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OPKO Surpasses 50% Enrollment in First Phase 3 Trial of RayaldyTM (CTAP101 Capsules)

MIAMI--(BUSINESS WIRE)-- OPKO Health, Inc. (NYSE: OPK), has surpassed 50% enrollment in the first phase 3 trial of *Rayaldy*™ to treat patients with secondary hyperparathyroidism (SHPT), stage 3 or 4 chronic kidney disease (CKD) and vitamin D insufficiency. This trial is the first of two identical randomized, double-blind, placebo controlled, multi-site studies intended to establish the safety and efficacy of *Rayaldy*™ as a new treatment for SHPT in the targeted population. The endpoints of both studies, which will be conducted in parallel, include vitamin D status and changes in serum calcium, serum phosphorus and plasma intact parathyroid hormone (PTH).

Each of the phase 3 trials will involve 210 patients recruited at approximately 40 sites in the U.S. These patients are being stratified by CKD stage and randomized in a 2:1 fashion to receive six months of treatment with either *Rayaldy*™ or placebo. Dosing with *Rayaldy*™ is titrated, as necessary, to achieve the desired blood concentration and the targeted reduction in PTH.

"*Rayaldy*™ is being developed as a much needed and safer alternative to currently used activated vitamin D hormones," commented Dr. David Bushinsky, Chief of Nephrology at the University of Rochester. "Activated vitamin D hormone therapy is problematic in CKD patients with secondary hyperparathyroidism arising primarily from vitamin D insufficiency since it further stimulates catabolism (breakdown) of the available vitamin D stores and is often associated with hypercalcemia, a side effect linked to vascular calcification."

"Secondary hyperparathyroidism develops in CKD patients due to vitamin D insufficiency or declining kidney function," explained Joel Z. Melnick, M.D., Vice President, Clinical Research and Development of OPKO's Renal Division. "Most CKD patients have insufficient stores of vitamin D due to the abnormal upregulation of CYP24, an enzyme which specifically destroys vitamin D and its metabolites. Many recent studies in CKD patients have demonstrated that over-the-counter and presently available prescription vitamin D supplements cannot reliably raise blood vitamin D prohormone levels or effectively treat SHPT. In contrast, our phase 2b trial has demonstrated that *Rayaldy*™ effectively and safely treats both SHPT and the underlying vitamin D insufficiency."

About *Rayaldy*™

Rayaldy™ is a first-in-class vitamin D prohormone treatment being developed for SHPT in stage 3 and 4 CKD patients with 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 CYP24, a cytochrome P-450 enzyme that reduces the PTH lowering potency of current vitamin D supplements. Activation of the product by the kidney is tightly regulated, preventing excessive elevation of serum calcium and related side effects which encumber current vitamin D hormone therapies and promote vascular and renal calcification. Once approved, *Rayaldy*™ will address the approximately 4 million CKD stage 3 and 4 patients in the U.S. and many more, elsewhere, with 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 different 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 eight million patients with moderate (stages 3 and 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 prohormones, collectively 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.

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 hormones 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.

About OPKO Health, Inc.

OPKO is a multi-national biopharmaceutical and diagnostics company that seeks to establish industry-leading positions in large and rapidly growing medical markets by leveraging our discovery, development and commercialization expertise and our novel and proprietary technologies. For more information, visit http://www.opko.com or contact Steven D. Rubin or Juan F. Rodriguez at 305-575-4100.

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. 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 enrollment of patients for or the results of the Phase 3 clinical trials for Rayaldy™ may not be completed on a timely basis or at all, may not be successful or achieve the expected results or effectiveness, and 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 Rayaldy™, and that Rayaldy™ may not have advantages over presently marketed products, including the currently used activated vitamin D hormone and over-the-counter and prescription 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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Source: OPKO Health, Inc.