# Ascendis Pharma Announces Once-weekly TransCon™ Growth Hormone Demonstrated Superiority on Primary Endpoint Compared to a Daily Growth Hormone in Phase 3 heiGHt Trial for Pediatric Growth Hormone Deficiency

March 4, 2019 at 6:30 AM EST

***- TransCon hGH demonstrated comparable safety and tolerability to a daily hGH -***

***- Potential once-weekly treatment option to overcome long-standing challenges with administration of daily hGH -***

***- Currently no available long-acting growth hormone treatment in the US or Europe -***

***- Ascendis Pharma to host conference call and webcast today at 8:00 a.m. Eastern time -***

COPENHAGEN, Denmark, March 04, 2019 (GLOBE NEWSWIRE) -- Ascendis Pharma A/S (Nasdaq: ASND), a biopharmaceutical company that utilizes its innovative TransCon technology to address unmet medical needs, today announced positive top-line results from the phase 3 heiGHt Trial, a randomized, open-label, active-controlled trial that compared once-weekly TransCon Growth Hormone (hGH) to a daily growth hormone (Genotropin®) in children with pediatric growth hormone deficiency (GHD).

The trial met its primary objective, demonstrating that TransCon hGH was observed to be non-inferior and, additionally, superior to the daily hGH on the primary endpoint of annualized height velocity (AHV) at 52 weeks. In the primary analysis of the intent-to-treat population using ANCOVA, TransCon hGH demonstrated an AHV of 11.2 cm/year compared to 10.3 cm/year for the daily hGH. The treatment difference was 0.86 cm/year with a 95 percent confidence interval of 0.22 to 1.50 cm/year. The AHV for TransCon hGH was significantly greater than the daily hGH (p=0.0088).

The AHV was greater for TransCon hGH than for the daily hGH at each visit, with the treatment difference reaching statistical significance from and including week 26 onward. The incidence of poor responders (AHV < 8.0 cm/year) was 4 percent and 11 percent in the TransCon hGH and daily hGH arms, respectively. All sensitivity analyses completed from the trial support the primary outcome, indicating the robustness of these results.

Results from the trial indicate that TransCon hGH was generally safe and well-tolerated, with adverse events consistent with the type and frequency observed with daily hGH therapy and comparable between arms of the trial. Key safety observations:

- No serious adverse events related to study drug were observed in either arm
- One serious adverse event was observed in each arm (representing 1.0 percent for TransCon hGH and 1.8 percent for daily hGH), both determined to be unrelated to study drug
- No treatment-emergent adverse events leading to discontinuation of study drug were observed in either arm

“The heiGHt Trial results announced today represent a potential breakthrough for patients and future treatment options for growth hormone deficiency,” said Jan Mikkelsen, Ascendis Pharma’s President and Chief Executive Officer. “The heiGHt Trial demonstrated that TransCon hGH had superior efficacy, as well as comparable safety and tolerability to daily growth hormone. We believe these results provide a validation of our TransCon technology platform, which forms the basis of our endocrinology pipeline and has potential application in other therapeutic areas.”

Additional preliminary analyses from the heiGHt Trial:

- No neutralizing antibodies detected, and low level (<10 percent) of low-titer non-neutralizing antibodies was similar between the two arms
- Height standard deviation score (SDS) at 52 weeks increased over baseline by 1.05 for TransCon hGH and by 0.94 for the daily hGH, and the treatment difference in height SDS increased at each visit over 52 weeks
- Body Mass Index (BMI) SDS was stable over 52 weeks and was -0.03 for TransCon hGH and -0.40 for the daily hGH at week 52
- Mean hemoglobin A1c values were generally stable over the course of the trial and remained within the normal range for both arms
- Observed peak and trough insulin-like growth factor-1 (IGF-1) SDS values were 1.3 and -0.5 over 52 weeks, respectively, for TransCon hGH compared to an approximate average IGF-1 SDS of 0.0 for the daily hGH at week 52
- In a pre-defined subset of 11 subjects, IGF-1 levels were assessed during week 13 and results were similar to those reported in the TransCon hGH pediatric phase 2 trial
- Consecutive IGF-1 SDS values >2.0 were uncommon (<10 percent of subjects) and IGF-1 SDS >3.0 were rare (<3 percent of subjects)
- Adverse events leading to dose reduction (IGF-1 levels or clinical symptoms) occurred twice in the TransCon hGH arm (representing 1.9 percent) and once in the daily hGH arm (representing 1.8 percent)
- Two subjects in each treatment arm experienced mild injection site reactions that were considered adverse events

