Press Release

ASN Kidney Week 2018: Data Presented from Two Japanese Phase 3 Studies on Roxadustat in the Treatment of Anemia Associated with Chronic Kidney Disease in Patients on Dialysis

TOKYO and San Francisco, October 30, 2018 - Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") and FibroGen, Inc. (Nasdaq: FGEN, CEO: Thomas B. Neff, "FibroGen") today announced the presentation of data from two Japanese Phase 3 studies (1517-CL-0302 and 1517-CL-0307) of roxadustat (development code: ASP1517/FG-4592) for the treatment of anemia associated with Chronic Kidney Disease (CKD) in patients on dialysis at the American Society of Nephrology (ASN) Kidney Week 2018 that was held October 23 – 28, 2018 in San Diego, California.

The 1517-CL-0302 study evaluated the efficacy and safety of roxadustat in Japanese CKD patients on peritoneal dialysis (PD). In this study, roxadustat was well tolerated and achieved and maintained hemoglobin (Hb) levels within the target range in Japanese CKD patients on PD, with or without previous treatment with erythropoiesis-stimulating agents (ESAs). The 1517-CL-0307 study evaluated the efficacy and safety of roxadustat compared to darbepoetin alfa (genetical recombination) ("darbepoetin alfa") in the treatment of CKD anemia in patients on hemodialysis (HD) who had previously been treated with recombinant human erythropoietin (rHuEPO) or darbepoetin alfa. In this study, roxadustat effectively maintained Hb within the range of 10-12 g/dL in HD patients, and its efficacy was non-inferior to darbepoetin alfa. In both studies, the safety profile of roxadustat was consistent with previous studies in the CKD population.

"Anemia, a common complication of CKD, is associated with significant morbidity and mortality, and the condition can have a debilitating impact on the patients affected," said Salim Mujais, M.D., senior vice president and global therapeutic area head, Medical Specialties Development, Astellas. "The presented data from two Phase 3 studies conducted in Japanese patients, showing roxadustat to be well tolerated and efficacious, support the potential of roxadustat as a new oral therapeutic option for CKD patients with anemia, including those on HD and on PD. We look forward to continuing to advance the development of roxadustat and contributing to a treatment of anemia associated with CKD."

The followings are highlights of key data from these two Phase 3 studies of roxadustat:

1517-CL-0302 study

Title: Phase 3, Multicenter, Open-Label Study of Intermittent Oral Roxadustat in Peritoneal Dialysis CKD Patients with Anemia

(Publication #: SA-OR075, Oral abstract session on Saturday, October 27 from 5:54 p.m. to 6:06 p.m. PT at San Diego Convention Center, Room 2)

Study design

- This multicenter 24-week, randomized, open-label Phase 3 study enrolled Japanese CKD patients on PD with anemia in two groups based on prior ESA treatment.
- Patients not previously treated with ESA (ESA Naive) were randomized to roxadustat 50 mg or 70 mg; patients previously treated with ESA (ESA Conversion) were switched to roxadustat 70 mg or 100 mg depending on prior ESA dose.
- Dose was adjusted throughout the study to maintain the Hb levels at a target range of 10-12 g/dL.
- Efficacy endpoints were maintenance rate of target Hb level at Weeks 18-24, cumulative response rate at the end of treatment (two Hb thresholds, 10.0 g/dL and 10.5 g/dL; and Hb increase, ≥1.0 g/dL), average Hb levels at Weeks 18-24 and its change from baseline, and rate of rise in Hb levels from Week 0 to Week 4.
- Safety was assessed by occurrence of Adverse Events (AEs).

