Akebia and Keryx to Merge by Year's End

A new company is forming to produce treatments for patients with chronic kidney disease (CKD). Subject to antitrust considerations, the merger of Akebia Therapeutics (Cambridge, MA) and Keryx Biopharmaceuticals (Boston, MA) is expected to be complete by the end of the year. The new company will be called Akebia Therapeutics.

The merger is valued at $1.3 billion, notes Pitchbook, a financial newsletter. Under terms of the merger, Akebia shareholders will own a bit more than half of the combined firm, the website FierceBiotech reported.

The strategy behind the merger is severalfold. First, the merger establishes a renal company with an enhanced market position that neither company has alone. The combined company will open a larger marketplace, including Akebia's product candidate, Vadadustat (for anemia treatment) and Keryx's Auryxia, which is FDA approved for the control of serum phosphorus levels in adults with CKD who are on dialysis. According to a joint news release about the merger, the combined company will "provide nephrologists with a portfolio of renal products." Vadadustat is up for FDA approval.

The merging companies said they will have the potential to help patients across all stages of CKD, including both those who need and those who don't need dialysis, and could become a partner for the renal patient community as well as for companies developing renal products.

The merger will result in a new management team that has been developing and commercializing products for patients with kidney disease. John P. Butler, current CEO of Akebia, will lead as CEO. He formerly led Genzyme Corporation's renal business.

Keryx will appoint the chairperson of the Board of Directors of the combined company.

The new company will have $453 million in cash plus the potential for increasing revenues from Auryxia sales and cost synergies expected to be in the neighborhood of more than $250 million, according to Keryx and Akebia.

Up and Comer in Progressive Kidney Disease

XORTX Therapeutics, a company founded to focus on developing therapies to treat progressive kidney disease, has filed a pre-IND (Investigational New Drug) meeting request with the FDA. The company, based in Calgary, Alberta, filed pre-IND documents and secured a September 2018 meeting with the FDA to discuss development of its compound, XRx-008, for the treatment of autosomal dominant polycystic kidney disease (ADPKD). The company currently plans to advance XRx-008 through phase 2 clinical trials.

Said XORTX's CEO Allen Davidoff, MD: "We are excited to take this important first regulatory step in the development of the XRx-008 program for ADPKD. This request initiates the process of establishing communication and discussion with the FDA regarding our phase 2 clinical trial plans and defining the critical path for clinical development and marketing approval of this therapy for PKD patients."

In 2018 the company has been advancing its two key programs: the ADPKD program and the diabetic nephropathy program through phase 2 proof-of-concept clinical trials.

The company's stated aim is to identify and assess acquisition opportunities of companies that "have products for unmet needs and a higher than average probability of success."

XORTX is continuing to partner with emerging and large pharma companies through opportunities to co-develop drugs and is in-licensing as a way to pursue corporate partnerships. In-licensing occurs when a company takes on some of the financial or technological work of developing a product, in return for a share of sales revenue.

Expanding its outlook in the renal community, XORTX has also paired with the Polycystic Kidney Disease Foundation to support patients, the company announced.

JYNARQUE™ (tolvaptan)

experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Use in Patients with Hepatic Impairment: Because of the risk of serious liver injury, use is contraindicated in patients with a history, signs or symptoms of significant liver impairment or injury. This contraindication does not apply to uncomplicated polycystic liver disease which was present in 60% and 66% of patients in TEMPO 3:4 and REPRISE, respectively. No specific exclusion for hepatic impairment was implemented in TEMPO 3:4. However, REPRISE excluded patients with ADPKD who had hepatic impairment or liver function abnormalities other than that expected for ADPKD with typical cystic liver disease.

Use in Patients with Renal Impairment: Efficacy studies included patients with normal and reduced renal function. TEMPO 3:4 required patients to have an estimated creatinine clearance ≥60 mL/min, while REPRISE included patients with $eGFR_{CKD\text{-}Epi}$ 25 to 65 mL/min/1.73m^2.

