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OPKO Health Announces KDIGO Clinical Practice Guideline Update on CKD-MBD

Updated Guideline Highlights the Limitations of Current Treatments for Secondary Hyperparathyroidism in Patients with Stage 3 or 4 Chronic Kidney Disease and Acknowledges Rayaldee as a Novel Vitamin D Prohormone

MIAMI, June 22, 2017 (GLOBE NEWSWIRE) -- OPKO Health, Inc. (NASDAQ:OPK) today announced that the Kidney Disease Improving Global Outcomes (KDIGO) organization has updated its Clinical Practice Guideline for the Diagnosis, Evaluation, Prevention and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). (http://kdigo.org/wp-content/uploads/2017/02/2017-KDIGO-CKD-MBD-GL-Update.pdf)

The update amends the 2009 KDIGO Clinical Practice Guideline and presents revised positions on current standards of care for the treatment of secondary hyperparathyroidism (SHPT) in patients with CKD stages 3 or 4:

- **Calcitriol and (1α-hydroxylated) vitamin D analogs:** These therapies are no longer suggested for routine use and should be reserved for patients with stage 4 or 5 CKD with severe and progressive hyperparathyroidism. The guideline notes that recent randomized clinical trials of calcitriol and its analogs failed to demonstrate improvements in outcomes but demonstrated increased risk of hypercalcemia, leading KDIGO to conclude that the risk-benefit ratio was no longer favorable for routine usage in patients with stage 3 or 4 CKD.

- **Nutritional vitamin D:** Supplementation with ergocalciferol or cholecalciferol remains unproven as a treatment for SHPT.

The updated guideline acknowledges Rayaldee® (extended release calcifediol) as a novel vitamin D prohormone and mentions that it both increases serum levels of 25-hydroxyvitamin D and lowers PTH in patients with stage 3 or 4 CKD. Developed by OPKO Health, Rayaldee is the first and only FDA-approved extended-release prohormone to treat SHPT and it has a safety profile similar to that of placebo.[1]

“The updated guideline represents a needed shift in the way nephrologists manage secondary hyperparathyroidism in patients with stage 3 or 4 chronic kidney disease,” said Michael J. Germain, MD, Professor of Medicine, Tufts University School of Medicine and Nephrologist/Partner, Western New England Renal & Transplant Associates, PC, Springfield, MA. “SHPT is one of the most common complications of CKD and, unfortunately, it has also been historically difficult to treat due to a lack of an effective and appropriate, FDA-approved treatment option. Having this updated guidance and the availability of an option like Rayaldee are significant advancements for both patients and providers managing this

complex disease."

"The updated KDIGO guideline highlights the unmet needs that exist in the treatment of SHPT, and we are working with physicians and other health care professionals to address these needs with Rayaldee," said Charles W. Bishop, PhD, CEO of the OPKO Health Renal Division.

About Rayaldee

Rayaldee is indicated for the treatment of secondary hyperparathyroidism (SHPT) in adults with stage 3 or 4 CKD and vitamin D insufficiency, defined as serum total 25-hydroxyvitamin D less than 30 ng/mL. It is not indicated in patients with stage 5 chronic kidney disease or end-stage renal disease on dialysis.[2]

Potential side effects of Rayaldee include hypercalcemia (elevated serum calcium), which can also lead to digitalis toxicity, and adynamic bone disease with subsequent increased risk of fractures if intact PTH levels are suppressed by Rayaldee to abnormally low levels. Severe hypercalcemia may require emergency attention; symptoms of hypercalcemia may include feeling tired, difficulty thinking clearly, loss of appetite, nausea, vomiting, constipation, increased thirst, increased urination, and weight loss. Digitalis toxicity can be potentiated by hypercalcemia of any cause. Excessive administration of Rayaldee can cause hypercalciuria, hypercalcemia, hyperphosphatemia, or oversuppression of intact PTH. Common symptoms of vitamin D overdosage may include constipation, decreased appetite, dehydration, fatigue, irritability, muscle weakness, or vomiting. Patients concomitantly taking cytochrome P450 inhibitors, thiazides, cholestyramine, phenobarbital or other anticonvulsants may require dose adjustments and more frequent monitoring.

The most common adverse reactions in clinical trials (≥3% and more frequent than placebo) were anemia, nasopharyngitis, increased blood creatinine, dyspnea, cough, congestive heart failure and constipation.

About OPKO Health, Inc.

OPKO Health is a diversified healthcare company that seeks to establish industry leading positions in large, rapidly growing markets. Our diagnostics business includes BioReference Laboratories, the nation's third largest clinical laboratory with a core genetic testing business and a 400 person sales and marketing team to drive growth and leverage new products, including the 4Kscore® prostate cancer test and the Claros® 1 in office immunoassay platform. Our pharmaceutical business features RAYALDEE, an FDA approved treatment for SHPT in stage 3-4 CKD patients with vitamin D insufficiency (launched in November 2016), VARUBITM for chemotherapy induced nausea and vomiting (oral formulation launched by partner TESARO and IV formulation pending FDA approval), OPK88004, a once or twice weekly oxyntomodulin for type 2 diabetes and obesity, in Phase 2 clinical trials, among the new class of GLP-1 glucagon receptor dual agonists, and OPK88003, a selective androgen receptor modulator for benign prostatic hyperplasia (Phase 2). Our biologics business includes hGH-CTP, a once weekly human growth hormone in Phase 3 and partnered with Pfizer; and a long-acting Factor VIIa drug for hemophilia in Phase 2a. More information available at www.opko.com.

Cautionary Statement Regarding Forward-Looking Statements

This press release contains "forward-looking statements," as that term is defined under the Private Securities Litigation Reform Act of 1995 (PSLRA), which statements may be identified by words such as "expects," "plans," "projects," "will," "may," "anticipates," "believes," "should," "intends," "estimates," and other words of similar meaning, including statements regarding the benefits of RAYALDEE, its ability to increase both serum levels of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D and lower parathyroid hormone, whether RAYALDEE will fill a treatment gap in treatment of SHPT, as well as other non-historical statements about our expectations, beliefs or intentions regarding our business, technologies and products, financial condition, strategies or prospects. Many factors could cause our actual activities or results to differ materially from the activities and results anticipated in forward-looking statements. These factors include those described in our Annual Report on Form 10-K filed with the Securities and Exchange Commission and in our other filings with the Securities and Exchange Commission. The forward-looking statements contained in this press release speak only as of the date the statements were made, and we do not undertake any obligation to update forward-looking statements. We intend that all forward-looking statements be subject to the safe-harbor provisions of the PSLRA.

[1] Sprague SM, Crawford PW, Melnick JZ, et al. Use of extended-release calcifediol to treat secondary hyperparathyroidism in stages 3 and 4 chronic kidney disease. Am J Nephrol. 20 l 6;44:316-325.
[2] Rayaldee [prescribing information]. Miami, FL: OPKO Pharmaceuticals, LLC; July 2016.

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