OPKO continues to make progress with its program to build a company capable of long-term growth and increasing value to its investors and I would like to review several highlights.

Rolapitant

Rolapitant, a new molecule divested by Schering-Plough as a part of its merger with Merck & Company and acquired by OPKO, is now in the midst of a large scale international Phase III clinical trial. Rolapitant, designed to prevent the nausea and vomiting associated with cancer chemotherapy, has the advantage of working for several days after taking a single tablet. We met with the FDA to prepare for the Phase III trial and then decided to license this product to TESARO, Inc., a small company whose management previously had great experience in developing and marketing another drug for the same indication and eventually made their product the market leader even though it was fourth in its category to come to market. OPKO will receive milestone payments and significant royalties as the product goes through the approval process and comes to market. As part of the license agreement, OPKO also received shares in TESARO which recently filed a registration statement with the SEC in anticipation of “going public.” Along with rolapitant, OPKO also acquired another NK-1 inhibitor which had been in Phase II trials for chronic cough and bladder hyperactivity. OPKO is now exploring opportunities to develop this new molecule for these and other indications.

AntagoNAT – Natural Antisense Transcript Inhibitors

Early in 2011, OPKO acquired CURNA, Inc., a privately-held company with technology to up regulate the production of specific messenger RNA molecules which, in turn, produce specific proteins (enzymes or structural proteins) in deficient patients or others who could benefit from producing more of a given protein. Patients with a wide variety of illnesses such as cancer, heart disease, metabolic disorders and genetic anomalies could benefit from such drugs. This approach has now been validated in vitro for a large number of conditions and in animal models for several others. As an example, we have made several oligonucleotides which enhance the production of a protein deficient in Dravet’s syndrome, a disease without a viable treatment option which is characterized by frequent seizures beginning in infancy. We have now produced a mouse model with the same specific deficiency and shown that one of our new oligonucleotides can decrease the frequency of seizures in this model. We will study this potential drug in larger animals and begin pre-clinical toxicology studies in preparation for human trials. We are also developing and studying new oligonucleotides for other diseases.

Asthma and COPD

Work is continuing with our new drug to treat asthma, COPD and cystic fibrosis. Although it has already been administered to humans in an inhaled dosage form, we have decided to develop it first as an orally administered drug. Because of the continuing growth of this market and the need for new drugs such as ours which work with a completely different mechanism of action from those presently used, we are enthusiastic about its future importance. Additional pre-clinical toxicology studies are needed before resuming clinical trials for the oral dosage form.

Neurodegenerative Disorders

OPKO recently announced the license of a new molecule from The Scripps Research Institute which, in animal studies, has been shown to inhibit death of nerve cells in an animal model of Parkinson’s disease. The potential new drug inhibits the JNK kinase receptors which form part of the pathway leading to apoptosis (cell death). Because death of brain neural cells is common in a variety of neurodegenerative diseases such as Alzheimer’s and Parkinson’s disease, ALS and multiple sclerosis, we are keen to actively develop this product.

Molecular Diagnostics

OPKO has two new major platforms in the diagnostics area. We have previously announced a technology to develop simple new blood tests for a large number of diseases. For one of these, Alzheimer’s disease, we are
cooperating with Bristol-Myers Squibb to explore areas of possible cooperation on the Alzheimer’s test and for identifying patients with early stage cognitive impairment that are likely to progress to Alzheimer’s disease. More recently, we announced a collaboration with LabCorp for them to complete the development and then commercialize the Alzheimer’s test as a “laboratory-developed test.” LabCorp will then market this product under a profit-sharing arrangement with OPKO.

We have, during the past year, acquired a Boston-based company, Claros Diagnostics, Inc., which has developed a proprietary new platform utilizing microfluidics technology to perform point-of-care diagnostic tests. These tests require only a finger stick drop of blood which, applied to a credit-card size cassette, provide quantitative results within 10 minutes. The first test to be marketed, PSA for prostate cancer, has already been approved in Europe and is in the midst of trials in the U.S. prior to application for approval here. We believe this test has large commercial potential, as over 30 million PSA tests were performed in the U.S. last year and, although there is discussion as to the appropriate number of tests that should be performed, we think it will continue to be a valuable test. More recently, we licensed additional proprietary markers for prostate cancer which, used together with the PSA marker, provide more precise data as to the aggressiveness of a tumor which might be present. Published data on a large number of patients indicate that as many as 60% of the biopsies being performed can be avoided utilizing these new markers. We believe that our new prostate panel, developed and endorsed by leading urological surgeons, will be widely used. Naturally, our new microfluidics platform lends itself for use with a large number of tests and panels of tests (several can be put on each disposable card) and others are at different stages of development.

Commercial Activities

In addition to our significant research and development activities, we continue to expand the commercial side of our business. In December 2011, we acquired a specialty active pharmaceutical ingredients manufacturer in Israel, which is generating revenue and positive cash flow. We have also expanded our commercial activities in emerging markets and have acquired a second company in Chile which will function in a synergistic way with OPKO Chile, our existing Chilean subsidiary. Our Mexican subsidiary also continues to increase sales and profits. Through these subsidiaries, as well as future acquisitions in other countries, we hope to generate positive cash flow to support our research and development activities and to facilitate a distribution network for our diagnostic and pharmaceutical products.

Strategic Investments and Transactions

OPKO has and will likely continue to make investments in other early stage companies that we perceive to have valuable proprietary technology and significant potential to create value for OPKO as a shareholder.

The OPKO team thanks you for your support.

Very truly yours,

Phillip Frost, M.D.
Chairman and
Chief Executive Officer