



OPKO Health Announces Positive Top-Line Results of Phase 3 Efficacy and Safety Study of Somatrogon for the Treatment of Japanese Children with Growth Hormone Deficiency

MIAMI (June 9, 2020) – Following last October’s [announcement](#) of successful results of the global Phase 3 study of once-weekly somatrogon, an investigational agent for the treatment of pediatric growth hormone deficiency (pGHD), OPKO Health Inc. (NASDAQ: OPK) announced today that the Japan Phase 3 clinical trial met its primary and secondary objectives, and demonstrated that the efficacy and safety of somatrogon administered weekly was comparable to GENOTROPIN® (somatropin) for injection administered once-daily as measured by annual height velocity after 12 months of treatment in treatment-naïve Japanese pre-pubertal children with GHD. The findings were consistent with the results previously reported in the Phase 3 global study.

Using the Full Analysis Set, the least squared means for the annual height velocity was higher in the somatrogon group (9.65 cm/year) than in the GENOTROPIN group (7.87 cm/year). The point estimate of the treatment difference was 1.79 cm/year with the two-sided 95% confidence interval of (0.97, 2.60). Similarly, greater change in height standard deviation score from baseline at 12 months was observed for the somatrogon group (0.94) compared to the GENOTROPIN group (0.52), indicating that both somatrogon and GENOTROPIN were associated with catch-up growth in treated patients.

Most adverse events were mild to moderate in severity with no notable differences between the treatment groups, and weekly somatrogon administration was generally well-tolerated. A total of six serious adverse events were reported in four patients (two in the somatrogon arm and two in the GENOTROPIN arm). One patient in the GENOTROPIN group discontinued treatment in the study due to adverse events.

“We are pleased to announce positive top-line results from the Japanese Phase 3 clinical study of somatrogon. We have reached an additional clinical development milestone of somatrogon with the demonstration of comparable efficacy and safety of somatrogon administered once-weekly to daily administration of GENOTROPIN in pediatric patients with growth hormone deficiency,” said Phillip Frost, M.D., Chairman and Chief Executive Officer of OPKO. “Positive results in both the Japanese and pivotal global Phase 3 pediatric trials are promising for children with pGHD. Treatment with once-weekly somatrogon represents a significant advance, which has the potential to enhance patient adherence and quality of life.”

“The data from the Japan Phase 3 trial are very encouraging and point to the potential of bringing a once-weekly treatment option to children with pGHD. We are committed to furthering treatment advances for people living with rare growth hormone disorders and this is an exciting

advance that may help ease the daily disease burden for children and their caregivers,” said Brenda Cooperstone, M.D., Chief Development Officer, Rare Disease, Pfizer Global Product Development.

In 2014, Pfizer and OPKO entered into a worldwide agreement for the development and commercialization of somatrogon for the treatment of GHD. Under the agreement, OPKO is responsible for conducting the clinical program and Pfizer is responsible for registering and commercializing the product. The companies will evaluate the potential for additional pediatric and adult indications, as appropriate.

About the Study

The Phase 3 study of somatrogon in 44 treatment-naïve Japanese pre-pubertal children with pGHD was a 12-month, open-label, randomized, active-controlled, parallel-group study of the efficacy and safety of weekly somatrogon compared to recombinant human growth hormone (r-hGH), GENOTROPIN® (somatropin) for injection treatment administered once-daily. Eligible patients were randomized in a 1:1 ratio to receive either once-weekly somatrogon or GENOTROPIN administered once-daily (reference therapy, 0.025 mg/kg/day which is equivalent to 0.175 mg/kg/week). To obtain pharmacokinetic information of three different weekly doses in Japanese pGHD patients, somatrogon treated patients received 0.25 mg/kg/week for 2 weeks, followed by 0.48 mg/kg/week for 2 weeks followed by 0.66 mg/kg/week for the remaining 46 weeks. Somatrogon was administered subcutaneously using a single patient use, multi-dose, disposable, pre-filled pen, the same pen used in the global study, while GENOTROPIN was administered using approved commercial products in Japan.

Patients who completed the 12-month Main Study Period and met the inclusion criteria were given the opportunity to continue in a long-term open label extension period with once-weekly somatrogon until marketing approval. All patients in the GENOTROPIN group have been switched to weekly somatrogon treatment.

About Somatrogon

Somatrogon is a new molecular entity that contains the natural sequence of human growth hormone and one copy of the C-terminal peptide (CTP) from the beta chain of human chorionic hCG at the N-terminus and two copies at the C-terminus. The CTPs extend the half-life of the molecule. Somatrogon received Orphan Drug designation in the U.S. and the EU for the treatment of children and adults with growth hormone deficiency.

About Growth Hormone Deficiency

Growth hormone deficiency is a rare disease characterized by the inadequate secretion of growth hormone from the pituitary gland and affects one in approximately 4,000 to 10,000 people. In children, this disease can be caused by genetic mutations or acquired after birth. Because the patient's pituitary gland secretes inadequate levels of somatropin, the hormone that causes growth, his or her height may be affected and puberty may be delayed. Without treatment, he or she will have persistent growth attenuation, a very short height in adulthood and may experience other health problems.

About GENOTROPIN®

GENOTROPIN is a recombinant growth hormone as a replacement treatment option, approved in the United States for children who do not make enough growth hormone on their own, have the genetic condition called Prader-Willi syndrome (PWS), were born smaller than most other babies, have the genetic condition called Turner syndrome (TS) or have idiopathic short stature (ISS). GENOTROPIN is also approved in the United States to treat adults with growth hormone deficiency. GENOTROPIN is taken by injection just below the skin and is available in a wide range of devices to fit a range of individual dosing needs. GENOTROPIN is distributed by Pharmacia and Upjohn Co., a division of Pfizer, Inc.

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 release contains forward-looking information about a product candidate, somatrogon dosed once-weekly in pre-pubertal children with growth hormone deficiency (or GHD), including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications may be filed in any jurisdictions for somatrogon; whether and when any such applications may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether somatrogon will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of somatrogon; and competitive developments.

A further description of risks and uncertainties can be found in OPKO's Annual Reports on Form 10-K for the fiscal year ended December 31, 2019 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors", "Forward-Looking Information and Factors That May Affect Future Results", "Cautionary Statement Regarding Forward-Looking Statements", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.OPKO.com.

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