Ascendis Pharma A/S Announces Top-line Data from Fixed Dose Portion of Phase 2 Trial Demonstrating Potential of TransCon™ PTH as a Replacement Therapy for Hypoparathyroidism

April 19, 2020 at 4:00 PM EDT

– PaTH Forward Trial met key objectives and showed that TransCon PTH eliminated standard of care in 82 percent of subjects within four weeks –

– Conference call today at 6 p.m. Eastern Time to review data –

COPENHAGEN, Denmark, April 19, 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 positive top-line results from the four-week fixed dose, blinded portion of PaTH Forward, a global phase 2 trial evaluating the safety, tolerability and efficacy of TransCon PTH in adult subjects with hypoparathyroidism (HP).

TransCon PTH is an investigational long-acting prodrug of parathyroid hormone (PTH) in development as a once-daily replacement therapy for adult hypoparathyroidism designed to replace PTH at physiologic levels for 24 hours each day and address both short-term symptoms and long-term complications of HP.

A total of 59 subjects were randomized in a blinded manner to receive fixed doses of TransCon PTH at 15, 18 or 21 µg/day or placebo for four weeks using a ready-to-use prefilled pen injector planned for commercial presentation. All doses of TransCon PTH were well-tolerated, and no serious or severe adverse events were shown at any point. No treatment-emergent adverse events (TEAEs) led to discontinuation of study drug, and the overall incidence of TEAEs was comparable between TransCon PTH and placebo. Additionally, there were no drop-outs during the four-week fixed dose period.

In the per protocol analysis (n=57), TransCon PTH eliminated standard of care (i.e. off active vitamin D and ≤ 500 mg per day of calcium supplements) in 100 percent of subjects in the highest dose arm (21 µg/day) and 82 percent of subjects across all dosage arms.

A slide presentation with top-line data is available at the Investors & News section of the company's website here: https://investors.ascendispharma.com/static-files/facf3f5e-2f0a-490a-974e-c2920f92641b

"With TransCon PTH, our goal has always been to improve the lives of patients with hypoparathyroidism, by designing a replacement therapy that restores physiologic levels of PTH 24 hours a day and that sets a new standard of care," said David B. Karpf, M.D., Ascendis Pharma's Vice President of Clinical Development. "These PaTH Forward data show the potential to completely remove standard of care while maintaining normal serum and urinary calcium levels, which could represent a major advance for patients with this complex, debilitating disease."

These results from the fixed dose portion of PaTH Forward demonstrated that TransCon PTH increased serum calcium levels, enabled discontinuation of active D and continuous calcium reduction of supplements over the four-week period. TransCon PTH reduced urinary calcium excretion (as measured by Fractional Excretion of Calcium or FECa) despite increased serum calcium, and resulted in sustained reductions in serum phosphate and calcium-phosphate product. At four weeks, the 21 µg/day arm and the combined TransCon PTH dosage arms showed a statistically significant response (p-value <0.05) in the primary composite endpoint compared to placebo in the per protocol analysis.

Fifty-eight subjects continue in the open-label extension portion of the trial, where they receive a customized maintenance dose of TransCon PTH (6 to 30 µg per day). The company plans to report six-month data from the open-label extension portion of the trial during the third quarter of 2020.

"Hypoparathyroidism has a significant negative impact on over 200,000 patients worldwide and is one of the last hormonal insufficiency disorders without an effective replacement therapy. With TransCon PTH, we have a unique opportunity to make a meaningful difference for patients on a global basis," said Jan Mikkelsen, Ascendis Pharma's President and Chief Executive Officer.

Ascendis Pharma plans to engage with global regulatory authorities on next steps for development of TransCon PTH, and submit regulatory filings to initiate a global phase 3 trial in North America, Europe and Asia in the fourth quarter of 2020.

Conference Call Details

Date	Sunday, April 19, 2020
Time	6:00 p.m. Eastern Time/3:00 p.m. Pacific Time 12:00 a.m. CET (Monday, April 20)
Dial In (U.S.)	(844) 290-3904
Dial In (International)	+1 (574) 990-1036
Access Code	9794795

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 PaTH Forward

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™ Technology

TransCon refers to “transient conjugation.” The proprietary TransCon platform is an innovative technology to create new therapies that 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 release 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 TransCon PTH

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)

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.

Until recently, HP remained among the few hormonal insufficiency states not treated by replacement of the missing hormone. 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 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, Germany and Palo Alto, 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 our 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) our plans to report six-month data from the open-label extension portion of the PaTH Forward Trial during the third quarter of 2020, (ii) our plans to engage with global regulatory authorities on next steps for development of TransCon PTH, (iii) our plans to submit regulatory filings to initiate a global phase 3 trial of in North America, Europe and Asia in the fourth quarter of 2020, (iv) our ability to apply our TransCon platform to build a leading, fully integrated biopharma company, (v) our expectations regarding our ability to create new and potentially best-in-class therapies and (vi) our product pipeline and expansion into additional therapeutic areas. We 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 we make, including the following: unforeseen safety or efficacy results in our TransCon hGH, TransCon PTH and TransCon CNP or other development programs; unforeseen expenses related to the development and potential commercialization of TransCon hGH, TransCon PTH and TransCon CNP or other development programs, general and administrative expenses, other research and development expenses and our business generally; delays in the development of 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; our ability to obtain additional funding, if needed, to support our business activities and the effects on our 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 our business in general, see our current and future reports filed with, or submitted to, the U.S. Securities and Exchange Commission (SEC), including our 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 we may enter into or make. We do not assume any obligation to update any forward-

looking statements, except as required by law.

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