Odyssey Therapeutics Announces Publication Highlighting Differentiated Therapeutic Potential of TNFR2 Agonism

"Cutting Edge" article demonstrates that compared with IL-2, TNFR2 agonism promotes tissue-directed regulatory T-cell differentiation and lineage stability, as well as reduces autoimmune inflammation in preclinical models

Company's investigational TNFR2 agonist, OD-003, expected to complete IND-enabling studies in the first quarter of 2027

BOSTON, November 10, 2026 (GLOBE NEWSWIRE) — Odyssey Therapeutics, Inc. (Nasdaq: ODTX) ("Odyssey" or the "Company"), a clinical-stage biopharmaceutical company seeking to transform the standard of care for patients suffering from autoimmune and inflammatory diseases by developing medicines that precisely target disease pathology, today announced the publication of a research paper titled, "TNFR2 agonism increases tissue and effector Treg cells" in The Journal of Immunology. The manuscript was selected by the editors as a "Cutting Edge" article, highlighting the scientific significance of the findings.

The research, conducted in collaboration with investigators at the University Medical Center Mainz, used single-cell analyses to investigate how activation of tumor necrosis factor receptor 2 (TNFR2) influences regulatory T cells (Tregs), which play a critical role in controlling inflammation. The findings demonstrate that TNFR2 agonism expands Tregs and promotes their differentiation into specialized cells with tissue-homing potential and stability under inflammatory conditions. In mouse studies, TNFR2 agonism increased tissue-associated Treg populations and reduced disease severity in models of autoimmune inflammation. Consistent with these findings, experiments using human Tregs demonstrated that TNFR2 agonism promotes the expression of genes associated with tissue homing and suppressive function while preserving Treg lineage stability.

"A key challenge in harnessing Tregs therapeutically is directing their differentiation into stable populations capable of controlling inflammation in affected tissues," said Gary D. Glick, Ph.D., founder and chief executive officer of Odyssey Therapeutics. "These findings demonstrate that TNFR2 agonism

promotes the expansion of tissue-competent Tregs while preserving phenotype stability and enhancing immuno-suppressive ability. Together with evidence of reduced disease severity in preclinical models, this research strengthens the therapeutic rationale for OD-003, our TNFR2 agonist, as an investigational treatment for autoimmune and inflammatory diseases and supports the potential superiority of this approach to IL-2-based therapies."

Summary of key findings

The findings demonstrate that TNFR2 agonism:

- **Drives tissue-directed Treg differentiation.** A single dose tripled the proportion of PD-1+BATF+ Tregs among lung Tregs in mice (22% to 66%), an effect not observed with an IL-2 mutein.

- **Reduces autoimmune inflammation in preclinical models.** Treatment increased tissue Treg populations and reduced disease severity in models of skin inflammation and experimental autoimmune encephalomyelitis.

- **Preserves Treg lineage stability.** Human Tregs expanded with a TNFR2 agonist maintained demethylation of the FOXP3 CNS2 region, an epigenetic hallmark of Treg lineage stability. Functionally, they produced less IFN-γ, a proinflammatory cytokine, when challenged with inflammatory signals, supporting their ability to retain regulatory characteristics under inflammatory conditions.

- **Promotes tissue-like differentiation in human Tregs, including those from patients with systemic lupus erythematosus.** In vitro studies showed increased expression of markers associated with tissue adaptation and immune regulation, supporting the translational relevance of TNFR2 agonism.

Collectively, these findings highlight the therapeutic potential of TNFR2 agonism to promote stable, tissue-directed Treg populations for the treatment of autoimmune and inflammatory diseases and support the development of OD-003, Odyssey's investigational TNFR2 agonist. OD-003 is advancing through IND-enabling studies, with completion expected in the first quarter of 2027.

About Odyssey Therapeutics

Odyssey Therapeutics is a clinical-stage biopharmaceutical company seeking to transform the standard of care for patients suffering from autoimmune and inflammatory diseases by developing medicines that are designed to precisely target disease pathology. Since its founding in 2021, Odyssey has built a portfolio of internally discovered and developed medicines with its first program advancing through multiple clinical milestones. Odyssey's portfolio leverages the scientific expertise of its team of experienced drug hunters and a comprehensive suite of tools to efficiently advance product candidates that the Company believes have the potential to induce deep and durable remission for patients across several inflammatory diseases with unmet need.

For more information, please visit www.odysseytx.com and follow Odyssey on LinkedIn or X.

Forward-looking statements

This press release includes certain disclosures that contain "forward-looking statements" within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including, without limitation, statements regarding the interpretation and potential implications of published preclinical and human cell research on TNFR2 agonism; the potential of TNFR2 agonism to promote regulatory T-cell expansion, tissue-directed differentiation, and stability; the potential translation of these findings to human disease; the therapeutic potential of TNFR2 agonism for autoimmune and inflammatory diseases; and the development, potential efficacy and anticipated benefits of OD-003, including the expected timing of completion of IND-enabling activities.

Forward-looking statements may be identified by words such as "anticipate," "believe," "could," "expect," "intend," "goal," "may," "plan," "potential," "will," "would" and variations of these words or similar expressions, although not all forward-looking statements contain these identifying words. Forward-looking statements reflect Odyssey's current expectations and involve risks and uncertainties that could cause actual results to differ materially. These include the inherent limitations of preclinical and in vitro research; uncertainty regarding the translation of preclinical findings to clinical outcomes in humans; the possibility that OD-003 may not demonstrate the anticipated safety, efficacy or biological activity in future clinical trials; risks associated with completing IND-enabling activities and advancing OD-003 into clinical development; clinical, regulatory, competitive and third-party risks; and other factors described under "Risk Factors" in Odyssey's most recent Form 10-Q and other SEC filings. Odyssey undertakes no obligation to update these statements except as required by law.

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