

PRESS RELEASE

Dose Escalation Data from transcendIT-101, Ascendis Pharma's Phase 1/2 Trial of TransCon™ TLR7/8 Agonist in Patients with Advanced Solid Tumors, Presented at SITC 2022

- *Early signs of clinical activity were observed in patients receiving TransCon TLR7/8 Agonist as monotherapy or in combination with pembrolizumab; abscopal effect observed with monotherapy*
- *With a single injection, TransCon TLR7/8 Agonist demonstrated sustained target immune system engagement over weeks in injected and non-injected tumors, with no signs of systemic toxicity*

COPENHAGEN, Denmark, November 11, 2022 (GLOBE NEWSWIRE) – Ascendis Pharma A/S (Nasdaq: ASND) today disclosed new data from the dose-escalation portion of transcendIT-101, the company's Phase 1/2 open-label, multi-center trial of TransCon TLR7/8 Agonist in patients with advanced solid tumors. TransCon TLR7/8 Agonist is an investigational long-acting prodrug designed to provide sustained, localized release over weeks of resiquimod (a potent immune response modifier with clinically demonstrated anti-tumor activity) with low systemic exposure.

The dose escalation data from transcendIT-101, presented by Diwakar Davar, M.D. of the University of Pittsburgh Medical Center during the annual meeting of the Society for Immunotherapy of Cancer (SITC 2022), suggests that intratumoral TransCon TLR7/8 Agonist was safe and well-tolerated alone or in combination with pembrolizumab; that it demonstrated target immune system engagement in injected and non-injected tumors along with a systemic immune response; and that it showed early signs of clinical activity alone or in combination with pembrolizumab.

“We are very pleased to see intratumoral TransCon TLR7/8 Agonist administration working as designed to deliver prolonged, high local concentrations of resiquimod, steadily activating and intensifying the body's innate and adaptive immune responses over weeks with a single injection,” said Stina Singel, Senior Vice President, Head of Clinical Development, Oncology at Ascendis Pharma. “With these early signs of clinical activity, including monotherapy abscopal activity, and no signs of systemic toxicity, we look forward to continuing our work with investigators and patients to further assess TransCon TLR7/8 Agonist's ability to promote potent anti-tumoral responses while minimizing toxic systemic exposures.”

All 23 of the patients enrolled in the dose escalation portion of the trial had advanced or metastatic solid tumors that had progressed on prior treatments, 9 in the monotherapy cohort (intratumoral TransCon TLR7/8 Agonist alone) and 14 in the combination therapy cohort (intratumoral TransCon TLR7/8 Agonist plus the check-point inhibitor pembrolizumab). Two dose levels were evaluated: 0.3 mg/lesion and 0.5 mg/lesion. The recommended Phase 2 dose was declared at 0.5 mg/lesion for up to two lesions.

The Phase 1/2 transcendIT-101 trial (NCT04799054) is continuing to enroll patients, with dose expansion focused on investigating TransCon TLR7/8 Agonist in combination with pembrolizumab in 4 cancer types where increased Toll-like receptor (TLR) activity has potential to improve adaptive immune activation and host defense against cancers: head and neck squamous cell carcinomas (SCC); other HPV-associated cancers; melanoma; and cutaneous squamous cell carcinomas (cSCC).

SITC 2022 registrants can obtain the poster (#763) and oral presentation slides, both titled “Phase 1/2, Open-Label, Multicenter, First-in-Human Dose Escalation and Dose Expansion Study of TransCon TLR7/8 Agonist Alone or in Combination With Pembrolizumab in Patients With Locally Advanced or Metastatic Solid Tumor Malignancies: Initial Results From Phase 1 Dose Escalation (transcendIT-101) Trial,” from the SITC 2022 event website: <https://www.sitcancer.org/2022/home>.

About TransCon TLR7/8 Agonist

Immunotherapies can stimulate, intensify, and sustain the immune system’s natural ability to recognize and eliminate cancer cells, yet many patients do not respond to immunotherapies currently on the market, most of which are designed for intravenous administration and many of which have significant toxicity profiles at therapeutically effective doses. TransCon TLR7/8 Agonist is an investigational long-acting prodrug of resiquimod (a potent immune response modifier with clinically demonstrated anti-tumor activity) designed to provide sustained activation of intratumoral antigen-presenting cells driving tumor antigen presentation and induction of immune-stimulatory cytokines for weeks with a single intratumoral injection. Based on Ascendis Pharma’s innovative TransCon technology platform, TransCon TLR7/8 Agonist is comprised of 3 main components: resiquimod a small molecule agonist of Toll-like receptors (TLRs) 7 and 8, a TransCon hydrogel microparticle carrier, and a linker bound permanently to the hydrogel microparticle carrier on one end and transiently to resiquimod on the other. TransCon TLR7/8 Agonist leverages TransCon hydrogel to achieve sustained, localized release of resiquimod in the injected tumor over weeks, where it is designed to steadily activate and intensify the body’s innate and adaptive immune responses to eradicate cancer cells in both injected and distal tumors, while maintaining low systemic drug exposure.

About Ascendis Pharma A/S

Ascendis Pharma is applying its innovative TransCon platform to build a leading, fully integrated, global 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) TransCon TLR7/8 Agonist’s ability to provide sustained, localized release over weeks of resiquimod with low systemic exposure and steadily activate and intensify the body’s innate and adaptive immune responses over weeks with a single

injection, (ii) Ascendis' plan to work with investigators and patients to further assess TransCon TLR7/8 Agonist's ability to promote potent anti-tumoral responses while minimizing toxic systemic exposures, (iii) Ascendis' plans and expectations with respect to the ongoing Phase 1/2 transcendIT-101 trial, (iv) TransCon TLR7/8 Agonist's potential to improve adaptive immune activation and host defense against SCC, other HPV-associated cancers, melanoma and cSCC in combination with pembrolizumab, (v) TransCon TLR7/8 Agonist's ability to provide sustained activation of intratumoral antigen-presenting cells driving tumor antigen presentation and induction of immune-stimulatory cytokines for weeks with a single intratumoral injection, (vi) TransCon TLR7/8 Agonist's ability to leverage TransCon hydrogel to achieve sustained, localized release of resiquimod to eradicate cancer cells in both injected and distal tumors, while maintaining low systemic drug exposure, and (vii) Ascendis' use of its TransCon technologies and platform to create new and potentially best-in-class therapies and build a leading, fully integrated, global biopharma company. 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 its development programs or on-market products; unforeseen expenses related to commercialization of any approved Ascendis products; 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, including inflation, and the effects on its business from the worldwide COVID-19 pandemic and the ongoing conflict in the region surrounding Ukraine and Russia. 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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