The heiGHt Trial evaluated 161 treatment-naïve children with GHD randomized in a 2:1 ratio to receive either once-weekly TransCon hGH (0.24 mg/kg/week subcutaneously, n=105) or daily Genotropin (34 µg/kg/day or 0.24 mg/kg/week subcutaneously, n=56) for 52 weeks. Of the 161 subjects, two subjects, one from each arm, withdrew from the trial prior to the final visit.

TransCon hGH is designed to deliver unmodified hGH, the same growth hormone used in daily therapies, at a predictable rate over one week. Currently in the U.S. and Europe, the only GHD treatment option for patients and their families is daily hGH injections. Patients receiving daily therapy endure thousands of injections over the course of many years. This often leads to missed doses and patients who fail to meet expected outcomes.

“Results from the pivotal heiGHt Trial demonstrated that TransCon hGH was more effective than daily hGH, with comparable safety and tolerability observed. We are thankful to all those who participated in this important global trial,” said Jonathan Leff, M.D., Ascendis Pharma’s Chief Medical Officer. “Our goal is to alleviate the burden of daily injections so every child has a better opportunity to achieve normal adult height and overall endocrine health - and to look forward to a healthy future.”

These heiGHt Trial data will be presented for the first time as an oral presentation on Sunday, March 24 at ENDO 2019.

The TransCon hGH phase 3 program includes the heiGHt, fliGHt and enliGHten Trials. Top-line data for the fliGHt Trial, evaluating TransCon hGH in subjects who switch from daily hGH, are expected in the second quarter of 2019. The enliGHten Trial is a long-term extension that provides subjects from the heiGHt and fliGHt Trials with the opportunity to continue once-weekly TransCon hGH treatment.

Ascendis plans a clinical database lock for the TransCon hGH phase 3 program in the third quarter of 2019. Subsequently, the company intends to submit a Biologics License Application (BLA) with the U.S. Food and Drug Administration for TransCon hGH to treat pediatric GHD in the first half of 2020.

**Conference Call and Webcast Information**

Ascendis Pharma will host a conference call and webcast today at 8:00 a.m. Eastern Time (ET) to discuss the top-line heiGHt Trial results. Details include:

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| **Date** | March 4, 2019 |
| **Time** | 8:00 a.m. ET |
| **Dial In (U.S.)** | 844-290-3904 |
| **Dial In (International)** | 574-990-1036 |
| **Access Code** | 9556035 |

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

**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 pH and temperature conditions 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 Pediatric Growth Hormone Deficiency (GHD)**

Pediatric GHD is a serious orphan disease caused when the pituitary gland does not produce enough growth hormone. Children with GHD are not only characterized by short stature, but they also experience metabolic abnormalities, psychosocial challenges, cognitive deficiencies and poor quality of life.

For decades, the standard of care for GHD has been a daily subcutaneous injection of hGH, which improves growth and metabolic effects. For caregivers and patients, the treatment burden with daily injections is high, which leads to poor adherence and reduced overall treatment outcomes.

**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 rare disease endocrinology product candidates in clinical development and has established oncology as its second therapeutic area of focus. Additionally, Ascendis Pharma has multi-product collaborations with Sanofi in diabetes and Genentech in the field of ophthalmology and continues to expand into additional therapeutic areas for both internal and external development.

Ascendis is headquartered in Copenhagen, Denmark, with 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) the timing of our expected database lock and BLA submission for TransCon hGH, (ii) the timing of the topline data from the fliGHt Trial, (iii) our ability to apply our platform technology to build a leading, fully integrated biopharma company, (iv) our expectations regarding our ability to create new and potentially best-in-class therapies and (v) our product pipeline. 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 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 and potential commercial sale, if approved; and our ability to obtain additional funding, if needed, to support our business activities. 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 for the year ended December 31, 2017, which we filed with the SEC on March 28, 2018. 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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