Press Release

Launch of Evrenzo® (roxadustat) Tablets in Japan for the Treatment of Renal Anemia in Patients on Dialysis

- First-in-Class Orally Administered HIF-PH Inhibitor -

TOKYO, November 20, 2019 - Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced launch of Evrenzo® Tablet 20mg, 50mg and 100mg (generic name: roxadustat) in Japan, an oral HIF-PH (hypoxia-inducible factor prolyl hydroxylase) inhibitor, for the treatment of renal anemia in patients on dialysis.

Evrenzo® is a first-in-class orally administered HIF-PH inhibitor that corrects anemia by a mechanism of action that is different from that of erythropoiesis-stimulating agents (ESAs). Evrenzo® activates a response that occurs naturally when the body responds to reduced oxygen levels in the blood. The response activated by Evrenzo® involves the regulation of multiple, complementary processes to promote erythropoiesis and increase the blood's oxygen-carrying capacity.

Astellas has been developing roxadustat in collaboration with FibroGen, Inc. (Nasdaq: FGEN) under the license agreement. In Japan, the clinical development for roxadustat is being conducted by Astellas, and roxadustat is currently in Phase 3 for renal anemia in patients not on dialysis in addition to the approved indication of renal anemia in patients on dialysis.

Anemia is a frequent complication of chronic kidney disease (CKD), occurring in over 90% of patients on dialysis.[1] The number of patients on dialysis in Japan is increasing year by year and exceeded 330,000 in 2017.[2] CKD anemia can severely worsen the outcomes of kidney disease, increasing the rate of progression to renal failure[3] and the likelihood of cardiovascular complications.[4] It also significantly reduces patients' quality of life and their cognitive ability.[5]

By offering Evrenzo® in Japan as a new treatment option, Astellas will continue to contributing to treatment of renal anemia where unmet needs still remain.

Important Product Information

PRODUCT NAME	Evrenzo® Tablets 20mg Evrenzo® Tablets 50mg Evrenzo® Tablets 100mg
GENERIC NAME	Roxadustat
INDICATIONS	Renal anemia in patients on dialysis
DOSAGE AND ADMINISTRATION	*Patients not on erythropoiesis-stimulating agent treatment.* For adults, the usual dosage is 50mg, the starting dose, as roxadustat orally administered three times weekly. The dosage thereafter should be adjusted according to the patient's condition; however, the maximum dose should not exceed 3.0mg/kg. *Patients switching from erythropoiesis-stimulating agents.* For adults, the usual dosage is 70 or 100mg, the starting dose, as roxadustat orally administered three times weekly. The dosage thereafter should be adjusted according to the patient's condition; however, the maximum dose should not exceed 3.0mg/kg.
DATE OF APPROVAL	September 20, 2019
DATE OF NHI Drug Price Listing	November 19, 2019
DATE OF LAUNCH	November 20, 2019

Product photo

About Chronic Kidney Disease (CKD) and Anemia

CKD is a progressive loss of kidney function caused by damage to the kidneys resulting from conditions such as hypertension, diabetes, or immune-regulated inflammatory conditions.[6] Worldwide, more than 1 in 10 people are living with CKD.[7] In Japan, specifically, the prevalence of CKD has increased significantly over time.[8] Although CKD can occur at any age, it becomes more common in aging populations, and the prevalence is increasing. CKD is a critical worldwide healthcare issue that represents a large and growing unmet medical need.

Anemia is a frequent complication of CKD, occurring in over 90% of patients on dialysis. The number of patients on dialysis in Japan is increasing year by year and exceeded 330,000 in 2017. CKD anemia can severely worsen the outcomes of kidney disease, increasing the rate of progression to renal failure and the likelihood of cardiovascular complications. It also significantly reduces patients' quality of life and their cognitive ability. Currently, the main treatment options for anemia associated with CKD are ESAs and iron supplements

About Roxadustat

In addition to launch for renal anemia in patients on dialysis, roxadustat is currently in Phase 3 for renal anemia in patients not on dialysis in Japan. Roxadustat is approved for treatment of anemia associated with CKD in China in both dialysis-dependent and non-dialysis-dependent CKD patients. U.S. NDA and EU MAA preparation is underway. Roxadustat is also in Phase 3 clinical development in the U.S. and Europe and in Phase 2/3 development in China for anemia associated with myelodysplastic syndromes, and in Phase 2 for chemotherapy-induced anemia. For information about roxadustat studies, please visit clinicaltrials.gov at: https://clinicaltrials.gov/ct2/results?term=roxadustat&Search=Search.

Astellas and FibroGen are collaborating on the development 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.

1: Nakhoul G. et al.: Cleve Clin J Med 2016；83（8）：613-624

2: The Japanese Society for Dialysis Therapy: Annual Dialysis Data Report (as of December 31, 2017)

3: Mohanram A, Zhang Z, Shahinfar S,ET AL. Anemia and end-stage renal disease in patients with type 2 diabetes and nephropathy. *Kidney Int.* 2004 Sep;66(3):1131-8.

4: Weiner DE , Tighiouart H, Stark PC et al. Kidney disease as a risk factor for recurrent cardiovascular disease and mortality. *Am J Kidney Dis*. 2004 Aug;44(2):198-206.

5: Eriksson D et al. Cross-sectional survey in CKD patients across Europe describing the association between quality of life and anaemia. *BMC Nephrology*. 2016;17:97.

6: Ojo, A. Addressing the Global Burden of Chronic Kidney Disease Through Clinical and Translational Research. *Transactions of the American Clinical and Climatological Association*. 2014, No. 125, p. 229-246.

7: The Global Kidney Health Atlas. International Society of Nephrology (ISN). Available at: https://www.kidneycareuk.org/news-and-campaigns/news/estimated-1-10-people-worldwide-have-chronic-kidney-disease/. Last accessed August 2019.

8: Nagata M, Ninomiya T, Doi Y, Yonemoto K, Kubo M, Hata J, Tsuruya K, Iida M, Kiyohara Y. *Nephrol Dial Transplan*t. 2010, Aug, vol. 25, no.8, 2557-2564.

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

About FibroGen

FibroGen, Inc., headquartered in San Francisco, with subsidiary offices in Beijing and Shanghai, is a leading biopharmaceutical company discovering and developing a pipeline of first-in-class therapeutics. The company applies its pioneering expertise in hypoxia-inducible factor (HIF), connective tissue growth factor (CTGF) biology, and clinical development to advance innovative medicines for the treatment of anemia, fibrotic disease, and cancer. For more information, please visit www.fibrogen.com.

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

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