PRESS RELEASE

Ascendis Pharma Presents New Data and Updated Results from Phase 1/2 IL-Believe Trial at ASCO 2024

- *40% of efficacy-evaluable patients (2 out of 5) in the initial cohort of patients with anti-PD-1 refractory melanoma treated with TransCon IL-2 β/γ in combination with TransCon TLR7/8 Agonist exhibited confirmed clinical responses with no new safety signals*
- *45% of efficacy-evaluable patients (5 out of 11) whose disease progressed on check-point inhibitors exhibited confirmed clinical responses when treated with TransCon IL-2 β/γ as monotherapy or in combination treatment*

COPENHAGEN, Denmark, June 3, 2024 (GLOBE NEWSWIRE) – Ascendis Pharma A/S (Nasdaq: ASND) reported new and updated results from its ongoing Phase 1/2 IL-Believe Trial of TransCon IL-2 β/γ in a poster presentation at ASCO 2024, the annual meeting of the American Society of Clinical Oncology being held in Chicago May 31–June 4, 2024. Data included the first presentation of Phase 2 dose expansion Cohort 4 (TransCon IL-2 β/γ in combination with TransCon TLR7/8 Agonist) in post anti-PD-1 melanoma and new analyses of patients from dose escalation cohorts with prior disease progression on checkpoint inhibitors, along with biomarker studies correlating cytotoxic immune cell expansion and clinical benefit.

As of the April 16, 2024 data cutoff, confirmed clinical responses were observed in 40% (two out of five) of efficacy-evaluable patients from Cohort 4, suggesting potential synergy of Ascendis Pharma's two novel immunotherapy agents.

Of efficacy-evaluable patients with prior disease progression on checkpoint inhibitors to date in the IL-Believe Trial, confirmed clinical responses (per RECIST v1.1) were observed in 45% (five out of eleven) administered TransCon IL-2 β/γ doses ≥80 µg/kg every 3 weeks, suggesting clinical benefit in treatment-resistant settings.

- Monotherapy (n=4): 1 confirmed partial response (PR) in colorectal cancer
- Combination with pembrolizumab (n=2): 1 confirmed complete response and 1 confirmed PR in small-cell lung cancer
- Combination with TransCon TLR7/8 Agonist (n=5): 2 confirmed PRs in melanoma

Biomarker analysis demonstrated comparable, cytotoxic immune expansion between TransCon IL-2 β/γ monotherapy and combination therapy with pembrolizumab, indicating that administration of TransCon IL-2 β/γ expands cytotoxic lymphocytes and elevates levels of cytokines and chemokines in the blood without the corresponding expansion of T_{regs} or eosinophils (markers of toxicity). A statistically significant correlation of clinical benefit with both CD8+ T cell expansion and activation was observed, directly linking this pharmacodynamic effect to clinical activity.

In this trial, TransCon IL-2 β/γ alone or in combination with pembrolizumab or TransCon TLR7/8 Agonist was generally well tolerated with no new safety signals.

"We are very encouraged by the clinical response and safety profile for TransCon IL-2 β/γ and are pleased to see it working as designed to recruit and amplify the body's immune response with sustained immune activation without a corresponding increase in markers of toxicity," said Stina Singel, M.D., Ph.D., Ascendis Pharma's Executive Vice President and Head of Clinical Development, Oncology. "These new data in a heavily pre-treated population who progressed on or did not benefit from prior checkpoint inhibitors support TransCon IL-2 β/γ as the first biased IL-2 cytokine therapy to show not only monotherapy activity in a convenient outpatient setting every 3 weeks but also a direct correlation between clinical benefit and expansion of CD8+ T cells. We look forward to additional data readouts expected later this year from larger, indication-specific cohorts."

TransCon IL-2 β/γ is an investigational long-acting prodrug with sustained release of an IL-2Rβ/γ-selective analog (IL-2 β/γ), designed to address the known limitations of interleukin-2 (IL-2) cancer immunotherapy through prolonged activation of IL-2Rβ/γ with low C_{max}. The Phase 1/2 IL-Believe Trial is investigating the safety and tolerability of TransCon IL-2 β/γ alone or in combination with the checkpoint inhibitor pembrolizumab and/or chemotherapy or TransCon TLR7/8 Agonist in participants with locally advanced or metastatic solid tumors. The recommended Phase 2 dose (RP2D) for TransCon IL-2 β/γ in the IL-Believe trial is 120 µg/kg administered intravenously every three weeks in an outpatient setting in both the monotherapy and combination-therapy arms.

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) the potential synergy of TransCon IL-2 β/γ and TransCon TLR7/8 Agonist; (ii) the timing of data from indication-specific cohorts for TransCon IL-2 β/γ; (iii) the ability of TransCon IL-2 β/γ to address the known limitations of interleukin-2 (IL-2) cancer immunotherapy through prolonged activation of IL-2Rβ/γ; (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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