Ascendis Pharma A/S Presents 6-Month Open-Label Extension Data from Phase 2 PaTH Forward Trial of TransCon PTH in Adult Hypoparathyroidism at ENDO 2021

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Clinical data demonstrate the potential of TransCon PTH as a hormone replacement therapy for adults with hypoparathyroidism

COPENHAGEN, Denmark, March 23, 2021 (GLOBE NEWSWIRE) -- Ascendis Pharma A/S (Nasdaq: ASND), a biopharmaceutical company that utilizes its innovative TransCon™ technologies to create product candidates that address unmet medical needs, today presented the safety and efficacy results of TransCon PTH after six-months of treatment in patients with hypoparathyroidism enrolled in the open-label extension period (OLE) of the phase 2 PaTH Forward Trial, at the Endocrine Society's annual meeting, taking place virtually from March 20-23, 2021.

"The study demonstrated that a majority of subjects were able to achieve independence from conventional therapeutic supplements, while maintaining serum calcium in the normal range and having clinically meaningful improvements in urine calcium levels, bone turnover markers and bone mineral density and quality of life," said Mishaela Rubin, M.D. M.S., Associate Professor of Medicine in the Metabolic Bone Disease Unit at the Vagelos College of Physicians & Surgeons at Columbia University Irving Medical Center in New York City. "Importantly, we are presenting the first data on the treatment effect of TransCon PTH on the Hypoparathyroidism Patient Experience Scale (HPES). In this study, HPES scores all decreased from baseline to Week 26, indicating fewer and less impact of disease-specific symptoms. These data are promising and TransCon PTH may offer a new potential treatment option for patients with hypoparathyroidism, many of whom have their daily lives disrupted by the disorder."

Presentation Details and Data Highlights[1]
Presentation title: TransCon PTH as a Hormone Replacement Therapy for Patients with Hypoparathyroidism: 6-Month Update from the PaTH Forward Open-Label Extension in 58 subjects.
Oral session: Novel Treatments for Metabolic Bone Diseases; March 23, 2021 at 2:15 to 2:25 p.m. EDT.
Presenter: Mishaela Rubin, M.D. M.S.
Summary of findings: Six-month results from the PaTH Forward OLE demonstrated:

- Over 90 percent of subjects demonstrated independence from standard-of-care (calcium ≤ 500 mg/day and active vitamin D = 0 µg/day) and 76 percent of subjects eliminated all supplements while:
  - Maintaining mean serum calcium in the normal range
  - Reducing mean 24-hour urine calcium to within the normal range
  - Achieving sustained reductions in mean serum phosphate and calcium x phosphate product
  - Demonstrating enhanced quality of life on both SF-36 Functional Health Survey and HPES
  - Trending towards normalization of skeletal remodeling.
- TransCon PTH continues to be well-tolerated:
  - No adverse events of hypocalcemia or hypercalcemia requiring visit to hospital, emergency room or urgent care.

"All 58 subjects in the open-label extension have now completed 12 months of treatment on TransCon PTH without any additional dropouts, which is a reflection of patient comfort with this once-daily injection as a chronic therapy for hypoparathyroidism," said Mark Bach, M.D., Ph.D., Senior Vice President of Endocrine Medical Sciences at Ascendis Pharma. "TransCon PTH is a potential hormone replacement therapy that was designed to restore calcium metabolism and improve quality of life for people with hypoparathyroidism, and we plan to present the 12-month results at an upcoming scientific meeting."

In addition, to PaTH Forward, Ascendis Pharma is conducting the PaTHway Trial, a phase 3 clinical study evaluating the safety, tolerability and efficacy of TransCon PTH in adults with HP. Topline results are expected from PaTHway in the fourth quarter of 2021.

About the PaTH Forward Trial[1]

PaTH Forward is a global, phase 2, randomized, double-blind, placebo-controlled group trial evaluating the safety and efficacy of three fixed doses of TransCon PTH (15, 18 or 21 µg/day or placebo). The trial enrolled 59 adult subjects with chronic HP who received standard of care or were previously treated with PTH therapies. The goal of PaTH Forward is to evaluate TransCon PTH control of serum and urinary calcium and identify a titration regimen for complete withdrawal of standard of care (i.e., active vitamin D and calcium supplements). PaTH Forward has introduced a ready-to-use pre-filled pen injector and assesses disease-specific patient-reported outcomes. After four weeks of fixed dosing, all subjects were eligible to enter an open-label extension period with the opportunity to receive a customized maintenance dose of TransCon PTH to evaluate long-term safety and efficacy.

About TransCon PTH[2]

TransCon PTH is an investigational once-daily long-acting prodrug of parathyroid hormone (PTH[1-34]) in development as a treatment for adult hypoparathyroidism (HP) designed to restore PTH at physiologic levels for 24 hours each day to address both the short-term symptoms and long-term complications of the disease. TransCon PTH was granted Orphan Drug Designation (ODD) by the U.S. Food and Drug Administration (FDA) in June 2018, and in October 2020 was granted Orphan Designation by the European Commission for the treatment of hypoparathyroidism.

