PRESS RELEASE

# Ascendis Pharma A/S Announces Phase 3 PaTHway Trial of TransCon™ PTH in Adults with Hypoparathyroidism Met Primary and All Key Secondary Endpoints

- *For the primary composite endpoint, TransCon PTH demonstrated a response rate of 78.7% compared to 4.8% for control (p-value <0.0001).*
- *TransCon PTH demonstrated statistically significant improvements compared to control on all key secondary endpoints, which included measures evaluating patient-reported disease symptoms and impacts.*
- *TransCon PTH was generally well-tolerated, with no discontinuations related to study drug.*
- *On track to submit NDA during the third quarter and MAA during the fourth quarter of 2022.*
- *Conference call Monday, March 14th at 8:00 am ET.*

**COPENHAGEN, Denmark, March 13, 2022 (GLOBE NEWSWIRE) –** Ascendis Pharma A/S (Nasdaq: ASND) today announced that top-line data from the randomized, double-blind, placebo-controlled portion of its Phase 3 PaTHway Trial of TransCon PTH in adults with hypoparathyroidism (HP) demonstrated statistically significant improvement with TransCon PTH compared to control on the primary composite endpoint and all key secondary endpoints. The primary endpoint – defined as serum calcium levels in the normal range (8.3–10.6 mg/dL) and independence from conventional therapy (active vitamin D and >600 mg/day of calcium supplements) with no increase in prescribed study drug within the 4 weeks prior to the Week 26 visit – was achieved by 78.7% of TransCon PTH-treated patients (48 of 61), compared to 4.8% for patients (1 of 21) in control group (p-value <0.0001).

“Hypoparathyroidism is an area of major unmet medical need with an estimated 200,000 patients in the United States, Europe, and Japan. Conventional therapy with calcium supplements and active vitamin D is aimed at maintaining serum calcium in the normal range, with the hope of reducing short-term symptoms, and is not able to address the underlying disease. In addition, conventional therapy can lead to long-term complications that include severe diseases such as chronic kidney diseases, liver and basal ganglia calcifications, cardiovascular complications, and bone damage,” said Jan Mikkelsen, Ascendis Pharma’s President and CEO. “This is the first Phase 3 trial where more than three quarters of patients achieved control of their hypoparathyroidism, defined as normalization of serum calcium and independence from conventional therapy. This study also demonstrated statistically significant improvement in all pre-specified patient-reported symptom and quality-of-life domains.”

**Highlights of the Phase 3 PaTHway Trial Top-Line Data**

The PaTHway Trial is a Phase 3 double-blind, placebo-controlled trial of 82 dosed adults with chronic hypoparathyroidism randomized 3:1 (TransCon PTH:placebo).

**Primary Composite Endpoint:**

- 78.7% of TransCon PTH-treated patients (48 of 61) achieved serum calcium levels in the normal range (8.3–10.6 mg/dL) and independence from therapeutic levels of conventional therapy, compared to 4.8% for patients (1 of 21) in control group (p-value = <0.0001).

**Key Pre-Specified Secondary Endpoints:**

- Statistically significant decrease in patient-reported, disease-specific physical and cognitive symptoms compared to patients in control group, as shown on Hypoparathyroidism Patient Experience Scales (HPES) Symptom-Physical domain scores (p-value = 0.0038) and HPES Symptom-Cognitive domain scores (p-value = 0.0055).
- Statistically significant reduction in patient-reported disease impact compared to patients in control group, as shown on HPES Impact-Physical Functioning domain scores (p-value = 0.0046) and HPES Impact-Daily Life domain scores (p-value = 0.0061).
- Statistically significant improvements in patient-reported physical functioning compared to patients in control group, as shown on the SF-36v2® survey Physical Functioning subscale (p-value = 0.0347).

**Selected other analyses:**

- At Week 26, 95% of TransCon PTH-treated patients were able to discontinue conventional treatments with therapeutic levels of calcium supplements and active vitamin D.
- PaTHway patients had low levels of bone turnover at baseline. TransCon PTH-treated patients demonstrated increased levels of bone turnover markers at Week 26.

**Safety summary:**

- TransCon PTH was generally well tolerated, with no discontinuations related to study drug. Three patients discontinued during the treatment period – 2 from the placebo arm and 1 from the TransCon PTH arm.
- 82% of TransCon PTH patients and 100% of patients in control group reported treatment-emergent adverse events (TEAEs), the majority of which were Grade 1, 2 in severity.
- One serious related TEAE in the TransCon PTH arm was reported due to a dosing error.
- One death in the TransCon PTH arm was assessed as unrelated to study drug.
- TransCon PTH-treated patients showed a mean decrease in 24-hour urine calcium excretion into the normal range, from 390 mg/24 hours down to 220 mg/24 hours.

