OPKO Health Reports Interim Results for Two Ongoing RAYALDEE Studies

Phase 4 Head-to-Head Study in Patients with Stage 3 or 4 Chronic Kidney Disease
Phase 2 Trial in Patients with Stage 5 Chronic Kidney Disease on Dialysis

MIAMI (March 25, 2020) – OPKO Health, Inc. (NASDAQ: OPK) today reported interim results from an ongoing Phase 4 clinical trial comparing RAYALDEE® with three common treatment regimens for secondary hyperparathyroidism (SHPT) in adult patients with stage 3 or 4 chronic kidney disease (CKD) and vitamin D insufficiency, as well as interim results from an ongoing Phase 2 clinical trial exploring the safety and efficacy of a high-strength formulation of RAYALDEE as a new treatment for SHPT in adult patients with stage 5 CKD requiring hemodialysis and vitamin D insufficiency.

Phase 4 Head-to-Head Study in Patients with Stage 3 or 4 CKD

In this Phase 4 study, approximately 80 patients from multiple U.S. clinics will be treated for 2 months in a randomized, open-label fashion with RAYALDEE, high-dose cholecalciferol, immediate-release calcifediol, or a combination of paricalcitol and low-dose cholecalciferol. To date, 67 subjects have been enrolled and 62 have completed treatment. Enrollment is expected to be completed by the end of the second quarter of this year.

The interim results from all subjects undergoing or completing treatment indicate that a daily dose of 60 mcg of RAYALDEE is the only one of the four treatment regimens tested that reliably raises serum total 25-hydroxyvitamin D to the range of 50 to 100 ng/mL, a level required to effectively suppress elevated plasma intact parathyroid hormone (iPTH) in CKD patients (Ennis et at 2016, Strugnell et al 2019).

The mean iPTH reduction observed so far with RAYALDEE has exceeded 25% from pre-treatment baseline. Cholecalciferol, at a dose of 300,000 international units (IU) per month, and immediate-release calcifediol, at a dose of 265 mcg/month as approved in Europe, have raised mean serum 25-hydroxyvitamin D levels to just over 30 ng/mL and reduced mean plasma iPTH by less than 10%. The inability of cholecalciferol to raise serum 25-hydroxyvitamin D to the desired target range appears to be due to the higher body weights seen in CKD patients. The combination of paricalcitol (1 mcg per day escalating to 2 mcg per day) and cholecalciferol (800 IU per day) has had no effect on serum 25-hydroxyvitamin D, but has lowered plasma iPTH to approximately the same extent as RAYALDEE. Vitamin D receptor activators, such as paricalcitol, can effectively suppress iPTH without increasing serum 25-hydroxyvitamin D, but are no longer suggested for routine use in patients with stage 3 or 4 CKD according to the Kidney Disease Improving Global Outcomes (KDIGO) 2017 Clinical Practice Guideline Update for CKD-Mineral and Bone Disorder (CKD-MBD).

Final results from the ongoing Phase 4 trial are expected in the second half of 2020.

Phase 2 Trial in Patients with Stage 5 CKD on Dialysis

This Phase 2 trial is being conducted in two successive cohorts, the first of which will involve up to approximately 44 patients from multiple U.S. dialysis centers treated in a randomized, open-label fashion with either RAYALDEE or placebo for 26 weeks. The second cohort will involve approximately 300 patients in multiple countries treated in a randomized, double-blind fashion with one of three

different doses of RAYALDEE or placebo for 26 weeks, followed by another 26 weeks in an open label extension.

The goals of the first cohort are as follows: (1) to evaluate whether patients can tolerate the highest dose of RAYALDEE (900 mcg/week) to be used in the second cohort; (2) to verify that calcifediol, the active ingredient in RAYALDEE, can be activated in the absence of functional kidneys; and (3) to determine whether RAYALDEE is capable of treating SHPT in patients with end-stage renal disease.

