Press Release

Astellas Analysis Shows No Evidence of Increased Risk of Cardiovascular Events or Mortality with Roxadustat Compared with Erythropoiesis-Stimulating Agents (ESAs) at 59th ERA Congress 2022

Pooled Phase 3 data for anemia of CKD patients, incident dialysis or not receiving dialysis from the ALPINE Phase 3 clinical trial program

TOKYO, May 19, 2022 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced results from a pooled analysis of patients with symptomatic anemia associated with chronic kidney disease (CKD) who are non-dialysis-dependent (NDD) and incident dialysis-dependent (IDD) from four Phase 3 studies evaluating the safety and efficacy of EVRENZO™ (roxadustat). These data presented during a mini-oral session at the 59th European Renal Association (ERA) Congress, taking place between May 19–22, 2022, showed no evidence of an increased risk of cardiovascular events or mortality with roxadustat compared with standard of care, erythropoiesis-stimulating agents (ESAs).

Roxadustat was non-inferior to ESA for risk of a major adverse cardiovascular event (MACE) (95% confidence interval [CI]: 0.61, 1.02) and a major adverse cardiovascular event plus congestive heart failure or unstable angina requiring hospitalization (MACE+) (95% CI: 0.62, 0.98) with a consistent finding for all-cause mortality (ACM) (95% CI: 0.57, 1.05). Hazard ratios for MACE, MACE+ and ACM vs ESA were 0.79, 0.78 and 0.78, respectively, favoring roxadustat. Although treatment-emergent adverse events occurred commonly in both the roxadustat and ESA groups, patients rarely discontinued either study drug because of an adverse event.

"I've seen first-hand the effect anemia can have on those living with CKD, and it impacts almost every aspect of their daily lives," said Professor Jonathan Barratt, Ph.D., FRCP, Consultant Nephrologist at the University of Leicester, United Kingdom. "I'm pleased to present these data which demonstrate that, as an alternative oral treatment that controls anemia with a reduced need for IV iron compared to standard of care, roxadustat has the potential to alleviate the burden many living with this condition have – with no risk of increase in cardiovascular events or mortality when compared with the existing standard of care."

As a first-in-class orally administered inhibitor of hypoxia-inducible factor prolyl hydroxylase (HIF-PH), roxadustat increases hemoglobin levels with a mechanism of action that is different from that of ESAs. Roxadustat activates the body's natural protective response to reduced oxygen levels in the blood. This response involves the regulation of multiple, complementary processes that promote a coordinated erythropoietic response and increase the blood's oxygen-carrying capacity.

"Astellas is dedicated to addressing unmet medical needs and providing innovative solutions in nephrology," said Ahsan Arozullah, Senior Vice President and Head of Development Therapeutic Areas, Astellas. "These data presented today add to the extensive clinical

evidence available for roxadustat and provide further assurance to the nephrology community of the positive impact roxadustat can have for patients with symptomatic anemia associated with CKD."

Additional Astellas mini-oral presentations at the 59th ERA Congress 2022 include:

Title: Cardiovascular Safety of Roxadustat Versus Erythropoiesis-Stimulating Agents for Treatment of Anemia in Patients With Chronic Kidney Disease Incident to or Not Receiving Dialysis: Pooled subgroup Analysis of Four Phase 3 Studies (Abstract 2379)

Presenter: Jonathan Barratt, University of Leicester, United Kingdom

Title: Iron Parameters in Patients Treated With Roxadustat for Anemia Associated With Chronic Kidney Disease: Post Hoc Analysis of the Non-Dialysis-Dependent or Incident Dialysis Population From Four Phase 3 Studies (Abstract 1008)

Presenter: Luca De Nicola, University of Campania, Naples, Italy

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About the Pooled Phase 3 Studies (Abstract 631)
Safety results from eligible patients with anemia of CKD enrolled in four Phase 3, randomized, open-label studies (NDD [DOLOMITES] or ID-DD [SIERRAS, HIMALAYAS, ROCKIES]) were pooled and compared roxadustat with an ESA. In total, 2,142 patients were evaluated (1,083 roxadustat; 1,059 ESA; 616 NDD; 1,526 ID-DD) and the majority of patients were ESA-untreated at baseline.

About CKD and Anemia of CKD
CKD is a progressive disease characterized by gradual loss of kidney function that may eventually lead to kidney failure or end-stage renal disease, requiring dialysis or kidney transplant.[1] Many patients with CKD die of cardiovascular complications before progressing to kidney failure and as such the prevalence of early kidney disease is much greater than end-stage disease.[1,2] CKD impacts one in 10 people globally and is predicted to become the fifth most common cause of premature death globally by 2040.[3,4]

Anemia, a serious medical condition in which patients have insufficient red blood cells and low levels of hemoglobin, is a common complication that can be observed during CKD progression, affecting approximately 20% of CKD patients.[5,6] Anemia of CKD is associated with an increased risk of hospitalization, cardiovascular complications and death, and can also cause significant fatigue, cognitive dysfunction and reduced quality of life.[7,8] ESAs and blood transfusions are used for treating severe anemia, however, they may reduce a patient's opportunity for kidney transplant and can increase the risk of infection and/or complications such as heart failure and allergic reactions.[9,10]

About Roxadustat
Roxadustat, an oral medicine, is the first in a new class of medicines, HIF-PH inhibitors, that promote erythropoiesis, or red blood cell production, through increased endogenous production of erythropoietin; improved iron absorption and mobilization; and downregulation of hepcidin. Roxadustat is also in Phase 3 clinical development for anemia associated with myelodysplastic syndromes and Phase 2 for chemotherapy-induced anemia.

Roxadustat is approved in EU member states, including the European Economic Area countries, as well as in Great Britain, Japan, Kuwait, United Arab Emirates, Russia, China, Chile, and South Korea for the treatment of anemia of CKD in adult patients on dialysis and not on dialysis. Several other licensing applications for roxadustat have been submitted by Astellas and AstraZeneca to regulatory authorities across the globe and are currently in review.

Astellas and FibroGen are collaborating on the development and commercialization of roxadustat for the potential treatment of anemia of CKD in territories including Japan, Europe, Turkey, Russia and the Commonwealth of Independent States, the Middle East, and South Africa. FibroGen and AstraZeneca are collaborating on the development and commercialization of roxadustat for the potential treatment of anemia of CKD in the US, China, other markets in the Americas, in Australia/New Zealand and Southeast Asia.

Important Safety Information
The full European Summary of Product Characteristics (SPC/SmPC) for roxadustat will be available from the European Medicines Agency at https://www.ema.europa.eu/en/documents/product-information/evrenzo-epar-product-information_en.pdf.[11]

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.

Astellas 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) that is included in this press release is not intended to constitute an advertisement or medical advice.

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