About Hypoparathyroidism (HP) [3,4,5,6,7,8]

Hypoparathyroidism (HP) is a rare endocrine disorder characterized by insufficient levels of parathyroid hormone (PTH), resulting in low calcium and elevated phosphate levels in the blood. HP affects approximately 200,000 patients in the United States, Europe, Japan and South Korea, the majority of whom develop the condition following damage or accidental removal of the parathyroid glands during thyroid surgery. Patients often experience decreased quality of life. In the short term, symptoms include weakness, severe muscle cramps (tetany), abnormal sensations such as tingling, burning and numbness (paresthesia), memory loss, impaired judgment and headache. Over the long term, this complex disorder can increase risk of major complications, such as extraskeletal calcium depositions occurring within the brain, lens of the eye, and kidneys, which can lead to impaired renal function.

HP remains among the few hormonal insufficiency states without a replacement therapy that restores the missing hormone at physiologic levels. Standard of care with active vitamin D analogs and calcium supplementation do not fully control the disease and may contribute to risk of renal disease. As a result, patients with HP have an estimated 4-fold to 8-fold greater risk of renal disease compared to healthy controls.

About TransCon™ Technology

TransCon refers to “transient conjugation.” The proprietary TransCon platform is an innovative technology to create new therapies that are designed to potentially optimize therapeutic effect, including efficacy, safety and dosing frequency. TransCon molecules have three components: an unmodified parent drug, an inert carrier that protects it, and a linker that temporarily binds the two. When bound, the carrier inactivates and shields the parent drug from clearance. When injected into the body, physiologic conditions (e.g., pH and temperature) initiate the release of the active, unmodified parent drug in a predictable manner. Because the parent drug is unmodified, its original mode of action is expected to be maintained. TransCon technology can be applied broadly to a protein, peptide or small molecule in multiple therapeutic areas, and can be used systemically or locally.

About Ascendis Pharma A/S

Ascendis Pharma is applying its innovative TransCon technologies to build a leading, fully integrated biopharmaceutical company focused on making a meaningful difference in patients’ lives. Guided by its core values of patients, science and passion, the company utilizes its TransCon technologies to create new and potentially best-in-class therapies.

Ascendis Pharma currently has a pipeline of three independent endocrinology rare disease product candidates and one oncology product candidate in clinical development. The company continues to expand into additional therapeutic areas to address unmet patient needs.

Ascendis is headquartered in Copenhagen, Denmark, with additional offices in Heidelberg and Berlin, Germany, Palo Alto and Redwood City, California, and Princeton, New Jersey.

Please visit www.ascendispharma.com (for global information) or www.ascendispharma.us (for U.S. information.)

Forward-Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this press release regarding Ascendis’ future operations, plans and objectives of management are forward-looking statements. Examples of such statements include, but are not limited to, statements relating to (i) Topline results expected from PaTHway in the fourth quarter of 2021; (ii) Ascendis’ ability to apply its platform technology to build a leading, fully integrated biopharmaceutical company, (iii) Ascendis’ product pipeline and expansion into additional therapeutic areas and (iv) Ascendis’ expectations regarding its ability to utilize its TransCon technologies to create new and potentially best-in-class therapies. Ascendis may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in the forward-looking statements and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions, expectations and projections disclosed in the forward-looking statements. Various important factors could cause actual results or events to differ materially from the forward-looking statements that Ascendis makes, including the following: unforeseen safety or efficacy results in its oncology programs, TransCon hGH, TransCon PTH and TransCon CNP or other development programs; unforeseen expenses related to the development and potential commercialization of its oncology programs, TransCon hGH, TransCon PTH and TransCon CNP or other development programs, selling, general and administrative expenses, other research and development expenses and Ascendis’ business generally; delays in the development of its oncology programs, TransCon hGH, TransCon PTH and TransCon CNP or other development programs related to manufacturing, regulatory requirements, speed of patient recruitment or other unforeseen delays; dependence on third party manufacturers to supply study drug for planned clinical studies; Ascendis’ ability to obtain additional funding, if needed, to support its business activities and the effects on its business from the worldwide COVID-19 pandemic. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to Ascendis’ business in general, see Ascendis’ Annual Report on Form 20-F filed with the U.S. Securities and Exchange Commission (SEC) on March 10, 2021 and Ascendis’ other future reports filed with, or submitted to, the SEC. Forward-looking statements do not reflect the potential impact of any future in-licensing, collaborations, acquisitions, mergers, dispositions, joint ventures, or investments that Ascendis may enter into or make. Ascendis does not assume any obligation to update any forward-looking statements, except as required by law.

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