Press Release

Roxadustat Demonstrates Non-Inferiority to Darbepoetin in Phase 3 DOLOMITES Study of Anemia in Non-Dialysis-Dependent Adult Patients with Chronic Kidney Disease

- Study meets primary endpoint demonstrating non-inferiority of roxadustat to darbepoetin in correction and maintenance of hemoglobin levels

- Findings presented today in oral session at the European Renal Association-European Dialysis and Transplant Association Virtual Congress 2020

TOKYO, June 8, 2020 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced results from the Phase 3 DOLOMITES study, evaluating the efficacy and safety of roxadustat compared with darbepoetin alfa for the treatment of anemia in non-dialysis dependent (NDD) adult patients with stage 3–5 chronic kidney disease (CKD) (Abstract: MO001). The data presented during an oral presentation at the 57th European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Virtual Congress, taking place between June 6–9, 2020, showed non-inferiority of roxadustat to darbepoetin alfa in the correction of hemoglobin levels during the first 24 weeks of treatment (89.5% vs 78.0%; a difference of 11.51% [95% confidence interval (CI): 5.66%, 17.36%]), meeting the study's primary endpoint with a lower bound of the 95% CI >0.

Secondary endpoints were hierarchically tested for non-inferiority and superiority. Superiority of roxadustat to darbepoetin alfa was demonstrated by a decrease in low-density lipoprotein cholesterol with a least square mean (LSM) difference of -0.403 mmol/L (95% CI: -0.510, -0.296; [P<0.01]) and in time to first intravenous iron use with a hazard ratio (HR) of 0.45 (95% CI: 0.26, 0.78; [P=0.004]). The non-inferiority of roxadustat to darbepoetin alfa was demonstrated for mean arterial pressure with a LSM difference of -0.372 mmHg (95% CI: -1.587, 0.842) and time to occurrence of hypertension (HR=0.83; [95% CI: 0.56, 1.22]). Regarding safety, the overall incidence of treatment emergent adverse events was comparable between roxadustat and darbepoetin alfa (91.6% and 92.5%, respectively). A non-confirmatory analysis of adjudicated major adverse cardiovascular event (MACE)/MACE plus hospitalized unstable angina and

hospitalized congestive heart failure (MACE+) outcomes showed HR point estimates of 0.81 (95% CI: 0.52, 1.25) and 0.90 (95% CI: 0.61, 1.32).

“The goal of treatment for anemia in CKD is to raise and stabilize hemoglobin levels, yet as many as half of CKD anemia patients have hemoglobin levels outside the recommended target values, often leaving them with debilitating symptoms that can make daily activities extremely challenging,” said Jonathan Barratt, Ph.D., FRCP, Consultant Nephrologist and the Mayer Professor of Renal Medicine at the University of Leicester, United Kingdom. “The DOLOMITES study results demonstrate the ability of roxadustat to correct and maintain hemoglobin levels in people with CKD anemia not on dialysis for up to 2 years.”

As a first-in-class orally administered inhibitor of hypoxia-inducible factor (HIF) prolyl hydroxylase (PH), roxadustat increases hemoglobin levels with a mechanism of action that is different from that of erythropoiesis-stimulating agents (ESAs). As a HIF-PH inhibitor, 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 erythropoiesis and increase the blood’s oxygen-carrying capacity.

“The DOLOMITES study data add to the body of evidence supporting the efficacy of roxadustat in adult CKD patients with anemia who are not dialysis dependent, this time versus an active comparator, darbepoetin,” said Bernhardt G Zeiher, M.D., Chief Medical Officer, Astellas. “This study, designed to assess the novel mechanism of action of roxadustat in correcting and maintaining hemoglobin levels, reinforces Astellas’ commitment to turning innovative science into value for patients and addressing the unmet medical needs of people living with CKD and the added complication of anemia.”

