Press Release

Astellas Presents Fezolinetant Phase 2b Clinical Trial Results at Endocrine Society's Annual Meeting (ENDO)

- Investigational compound fezolinetant reduced frequency and severity of vasomotor symptoms in postmenopausal women -

TOKYO, March 26, 2019 - Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced results from a Phase 2b dose-finding study of fezolinetant, presented in an oral session (Abstract OR33-6) at ENDO 2019, the Endocrine Society's annual meeting in New Orleans. Fezolinetant, a selective neurokinin-3 (NK3) receptor antagonist, is an investigational oral, non-hormonal compound being studied for the treatment of vasomotor symptoms (VMS) – i.e., hot flashes and night sweats – in postmenopausal women. The study met the four FDA-recommended co-primary endpoints of mean decrease in frequency and mean decrease in severity of VMS at both week 4 and week 12 in most groups.

"Vasomotor symptoms can significantly impact a woman's quality of life and there are currently limited non-hormonal options for managing them," said Arthur Waldbaum, M.D., a gynecologist in Denver, Colo., specializing in women's health, and lead investigator for the Phase 2b study. "The study findings presented at ENDO are promising as they suggest that fezolinetant may have the potential to address these symptoms as early as one week."

In the Phase 2b study, 356 women were randomized to receive either placebo or fezolinetant doses ranging from 15 – 90 mg twice daily (BID) or 30 – 120 mg once daily (QD).

Most groups were statistically significant from placebo in mean change in the frequency and severity of moderate-to-severe VMS at both week 4 and week 12. Results were maintained throughout the 12-week treatment period, with a return to baseline once treatment was stopped.

"We are encouraged by these results showing fezolinetant to be a potential non-hormonal therapeutic agent for women living with moderate-to-severe hot flashes," said Salim Mujais, M.D., Senior Vice President and Therapeutic Area Head, Medical Specialties, Astellas. "Further, these results suggest once-daily dosing – including the lower doses – produced similar reductions in severity and frequency of VMS to the twice-daily dosing. We look forward to studying fezolinetant in Phase 3 clinical trials, scheduled to begin later this year."

Fezolinetant significantly reduced VMS frequency compared to placebo, showing between -1.9 to -3.5 mean change per day from baseline for the BID doses and between -2.3 to -3.0 mean change per day for the QD doses at week 4. At week 12, fezolinetant demonstrated reduced VMS frequency compared to placebo, showing

between -1.8 to -2.6 mean change per day for the BID doses and between -2.1 to -2.6 mean change per day for the QD doses. The percentage reduction in VMS frequency from baseline to week 12 was between 74.3 to 86.9 percent for the BID doses and between 75.1 to 77.9 for the QD doses versus a 55 percent reduction for placebo.

Additionally, fezolinetant showed improvement in VMS severity compared to placebo, with a mean change per day range of -0.5 to -1.0 for the BID doses and -0.4 to -0.7 for the QD doses at week 4. At week 12, fezolinetant demonstrated improvement in VMS severity compared to placebo, with a mean change per day range of -0.3 to -0.6 for the BID doses and -0.2 to -0.5 for the QD doses.

Overall treatment-emergent adverse event (TEAE) rates were similar across groups and mostly mild or moderate. There were no deaths or treatment-related serious adverse events (SAEs) reported. Common TEAEs (greater or equal to 5 percent in any treatment arm) include headache, nausea, urinary tract infection, diarrhea, upper respiratory tract infection, fatigue, viral upper respiratory tract infection, sinusitis and cough. There were no reports of endometrial hyperplasia. Nine patients (less than 3 percent) treated with the higher doses of fezolinetant saw brief increases in the liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST). There were no cases of bilirubin greater than two times the upper limit of normal. Patients returned to baseline levels after discontinuation of dosing. No other clinically meaningful changes were noted in the vital signs and laboratory tests, electrocardiogram parameters, or plasma bone marker concentrations.

About Fezolinetant
Fezolinetant is an investigational oral, non-hormonal compound being developed for the treatment of moderate-to-severe VMS, including hot flashes and night sweats. Fezolinetant works by blocking neurokinin B (NKB) signaling and normalizing KNDy (kisspeptin/NKB/dynorphin) neuron activity, which modulates the temperature control center and reduces the frequency and severity of hot flashes.

About Vasomotor Symptoms (VMS)
Globally, approximately 57 percent of women 40 to 64 years of age have reported the occurrence of hot flashes and sweating.[1] VMS can have a considerable effect on women's comfort and sleep and can lead to anxiety, irritability, loss of productivity and depression.[2] Hot flashes are also the most common symptom for women transitioning through menopause.[3]

About the Phase 2b study
The Phase 2b study is a randomized, double-blind, placebo-controlled, dose-ranging study. The study enrolled postmenopausal women 40 to 65 years of age suffering at least 50 moderate-to-severe hot flashes per week. In the study, 356 women were randomized to one of the following doses: fezolinetant 15, 30, 60 or 90 mg twice daily or 30, 60, 120 mg once daily. For more information about this study, visit www.clinicaltrials.gov [NCT03192176].
The safety and efficacy of the agent discussed herein are under investigation and have not been established. There is no guarantee that the agent will receive regulatory approval and become commercially available for the uses being investigated.

About Astellas
Astellas Pharma Inc., based in Tokyo, Japan, is a company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. 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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