aTyr Pharma Announces Publication Demonstrating Efzofitimod's Immunomodulatory Activity in Science Translational Medicine

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Peer-reviewed publication validates efzofitimod's unique anti-inflammatory mechanism of action on macrophages through neuropilin-2 (NRP2) receptor.

Scientific insights further strengthen the rationale for clinical program for efzofitimod in interstitial lung disease (ILD).

SAN DIEGO, March 12, 2025 (GLOBE NEWSWIRE) -- aTyr Pharma, Inc. (Nasdaq: ATYR) ("aTyr" or the "Company"), a clinical stage biotechnology company engaged in the discovery and development of first-in-class medicines from its proprietary tRNA synthetase platform, today announced a publication demonstrating the mechanism of action for its lead therapeutic candidate, efzofitimod, in the journal *Science Translational Medicine*. The publication, entitled, "A human histidyl-tRNA synthetase splice variant therapeutic targets NRP2 to resolve lung inflammation and fibrosis," is available on the journal's website and at: https://www.science.org/doi/10.1126/scitranslmed.adp4754.

"We are pleased to publish this extensive manuscript detailing the preclinical data supporting the development of efzofitimod, which includes all of the data generated for this novel drug candidate from concept to clinic," said Leslie A. Nangle, Ph.D., Vice President, Research at aTyr. "This peer-reviewed publication in a highly regarded journal such as *Science Translational Medicine* validates the immunomodulatory activity and extracellularly mediated mechanism of efzofitimod in reducing inflammation and fibrosis. Furthermore, this validation considerably expands the basis for the application of efzofitimod in chronic inflammatory conditions, as well as encourages the potential development of other tRNA synthetase-based therapeutics for disease intervention."

The publication presents the foundational science, detailed preclinical studies and discovery work behind efzofitimod, a first-in-class immunomodulator derived from a splice variant of histidyl-tRNA synthetase (HARS), which is enriched in human lung and is upregulated by inflammatory cytokines in lung and immune cells. The article also describes the specific and selective binding for efzofitimod to neuropilin-2 (NRP2), a cellular receptor highly expressed by myeloid cells in active sites of inflammation. Through this binding, efzofitimod inhibits the expression of pro-inflammatory receptor and cytokines, thereby downregulating inflammatory pathways in macrophages. This mechanism can subsequently disrupt the cycle of chronic inflammation and fibrosis.

"This publication is a culmination of our innovative drug discovery process and serves as a testament to the overwhelming amount of preclinical work that provides evidence for the immunomodulatory activity for efzofitimod," said Sanjay S. Shukla, M.D., M.S., President and Chief Executive Officer of aTyr. "This scientific work along with the compelling clinical proof-of-concept generated for efzofitimod in pulmonary sarcoidosis supports the ongoing clinical development program in interstitial lung disease (ILD) and further strengthens the rationale to target ILD in their inflammatory stages using this novel therapeutic agent."

Efzofitimod is currently being investigated in the global pivotal Phase 3 EFZO-FIT™ study in pulmonary sarcoidosis, a major form of ILD, and the Phase 2 EFZO-CONNECT™ study in systemic sclerosis (SSc, or scleroderma-related ILD). Efzofitimod has received orphan drug designation in the U.S., E.U. and Japan for sarcoidosis and Fast Track designation in the U.S. for pulmonary sarcoidosis and orphan drug designation in the U.S. and E.U. for SSc and Fast Track designation in the U.S. for SSc-ILD.

About Efzofitimod

Efzofitimod is a first-in-class biologic immunomodulator in clinical development for the treatment of interstitial lung disease (ILD), a group of immune-mediated disorders that can cause inflammation and fibrosis, or scarring, of the lungs. Efzofitimod is a tRNA synthetase derived therapy that selectively modulates activated myeloid cells through neuropilin-2 to resolve inflammation without immune suppression and potentially prevent the progression of fibrosis. aTyr is currently investigating efzofitimod in the global Phase 3 EFZO-FIT™ study in patients with pulmonary sarcoidosis, a major form of ILD, and in the Phase 2 EFZO-CONNECT™ study in patients with systemic sclerosis (SSc, or scleroderma)-related ILD. These forms of ILD have limited therapeutic options and there is a need for safer and more effective, disease-modifying treatments that improve outcomes.

About aTyr

aTyr is a clinical stage biotechnology company leveraging evolutionary intelligence to translate tRNA synthetase biology into new therapies for fibrosis and inflammation. tRNA synthetases are ancient, essential proteins that have evolved novel domains that regulate diverse pathways extracellularly in humans. aTyr's discovery platform is focused on unlocking hidden therapeutic intervention points by uncovering signaling pathways driven by its proprietary library of domains derived from all 20 tRNA synthetases. aTyr's lead therapeutic candidate is efzofitimod, a first-in-class biologic immunomodulator in clinical development for the treatment of interstitial lung disease, a group of immune-mediated disorders that can cause inflammation and progressive fibrosis, or scarring, of the lungs. For more information, please visit www.atyrpharma.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are usually identified by the use of words such as "anticipate," "believes," "designed," "could," "can," "expects," "intends," "may," "plans," "potential," "will," and variations of such words or similar expressions. We intend these forward-looking statements to be covered by such safe harbor provisions for forward-looking statements and are making this statement for purposes of complying with those safe harbor provisions. These forward-looking statements include, among others, statements regarding the clinical development for efzofitimod, including the immunomodulatory activity and unique anti-inflammatory mechanism of action on macrophages through NRP2, the ability of efzofitimod to resolve lung inflammation and fibrosis, and the potential for the ongoing clinical program for efzofitimod in ILD, including pulmonary sarcoidosis and SSc-ILD. These forward-looking statements

also reflect our current views about our plans, intentions, expectations, strategies and prospects, which are based on the information currently available to us and on assumptions we have made. Although we believe that our plans, intentions, expectations, strategies and prospects, as reflected in or suggested by these forward-looking statements, are reasonable, we can give no assurance that the plans, intentions, expectations, strategies or prospects will be attained or achieved. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. Furthermore, actual results may differ materially from those described in these forward-looking statements and will be affected by a variety of risks and factors that are beyond our control including, without limitation, uncertainty regarding geopolitical and macroeconomic events, risks associated with the discovery, development and regulation of efzofitimod, the risk that we or our partners may cease or delay preclinical or clinical development activities for efzofitimod for a variety of reasons (including difficulties or delays in patient enrollment in planned clinical trials), the possibility that existing collaborations could be terminated early, and the risk that we may not be able to raise the additional funding required for our business and product development plans, as well as those risks set forth in our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and in our other SEC filings. Except as required by law, we assume no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

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