

## PRESS RELEASE

Date 9 May 2016

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Subject Vifor Fresenius Medical Care Renal Pharma acquires marketing rights to RAYALDEE®

### **Vifor Fresenius Medical Care Renal Pharma and OPKO Health enter into Agreement for OPKO's RAYALDEE®**

**Vifor Fresenius Medical Care Renal Pharma (VFMCRP), a common company of Galenica and Fresenius Medical Care, and OPKO Health (NYSE: OPK), have entered into a collaboration and license agreement for the development and commercialisation of RAYALDEE® in Europe, Canada, Mexico, Australia, South Korea and certain other international markets for the treatment of secondary hyperparathyroidism (SHPT) in patients with chronic kidney disease (CKD) and vitamin D insufficiency. Under the terms of the agreement, the parties will also collaborate to develop and commercialise RAYALDEE® for the treatment of SHPT in dialysis patients, and OPKO has granted VFMCRP an option to acquire rights to the US market for treatment of dialysis patients.**

SHPT is a common disorder in CKD patients triggered by vitamin D insufficiency, which can cause reduced vitamin D hormone production, decreased intestinal absorption of dietary calcium, increased secretion of parathyroid hormone (PTH), and metabolic bone disease. Using current treatment options, most patients underachieve control of both vitamin D insufficiency and SHPT, leading to a range of bone and mineral disorders.

RAYALDEE® is an oral vitamin D prohormone treatment in a modified release capsule being developed by OPKO. VFMCRP has entered into an exclusive license agreement with OPKO to co-develop and commercialize RAYALDEE® in leading markets around the world, including Europe (except Russia), Canada, Mexico, Australia and South Korea. OPKO retains all rights in the US, Latin America (excluding Mexico), Russia, China, Taiwan and Japan. Furthermore OPKO has granted VFMCRP an option to acquire rights to the US market for treatment of dialysis patients. The two companies will also collaborate to prepare the Marketing Authorization Application (MAA) submission to the European Medicines Agency (EMA).

Currently the management of bone and mineral disorders in CKD patients remains a challenge for physicians despite the treatment options already available to them. The clinical data for RAYALDEE® show promising safety and efficacy and, therefore, once approved, RAYALDEE® will become an important additional step in the care of chronic kidney disease patients.

OPKO submitted a New Drug Application (NDA) for RAYALDEE® to the US Food and Drug Administration (FDA) in 2015 for the treatment of SHPT in patients with stage 3 or 4 CKD and vitamin D insufficiency. On 29 March 2016, the FDA indicated in a Complete Response Letter (CRL) that observations of deficiencies at OPKO's third-party contract manufacturer were issued on March 25, 2016, as a result of an FDA field inspection initiated on March 14, 2016. The observations were not specific to RAYALDEE® manufacturing. The CRL did not cite any safety, efficacy or labelling issues with regard to RAYALDEE®, nor did it request that additional studies be conducted prior to FDA approval. OPKO subsequently resubmitted its NDA to the FDA, and the FDA accepted OPKO's resubmission on April 22, 2016. The new Prescription Drug User Fee Act (PDUFA) date is October 22, 2016.

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The NDA is supported by data from three randomized, double-blind, placebo-controlled studies and one open label extension study conducted in the targeted patient population at 105 US sites. These studies met all primary efficacy and safety endpoints, confirming the anticipated product profile of RAYALDEE's ability to correct vitamin D insufficiency and treat SHPT without meaningfully increasing serum calcium or phosphorus levels.

Under the agreement, VFMCRP will make an upfront payment to OPKO of USD 50 million, plus up to an additional USD 52 million in regulatory and launch milestones, and USD 180 million in sales-based milestones. In addition, VFMCRP will pay OPKO tiered, double-digit royalties on sales of the product. In the event VFMCRP exercises its option for rights to the US dialysis market, VFMCRP will pay OPKO additional commercial-based milestones, as well as double-digit royalties.

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***Galenica** is a diversified Group active throughout the healthcare market which, among other activities, develops, manufactures and markets pharmaceutical products, runs pharmacies, provides logistical and database services and sets up networks. With its two Business units Vifor Pharma and Galenica Santé, the Galenica Group enjoys a leading position in all its core business activities. A large part of the Group's income is generated by international operations. Galenica is listed on the Swiss Stock Exchange (SIX Swiss Exchange, GALN, security number 1,553,646). Additional information concerning the Galenica Group can be found at [www.galenica.com](http://www.galenica.com).*

***Fresenius Medical Care** is the world's largest provider of products and services for individuals with renal diseases of which about 2.8 million patients worldwide regularly undergo dialysis treatment. Through its network of 3,418 dialysis clinics, Fresenius Medical Care provides dialysis treatments for 294,381 patients around the globe. Fresenius Medical Care is also the leading provider of dialysis products such as dialysis machines or dialyzers. Along with the core business, the company focuses on expanding the range of additional medical services in the field of care coordination. For more information about Fresenius Medical Care, visit the company's website at [www.freseniusmedicalcare.com](http://www.freseniusmedicalcare.com).*

***Vifor Fresenius Medical Care Renal Pharma Ltd.**, a common company of Galenica and Fresenius Medical Care, develops and commercialises innovative and high quality therapies to improve the life of patients suffering from Chronic Kidney Disease (CKD) worldwide. The company was founded at the end of 2010 and is owned 55% by Galenica and 45% by Fresenius Medical Care.*

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**OPKO Health, Inc.** is a diversified healthcare company that seeks to establish industry-leading positions in large, rapidly growing markets. OPKO's diagnostics business includes BioReference Laboratories, the third-largest clinical laboratory in the US with a core genetic testing business and a 420-person sales force to drive growth and leverage new products, including the 4Kscore® prostate cancer test and the Claros® 1 in office immunoassay platform. OPKO's pharmaceutical business features RAYALDEE, a treatment for SHPT in stage 3-4 CKD patients with vitamin D insufficiency, and VARUBI™ for chemotherapy-induced nausea and vomiting (oral formulation approved by FDA and launched by partner Tesaro, IV formulation in Phase 3). OPKO's biologics business includes hGH-CTP, a once-weekly human growth hormone injection (in Phase 3 and partnered with Pfizer), and a long-acting Factor VIIa drug for hemophilia (in Phase 2a). OPKO also has production and distribution assets worldwide, multiple strategic investments and an active business development strategy. More information is available at [www.opko.com](http://www.opko.com).

**RAYALDEE®** (calcifediol) extended-release capsules are being developed for the treatment of SHPT in adult patients with stage 3 or 4 CKD and serum total 25-hydroxyvitamin D levels less than 30 ng/mL. RAYALDEE® has a proprietary formulation designed to raise serum total 25-hydroxyvitamin D (prohormone) concentrations to targeted levels (at least 30 ng/mL) and to reduce elevated iPTH (intact parathyroid hormone).

**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 US, 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.

**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 25D. 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.

**Secondary Hyperparathyroidism (SHPT)** is a condition commonly associated with CKD in which the parathyroid glands secrete excessive amounts of parathyroid hormone (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 advanced CKD.