

PRESS RELEASE

Ascendis Pharma Oncology Program Update Highlights Latest Clinical Data for Product Candidates

- *TransCon IL-2 β/γ in Phase 1 clinical trial showed monotherapy clinical activity in heavily pre-treated cancer patients with clear dose dependent response on cytotoxic immune cells*
- *TransCon IL-2 β/γ administered every 3 weeks was generally well tolerated, with no meaningful effect on T_{regs} and eosinophils.*
- *At the TransCon IL-2 β/γ recommended Phase 2 dose (RP2D), no dose limiting toxicity (DLT), vascular leak syndrome, or grade 3/4 cytokine release syndrome observed*
- *Further follow-up for the TransCon TLR7/8 Agonist monotherapy cohort showed additional abscopal responses*
- *Webcast of Ascendis' Oncology Program Update to begin at 10:00 am ET*

COPENHAGEN, Denmark, May 31, 2023 (GLOBE NEWSWIRE) – Ascendis Pharma A/S (Nasdaq: ASND) will today host an investor meeting highlighting the latest developments in the Company's Oncology programs, including clinical data updates and a review of clinical development strategy for the Company's two immuno-oncology product candidates, TransCon TLR7/8 Agonist and TransCon IL-2 β/γ . Both are designed to recruit innate and adaptive components of the immune system to maximize anti-cancer activity while reducing dose-limiting toxicities.

“TransCon IL-2 β/γ was designed by applying the TransCon technology together with protein bioscience to solve problems with aldesleukin that have eluded industry for many decades - to create a well-tolerated IL-2 therapy that has the potential to effectively activate the immune system to drive anti-cancer activity without dosing complexity that limits aldesleukin use. Today we are reporting for the first-time clinical data supporting the successful design for TransCon IL-2 β/γ ,” said Jan Mikkelsen, Ascendis Pharma's President and CEO.

“We are excited to highlight the progress we have made across our two immuno-oncology product candidate programs, TransCon IL-2 β/γ and TransCon TLR7/8 Agonist,” said Stina Singel, M.D., Ph.D., Executive Vice President, Head of Clinical Development, Oncology at Ascendis Pharma. “The clinical data shared today from both programs showed an acceptable safety profile and single-agent clinical activity. Data from indication-specific cohorts, including melanoma, head-and-neck, and non-small cell lung cancer are expected in 2024.”

Today's meeting highlights include:

TransCon IL-2 β/γ program update from the Phase 1/2 IL-Believe Trial

- Phase 1 monotherapy dose escalation complete; 25 heavily pre-treated patients enrolled (median of 4 prior lines of systemic therapies).
- 120 $\mu\text{g}/\text{kg}$ IV every three weeks selected as monotherapy recommended Phase 2 dose (RP2D).
- Eight monotherapy patients dosed at RP2D; of the three efficacy evaluable patients to date, one partial response in a metastatic colorectal cancer patient, and one stable disease in a renal cell carcinoma patient (data cut April 28, 2023).
- At RP2D, TransCon IL-2 β/γ was generally well-tolerated with no DLT observed, no vascular leak syndrome and no grade 3 or 4 cytokine release syndrome.
- As designed, the non-alpha TransCon IL-2 β/γ expanded local and systemic cytotoxic immune effector cells (CD8+ T and NK cells) without clear effect on T_{regs} and eosinophils.
- RP2D for combination therapy with checkpoint inhibitor dose escalation data expected in the third quarter of 2023 and will be presented at a scientific congress in the fourth quarter.
- Enrollment continues in indication-specific cohorts for the Phase 2 portion of the IL-Believe trial.

TransCon TLR7/8 Agonist program update from the Phase 1/2 transcendIT-101 Trial

- Additional follow-up indicates further clinical activity in patients receiving TransCon TLR7/8 Agonist as monotherapy or in combination with pembrolizumab. Results supporting selection of RP2D from transcendIT-101 were first reported at SITC 2022 last November.
- Preliminary results showed that TransCon TLR7/8 Agonist was well-tolerated both as a monotherapy and in combination with pembrolizumab.
- Enrollment continues in the Phase 2 portion of transcendIT-101 at the RP2D of 0.5 mg/lesion for up to two lesions, which is being evaluated in four indication-specific cohorts.

TransCon IL-2 β/γ is an investigational long-acting prodrug with sustained release of an IL-2R β/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-2R β/γ with low C_{max}.

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.

Oncology Program Update Meeting Webcast Information

Ascendis' 2023 Oncology Program Update Meeting will take place today starting at 10:00 am Eastern Time (ET). Those who would like to participate may access the live webcast [here](#). The link to the live webcast will also be available on the Investors & News section of the Ascendis Pharma website at <https://investors.ascendispharma.com>. A replay of the webcast will be available on this section of our 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, 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 Germany (Heidelberg, Berlin and Munich) and the United States (Palo Alto and Redwood City, California, and Princeton, New Jersey). 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) Ascendis' ability to create well-tolerated immune-oncology product candidates without dosing complexity that limits use of current therapies; (ii) the timing of data from indication-specific cohorts for TransCon IL-2 β/γ and TransCon TLR7/8 Agonist; (iii) the timing of dose escalation combination therapy data from the Phase 1/2 IL-Believe trial and its presentation at a scientific congress; (iv) Ascendis' ability to apply its TransCon technology platform to build a leading, fully integrated, global 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 its 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, including inflation, and the effects on its business from the worldwide COVID-19 pandemic and ongoing conflicts such as that 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 February 16, 2023 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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