PRESS RELEASE

Pivotal ApproaCH Trial of TransCon™ CNP (Navepegritide) Achieved Primary Objective, Demonstrated AGV Superior to Placebo

- *TransCon CNP demonstrated AGV superior to placebo with LS mean treatment difference of 1.49 cm/year at Week 52 (p<0.0001)*
- *For children aged 5-11 years TransCon CNP demonstrated a change from baseline AGV superior to placebo with LS mean treatment difference of 1.78 cm/year at Week 52 (p<0.0001)*
- *Other endpoints supportive that TransCon CNP may provide benefits beyond linear growth*
- *TransCon CNP was generally well-tolerated, with low frequency of injection site reactions (0.41 events per patient year), all mild*
- *Ascendis to host investor conference call Monday, September 16, at 8:00 a.m. E.T.*

COPENHAGEN, Denmark, September 16, 2024 (GLOBE NEWSWIRE) – Ascendis Pharma A/S (Nasdaq: ASND) today announced topline data from the pivotal double-blind placebo-controlled ApproaCH Trial of TransCon CNP (navepegritide), which included 84 children with achondroplasia (ages 2-11 years) randomized 2:1 (TransCon CNP:placebo). TransCon CNP is an investigational prodrug of C-type natriuretic peptide (CNP) administered once weekly and designed to provide sustained release and continuous exposure of active CNP. In the trial, children treated with once-weekly TransCon CNP demonstrated annualized growth velocity (AGV) superior to placebo. TransCon CNP also demonstrated statistically significant improvements in other growth parameters, including height Z-score and change from baseline AGV.

“Results of this pivotal trial demonstrate that once-weekly TransCon CNP can, if approved, address the need for an efficacious, safe, tolerable, and convenient treatment for children with achondroplasia,” said Ravi Savarirayan, M.D., at the Murdoch Children’s Research Center (Australia) and an investigator in the ApproaCH Trial. “I am excited about the possibilities TransCon CNP presents for a potential new treatment option for these children that will allow decreased injection frequency, improved compliance, and reduced caregiver burden.”

“TransCon CNP-treated children with achondroplasia exceeded the growth rate of the general population, suggesting that once-weekly TransCon CNP provides catch-up growth with safety and tolerability results comparable to placebo with a low incidence of injection-site reactions,” said Jan Mikkelsen, Ascendis Pharma’s President and Chief Executive Officer. “With SKYTROFA® and TransCon CNP, Ascendis is uniquely positioned to become the leader in the treatment of skeletal dysplasias and growth disorders.”

Highlights of the ApproaCH Trial Topline Data

Primary Endpoint

- For the primary endpoint of AGV at Week 52, children treated with TransCon CNP (n=57) demonstrated an LS mean AGV of 5.89 cm/year compared to 4.41 cm/year in the placebo arm (n=27), an LS mean difference of 1.49 cm/year ($p<0.0001$).
- Sub-group analyses:
    - Children aged 2 to <5 years treated with TransCon CNP (n=21) demonstrated an LS mean AGV at Week 52 of 6.07 cm/year compared to 5.06 cm/year in the placebo arm (n=10), an LS mean difference of 1.02 cm/year ($p=0.0084$).
    - Children aged 5-11 years treated with TransCon CNP (n=36) demonstrated an LS mean AGV at Week 52 of 5.79 cm/year compared to 4.02 cm/year in the placebo arm (n=17), an LS mean difference of 1.78 cm/year ($p<0.0001$).

AGV Change from Baseline

- Children aged 2 to <5 years, treated with TransCon CNP (n=19) demonstrated a change from baseline AGV at Week 52 of 1.57 cm/year compared to 0.43 cm/year in the placebo arm (n=10), an LS mean difference of 1.15 cm/year ($p=0.0047$).
- Children aged 5-11 years, treated with TransCon CNP (n=35) demonstrated a change from baseline AGV at Week 52 of 2.29 cm/year compared to 0.52 cm/year in the placebo arm (n=17), an LS mean difference of 1.78 cm/year ($p<0.0001$).

Secondary Endpoints

- For the secondary endpoint of change in ACH Height Z-score, children treated with TransCon CNP (n=57) demonstrated an LS mean change from baseline ACH Height Z-score of 0.30 compared to 0.01 in the placebo arm (n=27), an LS mean difference of 0.28 ($p<0.0001$).
- For the secondary endpoint of change in CDC Height Z-score, children treated with TransCon CNP (n=55) demonstrated an LS mean change from baseline CDC Height Z-score of 0.15 compared to -0.15 in the placebo arm (n=27), an LS mean difference of 0.30 ($p=0.0003$).