Study results

- 56 patients were enrolled (13 ESA Naive; 43 ESA Conversion).
- Efficacy endpoints:
    - Hb maintenance rates were 92.3% (95% CI: 64.0, 99.8; ESA Naive) and 74.4% (95% CI: 58.8, 86.5; ESA Conversion).
    - Maintenance rates of patients with at least one Hb value at Weeks 18-24 were 92.3% (95% CI: 64.0, 99.8; ESA Naive) and 86.5% (95% CI: 71.2, 95.5; ESA Conversion).
    - In the ESA Naive Group, cumulative response rate for both Hb thresholds was 100.0%.
    - Mean of average Hb levels at Weeks 18-24 were 11.05 g/dL (95% CI: 10.67, 11.42; ESA Naive) and 10.93 g/dL (95% CI: 10.73, 11.13; ESA Conversion).
    - Mean change in average Hb at Weeks 18-24 from baseline was 1.69 g/dL (95% CI: 1.06, 2.33; ESA Naive) and 0.14 g/dL (95% CI: -0.12, 0.39; ESA Conversion).
    - In the ESA Naive Group, mean (SD) rate of rise in Hb levels from Week 0 to Week 4 was 0.193 (0.203) and 0.556 (0.408) g/dL/week with roxadustat 50 mg and 70 mg, respectively.
- The most common treatment emergent adverse events (TEAEs) were nasopharyngitis, back pain, catheter site infection, diarrhea, vomiting, abdominal pain, conjunctivitis, constipation, nausea, and pruritus.

1517-CL-0307 study

Title: Phase 3, Randomized, Double-Blind, Active-Comparator (Darbepoetin Alfa) Conversion Study of Oral Roxadustat in CKD Patients with Anemia on Hemodialysis in Japan

(Publication #: TH-PO1151, Poster session on Thursday, October 25 from 10:00 a.m. to 12:00 noon PT at Exhibit hall)

Study design

- This multicenter, 24-week, randomized, double-blind, double-dummy, darbepoetin-controlled Phase 3 study enrolled Japanese CKD patients on HD for ≥12 weeks, with anemia converted from rHuEPO or darbepoetin alpha to roxadustat.
- Patients were randomized to roxadustat (70 mg and 100 mg) three times weekly or darbepoetin alfa (10-60 μg) once weekly; roxadustat dose was adjusted to maintain Hb between 10 and12 g/dL.
- Primary endpoint was the change of average Hb levels from baseline to Weeks 18-24. Roxadustat efficacy was confirmed if the 95% CI of average Hb at Weeks 18-24 was within the range of 10-12 g/dL. Non-inferiority to darbepoetin alfa was confirmed if the lower limit of the 95% CI of the difference in the means of change of average Hb levels from baseline to Weeks 18-24 between roxadustat and darbepoetin alfa was above -0.75 g/dL.
- Secondary endpoints included: average Hb levels of Weeks 18-24, proportion of patients who achieved an average Hb level of 10-12 g/dL at Weeks 18-24 (maintenance rate), and iron parameters (i.e., serum iron, ferritin, Transferrin Saturation (TSAT), transferrin, and Total Iron Binding Capacity (TIBC)).
- Safety was assessed as occurrence of AEs and ophthalmological examination (color fundus photography and optical coherence tomography (OCT)).

Study results

- 303 patients were randomized to roxadustat (n=151) or darbepoetin alfa (n=152).
- The mean average Hb at Weeks 18-24 was 10.99 g/dL (95% CI: 10.88, 11.10) with roxadustat, confirming its efficacy.
- The difference between roxadustat and darbepoetin alfa in change of average Hb levels from baseline to Weeks 18-24 was -0.02 g/dL (95% CI: -0.18, 0.15), confirming non-inferiority of roxadustat efficacy to darbepoetin alfa.
- Hb maintenance rates were 79.3% (95% CI: 72.0, 85.5; roxadustat) and 83.4% (95% CI: 76.5, 89.0; darbepoetin alfa).
- The proportion of patients with at least one Hb value maintained at Hb 10-12 g/dL at Weeks 18-24 were 95.2% (95% CI: 89.8, 98.2; roxadustat) and 91.3% (95% CI: 85.3, 95.4; darbepoetin alfa).
- Among patients taking roxadustat, serum iron, ferritin, and TSAT were clinically stable; and transferrin and TIBC increased through Week 4 and then remained stable. No remarkable changes in iron parameters occurred with darbepoetin alfa.

