Ascendis Pharma Announces Filing of Investigational New Drug (IND) Application for Initiation of a Global Phase 2 Trial for TransCon™ CNP in Children with Achondroplasia

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– TransCon CNP is designed to address all aspects of achondroplasia by providing continuous exposure to C-type natriuretic peptide (CNP) at safe and effective levels –

COPENHAGEN, Denmark, July 18, 2019 (GLOBE NEWSWIRE) -- Ascendis Pharma A/S (Nasdaq: ASND), a biopharmaceutical company that utilizes its innovative TransCon technologies to address significant unmet medical needs, today announced the filing of an investigational new drug (IND) application with the U.S. Food and Drug Administration (FDA) to initiate the ACcomplisH Trial, a global phase 2 trial designed to evaluate the safety and efficacy of TransCon CNP in children with achondroplasia.

"With the phase 2 ACcomplisH Trial, we aim to demonstrate that once-weekly TransCon CNP, which provides continuous exposure to CNP, is a potential therapeutic option for children with achondroplasia," said Jonathan Leff, M.D., Chief Medical Officer of Ascendis Pharma. "By delivering continuous levels of CNP, TransCon CNP is expected to help restore balance to the fibroblast growth factor receptor 3 pathway, thereby addressing not only height but the many skeletal complications and comorbidities that can have life-altering implications for children with achondroplasia. Our hope is to offer a potential new therapeutic option that addresses these challenges to improve the overall health and well-being of children with achondroplasia."

TransCon CNP is a long-acting prodrug of C-type natriuretic peptide (CNP) in development for children with achondroplasia. Phase 1 results demonstrated that TransCon CNP provided continuous exposure to CNP with a pharmacokinetic profile designed to maximize efficacy with once-weekly dosing. TransCon CNP was generally well tolerated at doses up to 150 µg/kg, with no serious adverse events or anti-CNP antibodies reported. TransCon CNP received Orphan Drug Designation (ODD) from the U.S. FDA in February 2019.

Achondroplasia is the most common form of dwarfism for which there is no FDA-approved therapy. Individuals living with achondroplasia may experience severe skeletal complications and comorbidities. For example, abnormal development of the vertebra can lead to sleep apnea, chronic back and leg pain from lower spine impingement and sudden infant death from cervical compression. Chronic ear infections due to abnormal eustachian tubes can lead to hearing loss and speech delay.

The ACcomplisH Trial is a global, phase 2, randomized, double-blind, placebo-controlled trial that will enroll approximately 60 children, ages 2 to 10 years, with achondroplasia. Subjects in each dose cohort will be randomized to receive TransCon CNP or placebo. Four doses of TransCon CNP will be tested sequentially, with the addition of a fifth dose, if needed, based on emerging data. The primary endpoint is annualized height velocity at 12 months. Key secondary endpoints include change in body proportionality at 12 months and change in body mass index at 12 months. All subjects who complete the ACcomplisH Trial will have the opportunity to receive TransCon CNP in a long-term extension trial. Ascendis expects to enroll the first subjects in the ACcomplisH Trial later this year.

The company is also conducting ACHieve, a natural history study that aims to provide important observational insights into the experience of children living with achondroplasia.

About TransCon™ Technology

TransCon is short for "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 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 a small molecule in multiple therapeutic areas, and can be used systemically or locally.

About Achondroplasia

Achondroplasia is the most common form of dwarfism, affecting approximately 250,000 people worldwide. Individuals living with achondroplasia may experience severe skeletal complications and comorbidities. For example, abnormal development of the vertebra can lead to sleep apnea, chronic back and leg pain from lower spine impingement and sudden infant death from cervical compression. Chronic ear infections due to abnormal eustachian tubes can lead to hearing loss and speech delay.

The condition is caused by an autosomal dominant activating mutation in the fibroblast growth factor receptor 3 (FGFR3) gene that leads to an imbalance in the effects of the FGFR3 and CNP signaling pathways. Preclinical and clinical data show that the CNP pathway stimulates growth. Increased CNP counteracts the effects of the FGFR3 mutation downstream, thus promoting bone growth.

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) our plans to initiate a Phase 2 trial of TransCon CNP in children with achondroplasia, (ii) our expectations regarding the results of our Phase 2 trial of TransCon CNP, (iii) insights we may obtain from our ACHieve natural history study; (iv) our ability to apply our platform technology to build a leading, fully integrated biopharma company, (v) our expectations regarding our ability to create potentially best-in-class therapies and (vi) 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 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, 2018, which we filed with the SEC on April 3, 2019. 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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