Selected Other Endpoints

- In the total trial population, treatment with TransCon CNP resulted in numerical improvements in health-related quality of life compared to placebo as measured in several Achondroplasia Child Experience Measure (ACEM) domains.
- Predefined sub-group analyses of ACEM-Physical Functioning demonstrated potential treatment effect, supported by muscle functionality test results.
- At baseline, parents of children generally reported lower burden of health-related quality of life (HRQoL) compared to the ACcomplisH Trial.
    - For children with HRQoL burden at baseline, a potential treatment effect was observed across several HRQoL domains of the ACEM measures.

Safety Summary

- TransCon CNP continues to show a safety profile comparable to placebo and was generally well-tolerated, with generally mild treatment-emergent adverse events (TEAEs), no evidence of hypotensive effect, and a low frequency of injection site reactions (0.41 events per patient year), all mild.
- No adverse events (AEs) led to discontinuation of TransCon CNP or withdrawal from the trial and no serious adverse events (SAEs) were assessed as related to TransCon CNP.

As of today, all 82 children who completed the double-blind period are continuing in the open-label extension of the ApproaCH Trial.

"On behalf of everyone at Ascendis, I want to thank the study participants, families, and clinical investigators contributing to the efforts to improve treatment options for individuals living with achondroplasia," said Aimee Shu, M.D., Ascendis Pharma's Senior Vice President of Clinical Development, Endocrine & Rare Disease. "These data support our aspirations for TransCon CNP, and we look forward to working with regulatory authorities as we take the next steps to advance TransCon CNP as a potential new treatment option."

Ascendis plans to submit a New Drug Application (NDA) to the U.S. Food & Drug Administration for TransCon CNP for the treatment of children with achondroplasia during the first quarter of 2025 and a Marketing Authorisation Application (MAA) for the treatment of children with achondroplasia to the European Medicines Agency during the third quarter of 2025.

ApproaCH is a pivotal, multicenter, randomized, double-blind, placebo-controlled trial of once-weekly TransCon CNP versus placebo in 84 children with achondroplasia ages 2-11 years old. Patients were randomized 2:1 to receive TransCon CNP or placebo for 52 weeks at the 100µg/kg/week dose in the double-blind period, after which all participants could choose to receive TransCon CNP in an ongoing open-label extension at the 100µg/kg/week dose.

A slide presentation with these data can be found on the Investor Relations & News section of the Ascendis Pharma website: https://investors.ascendispharma.com.

Conference Call & Webcast Information

Ascendis Pharma will host a conference call and webcast on Monday, September 16, 2024, at 8:00 am Eastern Time (ET) to discuss the pivotal ApproaCH Trial results. Those who would like to participate may access the live webcast here, or register in advance for the teleconference here. The link to the live webcast will also be available on the Ascendis Pharma Investors & News website at https://investors.ascendispharma.com. A replay of the webcast will be available on this section of the Ascendis Pharma website shortly after conclusion of the event for 30 days.

About Ascendis Pharma A/S

Ascendis Pharma is applying its innovative TransCon technology platform 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, Ascendis uses its TransCon technologies to create new and potentially best-in-class therapies. Ascendis is headquartered in Copenhagen, Denmark and has additional facilities in Europe and the United States. Please visit 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) improvements in well-being and physical functioning supporting potential direct treatment effects of TransCon CNP, (ii) TransCon CNP's potential to meet the need for a treatment addressing the health and quality-of-life complications of achondroplasia, (iii) Ascendis' timing for submission of certain regulatory filings related to TransCon CNP, (iv) Ascendis' ability to apply its TransCon technology platform 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, distributors and service providers for Ascendis' products and product candidates; unforeseen safety or efficacy results in Ascendis' development programs or on-market products; unforeseen expenses related to commercialization of any approved Ascendis products; unforeseen expenses related to Ascendis' development programs; unforeseen selling, general and administrative expenses, other research and development expenses and Ascendis' business generally; delays in the development of its programs related to manufacturing, regulatory requirements, speed of patient recruitment or other unforeseen delays; Ascendis' ability to obtain additional funding, if needed, to support its business activities; the impact of international economic, political, legal, compliance, social and business factors. 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 February 7, 2024, 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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