- The most common TEAEs in both groups were nasopharyngitis, shunt stenosis, diarrhea, contusion, and vomiting.
- In ophthalmology evaluations, blinded review of color fundus photography images revealed new or worsening retinal hemorrhage occurred in 32.4% of patients receiving roxadustat and 36.6% of patients receiving darbepoetin alfa during treatment; no clinically meaningful changes in retinal thickness evaluated with OCT were observed from Week 0 through end of treatment in either of the treatment groups.
- No increased risk of ophthalmological abnormalities including retinal hemorrhages were observed in patients treated with roxadustat compared to darbepoetin alfa.
- Roxadustat was well tolerated with a safety profile similar to that of darbepoetin alfa and consistent with previous reports.

For more information about roxadustat studies, please visit to clinicaltrials.gov at: https://clinicaltrials.gov/ct2/results?term=roxadustat&Search=Search.

About Chronic Kidney Disease (CKD) and Anemia

CKD is estimated to affect more than 200 million people worldwide*[1] and specifically in Japan, the prevalence of CKD has increased significantly over time.*[2] Although CKD can occur at any age, it becomes more common in aging populations, and the prevalence is increasing. Anemia is a common complication of CKD and is associated with significant morbidity and mortality in dialysis and non-dialysis populations. In addition, CKD can be both a cause and a consequence of cardiovascular disease and is now a critical worldwide healthcare issue that represents a large and growing unmet medical need.

About Roxadustat

Roxadustat, discovered and developed by FibroGen, is a compound currently in Phase 3 development on a global basis as a potential therapy for anemia associated with CKD in both patients on dialysis and not on dialysis. Roxadustat is an orally administered small molecule inhibitor of hypoxia-inducible factor (HIF) prolyl hydroxylase activity. HIF is a protein transcription factor that induces the natural physiological response to conditions of low oxygen, "turning on" erythropoiesis (the process by which red blood cells are produced).

Astellas and FibroGen are collaborating on the development of roxadustat for the potential treatment of anemia in patients with CKD and myelodysplastic syndromes 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 patients with CKD in the U.S., China, and other markets.

Roxadustat is currently in Phase 3 clinical development for the treatment of anemia associated with myelodysplastic syndromes (MDS) in the U.S. and in Phase 2/3 development for MDS in China.

For information about roxadustat studies, please visit clinicaltrials.gov at this link: https://clinicaltrials.gov/ct2/results?term=roxadustat&Search=Search.

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[1] 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.

[2] 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. Roxadustat, the company's most advanced product candidate, is an oral small molecule inhibitor of HIF prolyl hydroxylase activity, completing worldwide Phase 3 clinical development for the treatment of anemia in chronic kidney disease (CKD), with a New Drug Application (NDA) currently under review by the State Drug Administration (SDA). Roxadustat is 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 (MDS). Pamrevlumab, an anti-CTGF human monoclonal antibody, is advancing towards Phase 3 clinical development for the treatment of idiopathic pulmonary fibrosis (IPF) and pancreatic cancer, and is currently in a Phase 2 trial for Duchenne muscular dystrophy (DMD). FibroGen is also developing a biosynthetic cornea in China. 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.

FibroGen Forward-looking Statements
This release contains forward-looking statements regarding FibroGen's strategy, future plans, and prospects, including statements regarding the development of the company's product candidates pamrevlumab and roxadustat, the potential safety and efficacy profile of our product candidates, and our clinical, regulatory, and commercial plans, and those of our partners. These forward-looking statements include, but are not limited to, statements about our plans, objectives, representations and contentions and are not historical facts and typically are identified by use of terms such as "may," "will", "should," "on track," "could," "expect," "plan," "anticipate," "believe," "estimate," "predict," "potential," "continue" and similar words, although some forward-looking statements are expressed differently. Our actual results may differ materially from those indicated in these forward-looking statements due to risks and uncertainties related to the continued progress and timing of our various programs, including the enrollment and results from ongoing and potential future clinical trials, and other matters that are described in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, and our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2018, filed with the Securities and Exchange Commission (SEC), including the risk factors set forth therein. Investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release, and we undertake no obligation to update any forward-looking statement in this press release, except as required by law.

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