March 12, 2019

Topline Results of Japanese Phase 3 Clinical Studies of the HIF-PH Inhibitor MT-6548 in Anemia due to CKD

Mitsubishi Tanabe Pharma Corporation (Head Office: Chuo-ku, Osaka; President & Representative Director: Masayuki Mitsuka) today announced the positive efficacy and safety topline results of two pivotal Japanese phase 3 clinical studies of the hypoxia inducible factor prolyl hydroxylase (HIF-PH) inhibitor MT-6548 (generic name: vadadustat) in subjects with anemia due to chronic kidney disease (CKD) who are non-dialysis dependent (NDD-CKD) or hemodialysis dependent (HD-CKD). In addition, two phase 3 single-arm studies were conducted in peritoneal dialysis (PD-CKD) subjects and hemodialysis subjects, with positive results. MT-6548 is a HIF-PH inhibitor that has been in-licensed from Akebia Therapeutics Inc., a US biopharmaceutical company located in Cambridge, Massachusetts.

In Japan, it is estimated that around 13 million people are afflicted with higher CKD meaning that a great many people are suffering from anemia due to CKD. Injectable erythropoiesis stimulating agent (ESA) is currently the standard of care. The further development of MT-6548, which makes possible once-a-day oral administration, is expected to make a contribution to the treatment of anemia due to CKD.

Mitsubishi Tanabe Pharma plans to file MT-6548 to NDA as a therapeutic medication for renal anemia in Japan in FY2019.
In addition, Mitsubishi Tanabe Pharma will also advance the development of MT-6548 in other Asian countries in which it has exclusive development and sales rights.

Topline results as follows:

- Study for NDD-CKD subjects with anemia due to CKD (J01)
  The Phase 3 randomized, open-label, active-controlled study was conducted with 304 NDD-CKD subjects with anemia due to CKD with a treatment duration of 52 weeks. Data from the planned analysis at 24 weeks is provided. The mean hemoglobin (Hb) level at week 20 and week 24 was 11.66 g/dL (95% CI 11.49, 11.84 g/dL) for MT-6548 group and 11.93 g/dL (95% CI 11.76, 12.10 g/dL) for Darbepoetin Alfa (Genetical Recombination), ESA (control) group. The difference in mean Hb was -0.26 g/dL (95% CI -0.50,

-0.02 g/dL) achieving the non-inferiority criterion of -0.75 g/dL and the study met its primary endpoint.
The incidence of adverse events (AE) was 72.2% in MT-6548 group and 73.2% in control group. The most common AEs in MT-6548 group were nasopharyngitis (14.6%), diarrhea (10.6%), constipation (5.3%), and contusion (5.3%). The incidence of serious adverse events (SAEs) was 13.9% in MT-6548 group and 14.4% in control group. No SAE was considered related to study drug. No deaths were reported in MT-6548 group, and one fatal myocardial infarction was reported in control group, which was assessed as not related to study drug.

・ Study for HD-CKD subjects with anemia due to CKD who had been receiving ESA therapy (J03)

The Phase 3 randomized, double-blinded, active-controlled study was conducted with 323 HD-CKD subjects with anemia due to CKD who had been receiving ESA therapy, with a treatment duration of 52 weeks. Data from the planned analysis at 24 weeks is provided (on going double-blind study).
The mean Hb level at week 20 and week 24 is 10.61 g/dL (95% CI 10.45, 10.76 g/dL) for MT-6548 group and 10.65 g/dL (95% CI 10.50, 10.80 g/dL) for control group. The difference in mean Hb was -0.05 g/dL (95% CI -0.26, 0.17 g/dL) achieving the non-inferiority criterion of -0.75 g/dL and the study met its primary endpoint.
The incidence of adverse events (AE) was 89.5% in MT-6548 group and 88.2% in control group. The most common AEs in MT-6548 group were nasopharyngitis (19.8%), diarrhea (10.5%), and shunt stenosis (8.0%). The incidence of serious adverse events (SAEs) was 13.0% in MT-6548 group and 10.6% in control group. No SAE was considered related to study drug.

・ Study for PD-CKD subjects with anemia due to CKD (J02)

The Phase 3 open-label, single-arm study was conducted with 42 PD-CKD subjects with anemia due to CKD.
The mean Hb level at week 20 and week 24 for MT-6548 group was 11.35 g/dL (95% CI 10.99, 11.70 g/dL). Therapeutic effect on anemia was revealed. 38 subjects (90.5%) experienced an AE, and 12 (28.6%) experienced an SAE. One SAE of fatal myocardial ischemia was assessed as possibly related to vadadustat.

・ Study for HD-CKD subjects with anemia due to CKD who had not been receiving ESA therapy (J04)
The Phase 3 open-label, single-arm study was conducted with 24 HD-CKD subjects with anemia due to CKD who had not been receiving ESA therapy. The mean Hb level at week 20 and week 24 for MT-6548 group was 10.75 g/dL (95% CI 10.35, 11.14 g/dL). Therapeutic effect on anemia was revealed. 23 subjects (95.8%) experienced an AE, and 7 (29.2%) experienced an SAE. No SAE was assessed as related to study drug, and no deaths were reported.

Additional data from the studies are expected to be presented at an upcoming medical meeting and published in a peer-reviewed publication.

Mitsubishi Tanabe Pharma Corporation
Corporate Communications Department
Media contacts: TEL:+81 6 6205 5119
Investor contacts: TEL:+81 6 6205 5110

◆Reference◆

About Vadadustat

Vadadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) currently in global Phase 3 development for the treatment of anemia due to chronic kidney disease. Vadadustat's proposed mechanism of action is designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with increased production of HIF, which coordinates the interdependent processes of iron mobilization and erythropoietin production to increase red blood cell production and, ultimately, improve oxygen delivery. Vadadustat is an investigational therapy and is not approved by the U.S. Food and Drug Administration or any other regulatory authority.

About Akebia Therapeutics Inc.

Akebia Therapeutics, Inc. is a fully integrated biopharmaceutical company focused on the development and commercialization of therapeutics for patients with kidney disease. The company was founded in 2007 and is headquartered in Cambridge, Massachusetts. For more information, please visit www.akebia.com, which does not form a part of this release.