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OPKO Announces Submission of Rayaldee™ New Drug Application to U.S. Food and Drug Administration

MIAMI--(BUSINESS WIRE)-- OPKO Health, Inc. (NYSE: OPK), today announced that it has submitted a New Drug Application (NDA) for oral Rayaldee to the U.S. Food and Drug Administration (FDA). The NDA requests marketing approval for Rayaldee for the prevention and treatment of secondary hyperparathyroidism (SHPT) in patients with stage 3 or 4 chronic kidney disease (CKD) and vitamin D insufficiency.

"The submission of this NDA represents a significant milestone in the development of Rayaldee, and it underscores our strong commitment to making improved therapies available to patients who suffer from chronic kidney disease," commented Dr. Phillip Frost, CEO and Chairman of OPKO. "We believe Rayaldee will be the first product to receive FDA approval for this important indication."

The Rayaldee application is supported by positive data from three randomized, double-blind, placebo-controlled studies and one open-label extension study conducted in the targeted patient population at a total of 105 U.S. sites. These studies met all primary efficacy and safety endpoints, as previously announced.

About Rayaldee™

Rayaldee is a first-in-class oral vitamin D prohormone treatment being developed for SHPT in patients with stage 3 or 4 CKD and vitamin D insufficiency. It has a proprietary modified-release formulation designed to gradually and reliably raise serum total 25-hydroxyvitamin D (prohormone) concentrations to targeted levels (at least 30 ng/mL) while avoiding upregulation of CYP24A1, a cytochrome P-450 enzyme which reduces the desired parathyroid hormone (PTH)-lowering efficacy. Gradual elevation of serum total 25-hydroxyvitamin D prevents excessive elevation of serum calcium and related vascular and renal calcification. Such side effects limit the value of current vitamin D hormone therapies. Rayaldee is expected to address the approximately 20 million patients in the U.S., and many more elsewhere, with stage 3 or 4 CKD, SHPT and vitamin D insufficiency.

About Chronic Kidney Disease

CKD is a condition characterized by a progressive decline in kidney function. The kidney is normally responsible for excreting waste and excess water from the body, and for regulating various hormones. CKD is classified in five stages — mild (stage 1) to severe (stage 5) disease — as measured by the kidney's glomerular filtration rate. According to the National Kidney Foundation, CKD afflicts over 26 million people in the U.S., including more than 20 million patients with moderate (stages 3 or 4) and severe (stage 5) forms of CKD. In stage 5 CKD, kidney function is minimal to absent and patients require regular dialysis or a kidney transplant for survival.

About Vitamin D Insufficiency

Vitamin D insufficiency is a condition in which the body has low vitamin D stores, characterized by inadequate blood levels of vitamin D prohormone, known as 25-hydroxyvitamin D. An estimated 70-90% of CKD patients have vitamin D insufficiency, which can lead to SHPT and resultant debilitating bone diseases. Vitamin D insufficiency has been associated with increased mortality in CKD.

About Secondary Hyperparathyroidism (SHPT)

SHPT is a condition commonly associated with CKD in which the parathyroid glands secrete excessive amounts of PTH. SHPT arises as a result of vitamin D insufficiency or impaired kidney function that prevents sufficient production of vitamin D hormone to properly regulate calcium and phosphorus metabolism, and PTH secretion. Prolonged elevation of blood PTH causes excessive calcium and phosphorus to be released from bone, leading to elevated serum calcium and phosphorus, softening of the bones (osteomalacia) and calcification of vascular and renal tissues. SHPT affects 40-60% of patients with moderate CKD and approximately 90% of patients with severe CKD. Vitamin D therapy for SHPT is associated with reduced mortality in CKD patients.

About OPKO

OPKO is a multinational biopharmaceutical and diagnostics company that seeks to establish industry leading positions in large, rapidly growing markets by leveraging its discovery, development and commercialization expertise and novel and proprietary

technologies. For more information, visit http://www.opko.com.

This press release contains "forward-looking statements," as that term is defined under the Private Securities Litigation Reform Act of 1995 (PSLRA), regarding product development efforts and other non-historical facts about our expectations, beliefs or intentions regarding our business, technologies and products, financial condition, strategies or prospects, including statements regarding our ability to obtain approval for, successfully launch and commercialize proprietary renal disease products, including Rayaldee, that the NDA will be accepted or approved, expectations about Rayaldee, that Rayaldee will effectively control secondary hyperparathyroidism in patients with stage 3 or 4 chronic kidney disease by correcting vitamin D insufficiency, whether Rayaldee is appropriate for patients with minimal functioning kidney mass and its efficacy during longer term administration, whether Rayaldee will be highly effective in correcting vitamin D insufficiency, allowing more reliable treatment of patients, whether it is the solution to secondary hyperparathyroidism associated with vitamin D insufficiency for the 20 million pre-dialysis CKD patients in the U.S. and elsewhere, market potential for Rayaldee, that Rayaldee will treat vitamin D insufficiency and gradually correct elevated PTH, without safety concerns, and that we will be able to successfully develop, obtain approval for and launch sales of Rayaldee. 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 filings with the Securities and Exchange Commission, as well as risks inherent in funding, developing and obtaining regulatory approvals of new, commercially-viable and competitive products and treatments, including the risks that the phase 3 clinical trials for Rayaldee may not generate data that would support the approval or marketing of this product for the indications being studied, that others may develop products which are superior to Rayaldee, and that Rayaldee may not have advantages or prove to be superior over presently marketed products, including the currently used high monthly doses of prescription vitamin D_2, activated vitamin D hormone and over-the-counter vitamin D supplements . In addition, forward-looking statements may also be adversely affected by general market factors, competitive product development, product availability, federal and state regulations and legislation, the regulatory process for new products and indications, manufacturing issues that may arise, patent positions and litigation, among other factors. 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.

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