OVERDOSAGE: Single oral doses up to 480 mg (4 times the maximum recommended daily dose) and multiple doses up to 300 mg once daily for 5 days have been well tolerated in trials in healthy subjects. There is no specific antidote for tolvaptan intoxication. The signs and symptoms of an acute overdose can be anticipated to be those of excessive pharmacologic effect: a rise in serum sodium concentration, polyuria, thirst, and dehydration/hypovolemia.

No mortality was observed in rats or dogs following single oral doses of 2000 mg/kg (maximum feasible dose). A single oral dose of 2000 mg/kg was lethal in mice, and symptoms of toxicity in affected mice included decreased locomotor activity, staggering gait, tremor and hypothermia.

In patients with suspected JYNARQUE overdosage, assessment of vital signs, electrolyte concentrations, ECG and fluid status is recommended. Continue replacement of water and electrolytes until aquaresis abates. Dialysis may not be effective in removing JYNARQUE because of its high binding affinity for human plasma protein (>98%).

To report SUSPECTED ADVERSE REACTIONS, contact Otsuka America Pharmaceutical, Inc. at 1-800-438-9927 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Manufactured by Otsuka Pharmaceutical Co., Ltd., Tokyo, 101-8535 Japan
Distributed and marketed by Otsuka America Pharmaceutical, Inc., Rockville, MD 20850 USA
JYNARQUE is a trademark of Otsuka Pharmaceutical Co., Ltd., Tokyo, 101-8535 Japan
© 2018, Otsuka Pharmaceutical Co., Ltd., Tokyo, 101-8535 Japan

April 2018 10US18IBR0001

Diabetes Drug Roundup

Manufacturers of two different diabetes drugs have reported positive results recently.

Jardiance (empagliflozin) consistently reduced the risk of new or worsening kidney disease versus placebo, reported a two-member diabetes pharmaceutical alliance.

Boehringer Ingelheim (Ridgefield, CT) and Eli Lilly (Indianapolis) joined forces in 2011 to form an alliance that centers on compounds in "several of the largest diabetes treatment classes," the companies noted.

The companies shared findings from two new analyses from the long-term EMPA-REG OUTCOME trial of empagliflozin. One analysis showed that patients taking the drug consistently reduced the risk of new or worsening kidney disease when compared with patients taking placebo. This finding held regardless of level of control over blood pressure, level of low-density lipoprotein cholesterol or HbA1C levels, individually or combined, and other factors, Nasdaq.com reported.

A separate analysis showed a consistent reduction in the risk of cardiovascular death compared with placebo in patients stratified to low, intermediate, high, and highest cardiovascular risk groups, MD magazine reported. Likewise, there were similar reductions in the risk of hospitalization for heart failure among the patient groups taking empagliflozin.

At the 2018 American Diabetes Association (ADA) 78th Scientific Sessions in Orlando, FL, Rogelio Braceras, MD, therapeutic area head of Clinical Development and Medical Affairs (Metabolism) for Boehringer Ingelheim, said the results on Jardiance are "very reassuring, very informative, because we are doing the CVD outcome studies for heart failure and also for kidney programs through the EMPA-REG," a trial in 42 countries, MD magazine reported.

In a study published online in Lancet *Diabetes & Endocrinology* (1), researchers from the United States and Australia found that canagliflozin, marketed as Invokana by Janssen Pharmaceuticals (Johnson & Johnson, J&J) reduced kidney decline and albuminuria more than a placebo treatment.The research team assessed a number of kidney markers including end stage renal disease, with results from two studies taken between November 2009 and March 2011 and between January 2014 and May 2015.

Reference

1. Perkovic V, et al. Canagliflozin and renal outcomes in type 2 diabetes: results from the CANVAS Program randomised clinical trials. *Lancet Diabetes Endocrinol* 2018; DOI: https://doi.org/10.1016/S2213-8587(18)30141-4