Ascendis Pharma A/S Announces Preliminary Six-Month Data from Open-Label Extension of Phase 2 PaTH Forward Trial and Files IND Amendment to Initiate Phase 3 PaTHway Trial of TransCon™ PTH in Adult Hypoparathyroidism

September 28, 2020 at 7:00 PM EDT

- Six-month data from PaTH Forward open-label extension support potential use of TransCon PTH as a hormone replacement therapy for adult hypoparathyroidism –

- Conference call Tuesday, September 29 at 8:00 a.m. Eastern Time to review data –

COPENHAGEN, Denmark, Sept. 29, 2020 (GLOBE NEWSWIRE) -- Ascendis Pharma A/S (Nasdaq: ASND), a biopharmaceutical company that utilizes its innovative TransCon technologies to address unmet medical needs, today announced preliminary six-month results from the open-label extension (OLE) portion of PaTH Forward, a global phase 2 trial evaluating the safety, tolerability and efficacy of TransCon PTH in adult subjects with hypoparathyroidism (HP).

"Today we announced preliminary clinical results which demonstrate that TransCon PTH can potentially provide a new treatment paradigm for over 150,000 HP patients in North America and Europe. These results showed that subjects in the trial continued on once-daily TransCon PTH independent of pill burden and consistently improved their quality of life, while at the same time demonstrating improvement in 24-hour urine calcium excretion and serum phosphate which may be associated with long-term complications[1,2]," said Jan Mikkelsen, President and CEO at Ascendis Pharma. "We have now filed an IND amendment to initiate the U.S. sites of the phase 3 PaTHway Trial evaluating TransCon PTH in adult patients with hypoparathyroidism, which will enable us to eventually provide this therapy to patients as soon as possible."

TransCon PTH is an investigational long-acting prodrug of parathyroid hormone (PTH) in development as a once-daily hormone replacement therapy for adult hypoparathyroidism designed to replace PTH at physiologic levels for 24 hours each day and addresses both short-term symptoms and long-term complications of HP. Fifty-nine subjects participated in the phase 2 PaTH Forward Trial and continued in the OLE, where they all received a customized maintenance dose of TransCon PTH (6 to 30 µg) with a ready-to-use, room temperature, prefilled pen injector. One subject randomized to placebo withdrew after completing the four-week double-blinded fixed-dose period for reasons unrelated to safety or efficacy of the study drug. All of the other 58 subjects remained on TransCon PTH at the time of the six month data cutoff.

IND Amendment Filed for Phase 3 PaTHway Trial
The company submitted an amendment to its investigational new drug application (IND) with the U.S. Food and Drug Administration (FDA) to initiate the U.S. sites of the PaTHway phase 3 clinical trial evaluating the safety, tolerability and efficacy of TransCon PTH in adults with HP following discussions with FDA and European regulatory authorities. The company expects to file the clinical trial application for the European arm later this year. The double-blind, placebo-controlled trial is expected to enroll approximately 76 subjects at sites in North America and Europe in order to obtain 68 evaluable subjects.

The primary composite endpoint of the PaTHway Trial at 26 weeks is the proportion of subjects with (1) serum calcium in the normal range, (2) independence from active vitamin D, and (3) taking ≤600 mg/day of calcium supplements.

Preliminary OLE Results of PaTH Forward Trial at 6 Months
Preliminary six-month results from the PaTH Forward OLE demonstrated:

- 91 percent of all subjects eliminated standard of care (defined as (1) off active vitamin D and (2) ≤500 mg per day of calcium supplements), including 76 percent who eliminated all supplements.
- 86 percent of all subjects normalized or reduced by 50 percent 24-hour urine calcium.
- 71 percent of all subjects achieved a response on the composite endpoint of (1) serum calcium in the normal range, (2) independence from active vitamin D, (3) taking ≤500 mg/day of calcium supplements, and (4) 24-hour urine calcium in the normal range or 50 percent reduction from baseline, including 74 percent of subjects who were randomized to TransCon PTH.
- All mean summary and subdomain SF-36® Health Survey scores normalized despite all mean scores starting below norms at baseline including subjects randomized to placebo who switched to TransCon PTH group at week 4. Importantly, subjects randomized to TransCon PTH demonstrated continued improvements from week 4 to month 6.
- All doses of TransCon PTH were well-tolerated, and no treatment-related serious or severe adverse events were observed at any point. No subjects had PTH treatment-emergent adverse events related to hyper- or hypocalcemia leading to emergency visit, urgent care visit, or hospitalization.
- Adherence to daily injections of TransCon PTH was 99.7 percent.

"For people living with hypoparathyroidism, this debilitating endocrine disease frequently disrupts daily activities, diminishes quality of life and often leads to long-term complications," Aimee Shu, M.D., Senior Medical Director, Clinical Development at Ascendis Pharma. "We are very encouraged by the results of TransCon PTH in the PaTH Forward Trial, which may eventually represent a new treatment paradigm for patients with this disorder."

A slide presentation with these data is available at the Investors & News section of the company's website here: https://investors.ascendispharma.com/

Conference Call Details

Date	September 29, 2020
Time	8:00 a.m. Eastern Time/5:00 a.m. Pacific Time/2:00 p.m. CEST
Dial In (U.S.)	(844) 290-3904
Dial In (International)	+1 (574) 990-1036
Access Code	8483406

A live webcast of the conference call will be available on the Investors and News section of the Ascendis Pharma website at www.ascendispharma.com. A webcast replay will be available on this website shortly after conclusion of the event for 30 days.

About the PaTH Forward Trial
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 the PaTHway Trial
PaTHway is a phase 3 clinical trial evaluating the safety, tolerability and efficacy of TransCon PTH in adults with HP. The trial is expected to enroll approximately 76 subjects at sites in North America and Europe in order to obtain 68 evaluable subjects. The primary composite endpoint of the PaTHway Trial at 26 weeks is the proportion of subjects with (1) serum calcium in the normal range, (2) independence from active vitamin D, and (3) taking ≤600 mg/day of calcium supplements. After 26 weeks, all subjects are eligible to enter an open-label extension period to evaluate long-term safety and efficacy.

About TransCon PTH[3]
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 replace 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) from the U.S. Food and Drug Administration (FDA) in June 2018.

About Hypoparathyroidism (HP) [4,5,6,7,8,9]
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 platform technology to build a leading, fully integrated biopharma 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 in clinical development and is advancing oncology as its second therapeutic area of focus. 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, and in Palo Alto and Redwood City, California.

For more information, please visit **www.ascendispharma.com.**

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) Ascendis' expectation to enroll approximately 76 subjects in the PaTHway phase 3 clinical trial at sites in North America and Europe, (ii) Ascendis' ability to apply its platform technology to build a leading, fully integrated biopharma 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 of 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' prospectus supplement filed on July 9, 2020 and Ascendis' current and future reports filed with, or submitted to, the U.S. Securities and Exchange Commission (SEC), including its Annual Report on Form 20-F filed with the SEC on April 3, 2020. 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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