during the menopausal transition, which may include trouble falling asleep or staying asleep potentially causing a negative impact on women's quality of life and limit their daily activities, including performance at work. [2,3] SDM may also be associated with negative effects on metabolism, body fat gain, poor cardiovascular health in later life, cognitive health decline, and depressive symptoms.[4,5] Current treatments do not specifically target sleep disturbances associated with menopause.

"By adding NIRVANA to our broad clinical development program, we are further exploring the potential of elinzanetant to address sleep disturbances associated with menopause,

an area of important unmet need in women's health," said Dr. Christian Rommel, member of the Executive Committee of Bayer AG's Pharmaceutical Division and Global Head of Research and Development.

"Sleep is an incredibly complex aspect of health and the human experience, and unfortunately, its importance is often underestimated and undervalued – for those experiencing menopause this is especially the case," said Hadine Joffe, M.D., M.Sc, Professor of Psychiatry in the Field of Women's Health based at Brigham and Women's Hospital in Boston, an experienced psychiatrist and sleep researcher in women's mental health..

The NIRVANA Phase II trial is a multi-center, double-blind, randomized, parallel-group, placebo-controlled interventional study. It is intended to randomize approximately 78 participants in eight countries to investigate the efficacy and safety of elinzanetant in women with sleep disturbances associated with menopause (SDM). The primary endpoint for the NIRVANA study is the efficacy of elinzanetant on Wakefulness After Sleep Onset (WASO) at week 4 as measured by polysomnography.

Additionally, Bayer announced positive topline results of the pivotal Phase III studies OASIS 1 and 2 evaluating the efficacy and safety of the investigational compound elinzanetant for the treatment of moderate to severe VMS associated with menopause versus placebo. Elinzanetant successfully met all four primary endpoints in both studies demonstrating statistically significant reductions in the frequency and severity of moderate to severe vasomotor symptoms (VMS, also known as hot flashes) from baseline to week 4 and 12 compared to placebo. Both studies also achieved all three key secondary endpoints showing a statistically significant reduction in the frequency of VMS from baseline to week 1, as well as statistically significant improvements in sleep disturbances and menopause-related quality of life compared to placebo. The safety profile observed in the OASIS 1 and 2 studies is overall consistent with previously published data[2,6] on elinzanetant.

About the NIRVANA Study

NIRVANA is an exploratory Phase II randomized, parallel-group treatment, double-blind study. The primary objective is to explore the efficacy of elinzanetant on sleep disturbances associated with menopause (SDM) as determined by polysomnography (PSG). PSG is a validated method to study sleep and underlying causes of sleep disturbances. Additional

objectives include exploring the efficacy of elinzanetant on SDM as determined by patient-reported outcomes and evaluating the safety of elinzanetant for the treatment of SDM. More information can be found at https://clinicaltrials.gov/study/NCT06112756.

The Phase II study NIRVANA is based on improvements in sleep disturbances observed in the Phase IIb study SWITCH-1, which investigated the efficacy and safety of four different doses of elinzanetant compared to placebo in women with moderate to severe vasomotor symptoms associated with menopause. It also indicated improvements in sleep disturbances as assessed by the global Pittsburgh Sleep Quality Index (PSQI) and the total Insomnia Severity Index (ISI) scores with elinzanetant 120 mg once daily compared to placebo. Full results have been published in March 2023 in Menopause - The Journal of the Menopause Society.[2]

About the OASIS Clinical Development Program

The Phase III clinical development program of elinzanetant, OASIS, currently comprises four Phase III studies: OASIS 1, 2, 3 and 4. The OASIS 1, 2 and 3 studies investigate the efficacy and safety of elinzanetant 120 mg in women with moderate to severe VMS associated with menopause. The OASIS 4 study is an expansion of the clinical phase III program and investigates the efficacy and safety of elinzanetant in women with moderate to severe VMS caused by endocrine therapy for treatment or prevention of breast cancer.

The design and dosing of the Phase III clinical development program is based on the positive data from two Phase II studies (RELENT-1 and SWITCH-1). RELENT-1 was a Phase Ib/IIa study investigating the safety, pharmacokinetics and preliminary efficacy of elinzanetant. SWITCH-1 was a Phase IIb study investigating the efficacy and safety of four different doses of elinzanetant compared to placebo in women with VMS.

About Elinzanetant

Elinzanetant is a first dual neurokinin-1,3 (NK-1,3) receptor antagonist, in late-stage clinical development for the non-hormonal treatment of moderate to severe VMS associated with menopause, administered orally once daily. Elinzanetant may address moderate to severe VMS by modulating a group of estrogen sensitive neurons in the hypothalamus region of the brain (the KNDy neurons) which, with the decrease of estrogen, become hypertrophic and lead to a hyperactivation of the thermoregulatory pathway, consequently disrupting body heat control mechanisms resulting in VMS. Elinzanetant may also decrease sleep disturbances associated with menopause.

About Menopause

By 2030, the world population of women experiencing menopause is projected to increase to 1.2 billion, with 47 million new women entering this phase each year.[7] Menopause is a transitional phase in women's lives, related to the progressive decline of ovarian function, and which usually occurs in women during their 40s or early 50s. It can also be the result of surgical or medical treatment, for example breast cancer treatment. The hormonal decline can lead to various symptoms which can substantially affect a woman's health, quality of life, healthcare utilization and work productivity. The most frequently reported and disruptive symptoms during the menopausal transition are VMS, sleep disturbances and mood changes. Addressing these symptoms is key to maintaining functional ability and quality of life in menopause which is highly relevant from both a healthcare and socio-economic perspective.

About Women's Healthcare at Bayer

Women's Health is in Bayer's DNA and as a global leader in women's healthcare Bayer has a long-standing commitment to delivering science for a better life by advancing a portfolio of innovative treatments. Bayer offers a wide range of effective short- and long-acting birth control methods as well as therapies for menopause management and gynecological diseases. Bayer is also focusing on innovative options to address the unmet medical needs of women worldwide and to broadening treatment choices such as in the area of menopause. Additionally, Bayer intends to provide 100 million women per year in low-and-middle income countries by 2030 with access to family planning by funding multi-stakeholder aid programs and by ensuring the supply of affordable modern contraceptives. This is part of the comprehensive sustainability measures and commitments from 2020 onwards and in line with the Sustainable Development Goals of the United Nations.

About Bayer

Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. Its products and services are designed to help people and the planet thrive by supporting efforts to master the major challenges presented by a growing and aging global population. Bayer is committed to driving sustainable development and generating a positive impact with its businesses. At the same time, the Group aims to increase its earning power and create value through innovation and growth. The Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2022, the Group employed

around 101,000 people and had sales of 50.7 billion euros. R&D expenses before special items amounted to 6.2 billion euros. For more information, go to www.bayer.com.

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