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OPKO Health Announces Topline Results from Phase 2 Trial Evaluating RAYALDEE to Treat Symptomatic COVID-19 Outpatients

Preliminary data indicate that improving vitamin D status with oral RAYALDEE results in earlier resolution of respiratory symptoms associated with COVID-19

MIAMI, Dec. 23, 2021 (GLOBE NEWSWIRE) -- **OPKO Health, Inc. (NASDAQ: OPK)** announces preliminary topline results from its Phase 2 trial with RAYALDEE® to treat mild-to-moderate COVID-19. This study builds on increasing medical evidence that vitamin D repletion therapy can mitigate the severity of upper respiratory tract infections and accelerate recovery from COVID-19.

RAYALDEE, after oral administration, gradually releases calcifediol, the natural storage form of vitamin D_3, to safely and reliably raise a patient's serum total 25-hydroxyvitamin D (25D) well above current targets of 20 or 30 ng/mL. RAYALDEE is approved in the U.S. and many European countries for treating secondary hyperparathyroidism in non-dialysis chronic kidney disease (CKD) patients by raising 25D to levels as high as 100 ng/mL.

In the Phase 2 trial, titled "A Randomized, Double-Blind Placebo-Controlled Study to Evaluate the Safety and Efficacy of **R**AYALDEE (calcifediol) **E**xtended-relea**s**e **C**aps**ul**e**s** to Treat Symptomatic Patients Infected with SARS-CoV-2 (**REsCue**)," 171 symptomatic COVID-19 outpatients were enrolled from multiple U.S. sites and randomized in a 1:1 ratio for 4 weeks of treatment with RAYALDEE or placebo and a 2-week follow-up. Dosing with RAYALDEE was designed to progressively raise serum 25D to 50 to 100 ng/mL by Day 7, beginning with 300 mcg on Days 1, 2 and 3 followed by 60 mcg per day on Days 4 through 27. COVID-19 symptoms were self-reported daily during the 42-day study using the FLU-PRO Plus© questionnaire, an outcome tool validated for upper respiratory tract infections. Blood samples and safety assessments were obtained at 7-day intervals.

One primary efficacy endpoint was reaching the targeted serum 25D level. By Day 7, mean serum 25D levels increased with RAYALDEE treatment to 82 ng/mL ($p<0.001$) and remained elevated for the duration of the trial, with 88% of subjects attaining the targeted level. In contrast, mean 25D declined slightly with placebo treatment.

A second primary efficacy endpoint was the benefit of raising serum 25D on the time to resolution of five COVID-19 symptoms: trouble breathing, chest congestion, dry or hacking cough, body aches and pains, and chills and shivering. The three symptoms related to respiratory function, evaluated together, resolved more quickly when serum 25D was

elevated at Days 7 and 14 (Wilcoxon p<0.05), with resolution of chest congestion occurring 3.4 days sooner (Wilcoxon p<0.05). In subjects achieving increases in serum 25D of at least 25 ng/mL, chest congestion resolution occurred 4 days earlier (Wilcoxon p< 0.05). The mean time to resolution for all five symptoms considered in aggregate was not significantly different between the treatment groups since symptoms unrelated to respiratory function were unresponsive to treatment.

The average age of enrolled subjects was 43; 57% were female, 93% White, 6% African-American,1% Other. Nearly 40% were obese and 79% overweight, based on body mass index (BMI) greater than 30 or 25, respectively. Approximately 30% had comorbidities, most commonly hypertension.

Safety endpoints included vital signs, physical examinations, adverse events, electrocardiograms and biochemical assessments, all of which showed no meaningful changes with treatment.

About RAYALDEE

RAYALDEE is an extended-release oral formulation of calcifediol, a prohormone of calcitriol, the active form of vitamin D_3. The product is the first and only medicine approved by the U.S. Food and Drug Administration (FDA) for raising serum total 25D and lowering blood levels of intact parathyroid hormone (iPTH). RAYALDEE, approved to treat secondary hyperparathyroidism (SHPT) in adults with stage 3 or 4 CKD and vitamin D insufficiency, was launched in the U.S. in November 2016.

About OPKO Health, Inc.

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 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," "could," "may," "anticipates," "believes," "should," "intends," "estimates," and other words of similar meaning, including the expected benefits of RAYALDEE, whether final data for the clinical study will be positive, whether RAYALDEE is capable of treating patients with COVID-19 including whether RAYALDEE could impact the SARS-CoV-2 virus, or have any impact on the severity of the disease or that it will effectively raise and maintain serum total 25D consistently at or above 50ng/mL, whether further clinical studies utilizing RAYALDEE to treat patients with COVID-19 will be conducted or, if conducted, will show positive results or results consistent with the REsCue trial, whether we will seek approval to commercialize RAYALDEE for COVID-19 patients and whether such approval, on an emergency use basis or otherwise, will be obtained, as well as other non-historical statements about our expectations, beliefs or intentions regarding our technologies and products, 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 the risks 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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