Astellas presentations at the ERA-EDTA Virtual Congress 2020 include:

Title: Roxadustat for the Treatment of Anaemia in Chronic Kidney Disease Patients Not on Dialysis: A Phase 3, Randomised, Open-Label, Active-Controlled Study (Abstract MO001)

Presenter: Dr. Jonathan Barratt, University of Leicester, United Kingdom

- Session date/time: Monday, June 8, 8:54–9:07 a.m. CET

Title: Ophthalmological Effects of Roxadustat in the Treatment of Anaemia in Chronic Kidney Disease Patients on Dialysis in a Phase 3, Randomised, Double-Blind, Active-Comparator Conversion Study (Abstract MO002)

Presenter: Dr. Yasir J. Sepah, Ocular Imaging Research and Reading Center, Sunnyvale, CA and Byers Eye Institute, Stanford School of Medicine, CA

- Session date/time: Monday, June 8, 9:07–9:17 a.m. CET

Title: Effect of Severe Renal Impairment or End-Stage Renal Disease on the Pharmacokinetics and Pharmacodynamics of Roxadustat, an Oral Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitor (Abstract SO052)

Presenter: Dorien Groenendaal-van de Meent, Astellas Pharma Europe B.V.

- Session date/time: Sunday, June 7, 3:57–4:07 p.m. CET

Title: A Qualitative Study of Patients' Preference for the Treatment of Anaemia Associated With Chronic Kidney Disease (Abstract P0865)

- Available to view on the ERA-EDTA Virtual Congress website starting Saturday, June 6

About the DOLOMITES Trial (Abstract MO001)

DOLOMITES is a Phase 3, randomized, open-label, active-controlled study to evaluate the efficacy and safety of roxadustat in comparison to darbepoetin alfa in the treatment of anemia in adult NDD CKD patients. The study enrolled 616 adult anemia patients with stage 3-5 CKD, of which 323 received roxadustat and 293 received darbepoetin alfa. The response in correction of hemoglobin levels was defined as achieving Hb≥11g/dL and Hb change from BL of ≥1g/dL if the BL Hb>8g/dL, and the change from BL in Hb levels of ≥2g/dL if the BL Hb≤8g/dL. For more information about this study, visit www.clinicaltrials.gov [NCT02021318].[1]

About CKD and Anemia

CKD is characterized by a progressive loss of kidney function caused by damage to the kidneys resulting from conditions such as hypertension, diabetes or immune-regulated inflammatory conditions.[2] Worldwide 1 in 10 people are living with CKD.[3] In Europe, 1 in 8 people are living with CKD,[3] of whom 1 in 5 are affected by anemia; this rate increases to 1 in 2 in people with the most severe CKD (CKD stage 5).[4] Globally, CKD is predicted to become the fifth most common cause of premature death by 2040.[5] It is a critical worldwide healthcare issue that represents a large and growing unmet medical need.

Anemia is a common complication of CKD,[6] resulting from the failing kidneys' ability to produce erythropoietin, reduced oxygen sensing, and increased hepcidin and iron deficiency resulting from chronic inflammation. It is associated with significant morbidity and mortality in dialysis and non-dialysis populations, increasing in both prevalence and severity as kidney disease worsens.[7] CKD

anemia increases the risk of adverse cardiovascular events, worsens renal outcomes and can negatively impact patients' quality of life.[8-10]

About Roxadustat

Roxadustat is approved and launched for the treatment of anemia associated with CKD in Japan in dialysis dependent (DD) patients and in China in both DD and NDD patients. A supplemental New Drug Application (sNDA) has been submitted in Japan for NDD patients and a New Drug Application (NDA) has been filed for the FDA review in the U.S. in both DD and NDD patients. In the EU, a marketing authorization application for roxadustat has been accepted for regulatory review for both DD and NDD patients.

Astellas and FibroGen are collaborating on the development and commercialization of roxadustat for the potential treatment of anemia in territories including Japan, Europe, 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 in the U.S., China and other markets in the Americas and in Australia/New Zealand as well as Southeast Asia.

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 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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Contacts for inquiries or additional information:

Astellas Portfolio Communications
Anna Otten
TEL: +1 (224) 205-6651 | Email: anna.otten@astellas.com

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