Interim results from 20 subjects who have completed at least 3 months of treatment indicate that all three goals are being met. Specifically, RAYALDEE is (1) well tolerated (absence of significant changes in serum calcium and phosphorus or increased incidence of adverse events), (2) activated (serum levels of calcitriol, the active metabolite, are elevated) and (3) capable of treating SHPT (≥30% decreases in iPTH are observed from pre-treatment baseline).

Full enrollment is expected in the second quarter of 2020, and final topline data are expected in the third quarter of 2020.

“We are pleased to announce positive preliminary data from the ongoing Phase 4 comparative trial, which suggest that RAYALDEE may more effectively raise serum total 25-hydroxyvitamin D to the level required to effectively suppress elevated iPTH,” commented Charles W. Bishop, PhD, Chief Executive Officer of OPKO’s Renal Division. “We are also pleased to announce positive proof-of-concept data from the ongoing Phase 2 trial. These data are at odds with conventional wisdom that calcifediol is unlikely to be activated in patients who lack functional kidneys, and, while early, they indicate that RAYALDEE may be useful in treating SHPT in the growing global population of dialysis patients.”

About RAYALDEE

RAYALDEE is an extended release formulation of calcifediol, a prohormone of calcitriol, the active form of vitamin D_3. The product is the only medicine approved by the U.S. Food and Drug Administration that raises serum total 25-hydroxyvitamin D and lowers blood levels of iPTH. RAYALDEE, approved to treat SHPT in adults with stage 3 or 4 CKD and vitamin D insufficiency, was launched in November 2016. It is not yet approved for patients with stage 5 CKD on dialysis.

About OPKO Health, Inc.

OPKO Health is a diversified healthcare company. In diagnostics, its BioReference Laboratories is one of the nation's largest full-service clinical laboratories; GeneDx is a rapidly growing genetic testing business; the 4Kscore® test is used to assess a patient’s individual risk for aggressive prostate cancer following an elevated PSA and to help decide about next steps such as prostate biopsy; Claros® 1 is a point-of-care diagnostics platform with a total PSA test approved by the FDA. In our pharmaceutical pipeline, RAYALDEE is our first pharmaceutical product to be marketed. OPK88003, a once-weekly oxyntomodulin for type 2 diabetes and obesity - reported positive data from a Phase 2 clinical trial. It’s among a new class of GLP-1/glucagon receptor dual agonists. OPK88004, a SARM (selective androgen receptor modulator) is currently being studied for various potential indications. The Company’s most advanced product utilizing its CTP technology, a once-weekly human growth hormone for injection, successfully met its primary endpoint and key secondary endpoints in a Phase 3 study and is partnered with Pfizer. OPKO also has research, development, production and distribution facilities abroad.

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," "could," "may," "anticipates," "believes," "should," "intends," "estimates," and other words of similar meaning, including product development efforts and the expected benefits of RAYALDEE, whether and when we will complete the clinical studies contemplated for RAYALDEE and whether final study data will be positive, our ability to develop and commercialize RAYALDEE, whether RAYALDEE is capable of treating SHPT in patients with end-stage renal disease, whether RAYALDEE will prove effective in treating patients with stage 5 CKD undergoing hemodialysis, whether RAYALDEE will be more effective than comparator products in raising serum total 25-hydroxyvitamin D to the range of 50 to 100 ng/mL and suppressing elevated plasma intact parathyroid hormone, 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 Reports on Form 10-K filed and to be filed with the Securities and Exchange Commission and in our other filings with the Securities and Exchange Commission, as well as liquidity issues and the risks inherent in funding, developing and obtaining regulatory approvals of new, commercially-viable and competitive products and treatments, the success of our relationship with our commercial partners for RAYALDEE, that earlier clinical results of effectiveness and safety may not be reproducible or indicative of future results, and that currently available over-the-counter and prescription products, as well as products under development by others, may prove to be as or more effective than our products for the indications being studied. 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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