**CKD Treatment News**

AbbVie (North Chicago, IL) has dissolved its partnership with Reata Pharmaceuticals (Irving, TX) after nine years. The two companies were working together to develop, among other drug candidates, the therapeutic agent bardoxolone methyl for chronic kidney disease (CKD). The compound was moving along the approval pipeline until the FDA received findings that patients in the CKD treatment arm of a phase 3 study exhibited heart-related side effects, FierceBiotech.com reported.

Now the drug is being tested in more specific populations: patients with autosomal dominant polycystic kidney disease, a genetic disorder, as well as in patients with CKD caused by Alport syndrome, also an inherited disease. If results from current trials prove positive, then Reata will be in a much better position financially, reports Stockhouse.com.

“The deal is important to us because we get the rights to commercialized CKD indications on a worldwide basis,” said Reata CEO Warren Huff in a corporate statement. “Now we have all the rights, except those in southeast Asia, to commercialized CKD indications on a worldwide basis,” Huff declared. “The deal is important to us because we get the rights to the treatments, including bardoxolone, an orally available semi-synthetic triterpenoid, based on the natural product oleanolic acid. Preclinical studies indicated that the compound acts as an activator of the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway. Nrf2 regulates expression of antioxidant proteins that protect against oxidative damage. Reata is also developing Nfr2 compounds to treat other diseases.

Another CKD drug candidate is moving to a phase 2 trial: DiaMedica Therapeutics’ (Minneapolis, MN) DM199, a synthetic form of human serine protease kallikrein, which plays an important role in kidney physiology, including blood flow, inflammation, fibrosis, and oxidative stress.

The phase 2 study will enroll about 60 patients with CKD. The two cohorts will include 1) patients with CKD caused by IgA nephropathy and 2) non-diabetic, hypertensive African Americans with CKD. African Americans are at greater risk for CKD than European Americans; those with the APOL1 gene are at even higher risk.

Primary endpoints of the study will include safety, tolerability, kidney function, and blood pressure. Kidney function will be evaluated by changes from the baseline level of estimated glomerular filtration rate and albuminuria, as measured by the ratio of urinary albumin to creatinine.

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**Clinical Trials Planned for FSGS, Diabetic Nephropathy Agents**

Two companies recently announced clinical trials for promising drug candidates for kidney diseases.

Goldfinch Bio (Cambridge, MA) is entering into an agreement with Osaka, Japan-based Takeda to develop a drug to treat rare and metabolic kidney diseases. The agreement will grant Takeda worldwide rights to the cannabinoid receptor 1 (CB1) monoclonal antibody, which inhibits CB1. Goldfinch says terms are not being disclosed.

The company will assume development and commercialization responsibilities for the drug. Takeda reserves the right, however, to request that Goldfinch Bio negotiate with Takeda for sub-licensing of Japanese rights to the pharmaceutical.

A therapeutic agent will be developed from the preclinical CB1 monoclonal antibody, which has been renamed GFB-024. Goldfinch plans to file a new drug application and begin a phase 1 study in the second half of 2020.

Preclinical data support the inhibition of CB1 signaling as a novel treatment of two kidney-related conditions tracking with the obesity epidemic, diabetic nephropathy and obesity-related glomerulopathies (ORG). The compound potentially will provide metabolic benefits, help prevent fibrosis, and preserve kidney function, the company says.

Diabetic nephropathy develops in 30% to 40% of patients who have diabetes and is a leading cause of morbidity, mortality, and kidney failure in the United States and worldwide. ORG is a rare kidney disorder characterized by significant proteinuria and progressive renal dysfunction.

The Phase 2a clinical trial of ZyVersa Therapeutics’ drug candidate VAR200 should begin by year’s end. ZyVersa, based in Weston, FL, targets podocyte cholesterol accumulation that results from impaired efflux of cholesterol from the cells, causing structural damage that affects kidney filtration. The treatment would benefit patients with focal segmental glomerulosclerosis.

The article “Kidney is the New Liver” states: “Within the past 5 years, renal drug development has been de-risked due to FDA’s acceptance of short-term surrogate endpoints, such as proteinuria, and the ability to segment patients into homogeneous groups through AI and machine learning from large patient data bases, such as Neptune. This has resulted in a surge of interest and investment in this area, as was seen in the past with liver disease”.

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Reference