Despite a higher mean serum calcium at Week 26, there was a significantly greater decrease in mean 24-hour urine calcium for TransCon PTH-treated patients compared to patients in control group.

Following an initial blinded study period of 26 weeks, for which top-line data are reported here, all 79 patients completing the blinded period opted to receive treatment with TransCon PTH in the ongoing open-label extension portion of the study for up to 3 years (156 weeks). As of today, all 79 patients continue in the open label extension portion of the PaTHway Trial.

"On behalf of everyone at Ascendis Pharma, I want to express my thanks to patients, clinical investigators, and others involved in conducting this study and providing data to support the efforts to advance a potential new treatment option for adults with hypoparathyroidism," said Aimee Shu, M.D., Ascendis Pharma's Vice President of Clinical Development, Endocrine Medicine. "We look forward to discussing the results from this trial and the longer-term data from the Phase 2 PaTH Forward Trial with regulatory agencies in the near future."

Ascendis plans to submit a New Drug Application (NDA) to the U.S. Food & Drug Administration for TransCon PTH for adults with hypoparathyroidism during the third quarter of 2022 and a Marketing Authorisation Application (MAA) to the European Medicines Agency during the fourth quarter of 2022. Top-line results for the Phase 3 PaTHway Japan Trial are expected in the third quarter of 2022. In addition, Ascendis plans to initiate a clinical trial of TransCon PTH in pediatric hypoparathyroidism during the fourth quarter of 2022.

**Conference Call & Webcast Information**

Ascendis Pharma will host a conference call and webcast Monday, March 14th at 8:00 am Eastern Time (ET) to discuss the top-line Phase 3 PaTHway Trial results. Details include:

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| **Date** | Monday, March 14, 2022 |
| **Time** | 8 a.m. Eastern Time / 5 a.m. Pacific Time / 1 p.m. CET |
| **Dial In (U.S.)** | +1 (844) 290-3904 |
| **Dial In (International)** | +1 (574) 990-1036 |
| **Access Code** | 6266285 |

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

**About TransCon PTH** [1]

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). TransCon PTH is 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 has been granted orphan drug designation in the United States and European Union for the treatment of HP.

**About Hypoparathyroidism** [2, 3, 4, 5, 6, 7]
Hypoparathyroidism (also called "hypopara" or 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, and Japan, most of whom develop the condition following damage to or accidental removal of the parathyroid glands during thyroid surgery. Conventional treatment with calcium supplements and active vitamin D (also called calcitriol) does not effectively address the short-term symptoms, long-term complications, or quality-of-life impacts of hypoparathyroidism.

Short-term symptoms include weakness, severe muscle cramps (tetany), abnormal sensations such as tingling, burning and numbness (paresthesia), memory loss, impaired judgment, and headache. Patients often experience decreased quality of life, and, over the long term, this complex disorder can increase risk of major complications, such as calcium deposits in the brain, blood vessels, eye, and other soft tissues – including the kidneys, which can lead to impaired renal function.

Current standard of care with active vitamin D and calcium supplements does not fully control the disease and may contribute to risk of renal disease. Patients with HP have an estimated 4-fold to 8-fold greater risk of renal disease compared to healthy populations. The disease is also associated with a 2-fold increased risk of depression or bipolar disorder compared to healthy populations. HP remains among the few hormonal insufficiency states without a replacement therapy that restores the missing hormone at physiologic levels.

**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 uses its TransCon technologies to create new and potentially best-in-class therapies. Ascendis is headquartered in Copenhagen, Denmark, and has additional facilities in Heidelberg and Berlin, Germany; Palo Alto and Redwood City, California; and Princeton, New Jersey. Please visit www.ascendispharma.com to learn more.

**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' plans to submit an NDA and MAA for TransCon PTH, (ii) the expected timing of top-line results for the Phase 3 Pathway Japan Trial, (iii) Ascendis' plans to initiate a clinical trial of TransCon PTH in pediatric patients with HP, (iv) Ascendis' ability to apply its platform technology to build a leading, fully integrated biopharma company, and (v) Ascendis' use of 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: dependence on third party manufacturers and distributors to supply TransCon hGH, the SKYTROFA® Auto-Injector and other study drug for commercial sales in the U.S. and clinical studies; unforeseen safety or efficacy results in its oncology programs, TransCon hGH, TransCon PTH and TransCon CNP or other development programs; unforeseen expenses related to commercialization of lonapegsomatropin-tcgd in the U.S., the co-pay program, and the further development of TransCon hGH, 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 2, 2022 and Ascendis' other future reports filed with, or submitted to, the SEC. Forward-looking statements do not reflect the potential impact of any future 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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