Press Release

Astellas' Fezolinetant Reduces Frequency and Severity of VMS Associated with Menopause in Women Considered Unsuitable for Hormone Therapy

Phase 3b DAYLIGHT study being presented at ESG 2023 demonstrated fezolinetant 45 mg achieved statistically significant reductions in the frequency and severity of moderate to severe vasomotor symptoms due to menopause and patient-reported sleep disturbance at 24 weeks

Women considered unsuitable included those with contraindications, who are averse to taking, have stopped taking or have conditions that suggest caution in using hormone therapy

Results will support health technology assessment and reimbursement dossiers throughout Europe

TOKYO, November 30, 2023 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, "Astellas") will present 24-week results from the Phase 3b DAYLIGHT clinical trial examining the efficacy and safety of fezolinetant, an investigational oral, nonhormonal compound being studied for the treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause in women considered unsuitable for hormone therapy, in an oral presentation on November 30 at the 15th Congress of the European Society of Gynecology in Amsterdam, The Netherlands (Abstract #12497). VMS, characterized by hot flashes and/or night sweats, are common symptoms of menopause.[1,2]

The study of more than 450 women considered unsuitable for hormone therapy met all primary and secondary endpoints at 24 weeks.

- For the primary endpoint of mean change from baseline in the frequency of moderate to severe VMS, fezolinetant 45 mg demonstrated a statistically significant reduction of -1.93 ($p<0.001$) compared to placebo.
- For the key secondary endpoint of mean change from baseline in the severity of moderate to severe VMS, fezolinetant 45 mg demonstrated a statistically significant reduction of -0.39 ($p<0.001$) compared to placebo.
- For the secondary endpoint of mean change from baseline in patient-reported sleep disturbance, fezolinetant 45 mg demonstrated a statistically significant reduction of -2.5 ($p<0.001$) compared to placebo.

Treatment-emergent adverse events (TEAEs) were reported by 65% of patients in the fezolinetant group compared to 61% in the placebo group. The most common TEAEs were COVID-19 (13.3% for fezolinetant vs. 12.8% for placebo), headache (8.8% for fezolinetant vs. 9.3% for placebo) and fatigue (5.8% for fezolinetant vs. 0.4% for placebo). Serious TEAEs occurred in 4.4% of patients in the fezolinetant group and 3.5% of patients in the placebo group.

Prof. Rossella Nappi, Full Professor of Obstetrics and Gynecology, Chief of the Research Center for Reproductive Medicine and Director of the Gynecological Endocrinology & Menopause Unit, IRCCS San Matteo Foundation, University of Pavia
"I know many women want options for managing hot flashes based on their medical history and personal choices, which is why these DAYLIGHT results are encouraging. The statistically significant reductions observed over the 24-week period demonstrate the potential fezolinetant has to help women who are experiencing VMS due to menopause yet cannot or choose not to take hormone therapy."

Marci English, Vice President, Head of BioPharma Development, Astellas
"DAYLIGHT is the first 24-week placebo-controlled efficacy study for fezolinetant. Astellas is committed to advancing innovative science, and these data provide further affirmation to healthcare providers of the positive impact fezolinetant can have on reducing the frequency and severity of VMS, as well as sleep disturbances over a longer period of time."

About DAYLIGHT
DAYLIGHT (NCT05033886) is a Phase 3b, randomized, double-blind, placebo-controlled, 24-week study to assess the efficacy and safety of fezolinetant 45 mg in menopausal women aged 40-65 suffering from moderate to severe VMS and considered unsuitable for hormone therapy (HT): contraindicated, averse (made informed choice not to take HT), stoppers (previously discontinued HT) and caution (based on prior medical history). The primary endpoint was mean change in the frequency of moderate to severe VMS from baseline to week 24. Secondary endpoints were mean change in severity of moderate to severe VMS from baseline to week 24 and mean change in patient-reported sleep disturbance on the Patient-Reported Outcomes Measurement Information System Sleep Disturbance (PROMIS SD) – Short Form 8b from baseline to week 24. A total of 453 women were enrolled at 69 sites in Canada, Europe and Turkey. Topline results of the DAYLIGHT study were announced in June 2023.

About Fezolinetant
Fezolinetant is an investigational oral, nonhormonal medicine in clinical development for the treatment of moderate to severe VMS associated with menopause. VMS are also known as hot flashes or night sweats. Fezolinetant works by blocking neurokinin B (NKB) binding on the kisspeptin/neurokinin/dynorphin (KNDy) neuron, helping restore the balance in the brain's temperature control center (the hypothalamus) to reduce the number and intensity of hot flashes and night sweats.[3,4,5] There is no guarantee the agent will receive regulatory approval in Europe or become commercially available for the uses being investigated.

About Astellas
Astellas Pharma Inc. is a pharmaceutical company conducting business in more than 70 countries around the world. We are promoting the Focus Area Approach that is designed to identify opportunities for the continuous creation of new drugs to address diseases with high unmet medical needs by focusing on Biology and Modality. Furthermore, we are also looking beyond our foundational Rx focus to create Rx+® healthcare solutions that combine our expertise and knowledge with cutting-edge technology in different fields of external partners. Through these efforts, Astellas stands on the forefront of healthcare change to turn innovative science into VALUE for patients. For more information, please visit our website at https://www.astellas.com/en.

Cautionary Notes
In this press release, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas' intellectual property rights by third parties. Information about pharmaceutical products (including products currently in development) which is included in this press release is not intended to constitute an advertisement or medical advice.

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References

[1] Utian WH. Psychosocial and socioeconomic burden of vasomotor symptoms in menopause: a comprehensive review. Health Qual Life Outcomes. 2005;3:47.

[2] Jones RE, Lopez KH, eds. *Human Reproductive Biology*. 4th ed. Waltham, MA: Elsevier, 2014:120.

[3] Depypere H, Timmerman D, Donders G, et al. Treatment of menopausal vasomotor symptoms with fezolinetant, a neurokinin 3 receptor antagonist: a phase 2a trial. *J Clin Endocrinol* Metab. 2019;104:5893-5905.

[4] Fraser GL, Lederman S, Waldbaum A, et al. A phase 2b, randomized, placebo-controlled, double-blind, dose-ranging study of the neurokinin 3 receptor antagonist fezolinetant for vasomotor symptoms associated with menopause. *Menopause.* 2020;27:382-392.

[5] Fraser GL, Hoveyda HR, Clarke IJ, et al. The NK3 receptor antagonist ESN364 interrupts pulsatile LH secretion and moderate levels of ovarian hormones throughout the menstrual cycle. *Endocrinology.* 2015;156:4214-4225.