aTyr Pharma Highlights New Literature Implicating Neuropilin Pathway In SARS-CoV-2 Infection

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Discovery that Neuropilin b1 domain acts as a binding site for SARS-CoV-2 Spike protein and aids viral entry.
Lead therapeutic candidate, ATYR1923, modulates Neuropilin pathway to dampen inflammatory responses.

SAN DIEGO, June 17, 2020 (GLOBE NEWSWIRE) -- aTyr Pharma, Inc. (Nasdaq: LIFE), a biotherapeutics company engaged in the discovery and development of innovative medicines based on novel immunological pathways, today highlighted new external research demonstrating the involvement of Neuropilin biology in SARS-CoV-2 infection. The company is currently investigating Neuropilin-2 (NRP2) receptor biology as a novel target for new product candidates for a variety of diseases, including cancer and inflammatory disorders. The company's lead therapeutic candidate, ATYR1923, selectively binds to NRP2 and is currently in clinical development for inflammatory lung diseases, including a Phase 2 study in patients with COVID-19 related severe respiratory complications.

A recent article published in the *New England Journal of Medicine* (Ackermann M., Verleden S.E., Kuehnel M., et al.) reports that lung tissue analyzed from patients who died from COVID-19 related respiratory failure shows an increase in the expression of Neuropilin-1 (NRP1) and NRP2, suggesting these genes are up-regulated in response to SARS-CoV-2 infection in active sites of inflammation.

Recent pre-publications from two independent teams of European researchers report the discovery that the SARS-CoV-2 Spike protein S1 directly binds to the b1 domain of Neuropilin receptors on the cell surface, including NRP1 and NRP2. These studies also demonstrate that preventing this binding interaction results in decreased cell infection. This interaction suggests that NRP1 and NRP2 may be important factors which modulate the infectivity of the SARS-CoV-2 viral entry in cells which express these co-receptors. The authors of these studies indicate that Neuropilins may be a target for therapeutic approaches to reduce SARS-CoV-2 viral infection. These findings, published on the preprint server bioRxiv, are in line to be peer reviewed. (http://doi.org/dx5d; 2020) (http://doi.org/dx5c; 2020)

"As we continue to learn more about the nature of the SARS-CoV-2 virus, Neuropilins have emerged as a second gene family involved in viral entry. These papers show that by serving as a binding site for the S1 protein, Neuropilins promote viral infection of cells in tissue culture," said noted Neuropilin biology researcher Dr. Robert M. Gemmill, Ph.D., the former Melvyn Berlinsky Chair of Cancer Research and Professor of Medicine Emeritus in the Division of Hematology/Oncology at the Medical University of South Carolina. "These findings suggest that the S1 binding domain of Neuropilins may be a therapeutic target and present the opportunity to explore a potential new treatment approach to SARS-CoV-2 infection."

"We are particularly inspired by these independent findings and they further validate ATYR1923's potential to play a role as a treatment for COVID-19. As ATYR1923 is a selective modulator of NRP2 and dampens inflammatory response, the discovery of the Neuropilin domain as a binding site to the S1 protein significantly strengthens the hypothesis that ATYR1923 may have the potential to directly modulate SARS-CoV-2 infectivity and disease pathology," said Dr. Sanjay Shukla, M.D., M.S., President and Chief Executive Officer of aTyr.

About NRP2

Neuropilin-2 (NRP2) is a cell surface receptor that plays a key role in lymphatic development and in regulating inflammatory responses. In many forms of cancer, high NRP2 expression is associated with worse outcomes. NRP2 can interact with multiple ligands and co-receptors through distinct domains to influence their functional roles, making it a potential drug target with multiple distinct therapeutic applications. NRP2 interacts with type 3 semaphorins and plexins to impact inflammation and with forms of vascular endothelial growth factor (VEGF) and their receptors, to impact lymphangiogenesis. In addition, NRP2 modulates interactions between CCL21 and CCR7 potentially impacting homing of dendritic cells to lymphoid organs. aTyr is currently investigating NRP2 receptor biology, both internally and in collaboration with key academic thought leaders, as a novel target for new product candidates for a variety of diseases, including cancer and inflammation.

About ATYR1923

aTyr is developing ATYR1923 as a potential therapeutic for patients with inflammatory lung diseases. ATYR1923, a fusion protein comprised of the immuno-modulatory domain of histidyl tRNA synthetase fused to the FC region of a human antibody, is a selective modulator of neuropilin-2 that downregulates the innate and adaptive immune response in inflammatory disease states. aTyr is currently enrolling a proof-of-concept Phase 1b/2a trial evaluating ATYR1923 in patients with pulmonary sarcoidosis, a form of interstitial lung disease. This Phase 1b/2a study is a multi-ascending dose, placebo-controlled, first-in-patient study of ATYR1923 that has been designed to evaluate the safety, tolerability, steroid sparing effect, immunogenicity and pharmacokinetics profile of multiple doses of ATYR1923. In response to the COVID-19 pandemic, aTyr recently initiated a Phase 2 clinical trial with ATYR1923 in COVID-19 patients with severe respiratory complications. This Phase 2 study is a randomized, double blind, placebo-controlled study that has been designed to evaluate the safety and preliminary efficacy of a single dose of ATYR1923.

About aTyr

aTyr is a biotherapeutics company engaged in the discovery and development of innovative medicines based on novel immunological pathways. aTyr's research and development efforts are concentrated on a newly discovered area of biology, the extracellular functionality and signaling pathways of tRNA synthetases. aTyr has built a global intellectual property estate directed to a potential pipeline of protein compositions derived from 20 tRNA synthetase genes and their extracellular targets. aTyr's primary focus is ATYR1923, a clinical-stage product candidate which binds to the neuropilin-2 receptor and is designed to down-regulate immune engagement in inflammatory lung diseases. For more information, please visit http://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 “anticipates,” “believes,” “estimates,” “expects,” “intends,” “may,” “plans,” “projects,” “seeks,” “should,” “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 statements regarding the potential therapeutic benefits and applications of ATYR1923; timelines and plans with respect to certain development activities (such as the initiation of clinical trials, clinical trial enrollment, the conduct of clinical trials and the announcement of top-line results) and certain development goals. 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 or strategies 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, the fact that NRP2 and SARS-CoV-2 biology are not fully understood, uncertainty regarding the COVID-19 pandemic, risks associated with the discovery, development and regulation of our product candidates, including the risk that results from clinical trials or other studies may not support further development and the fact that ATYR1923 is in the early stages of clinical development, the risk that we may cease or delay preclinical or clinical development activities for any of our existing or future product candidates for a variety of reasons (including difficulties or delays in patient enrollment in planned clinical trials), the possibility of unexpected expenses or other demands on our cash resources, 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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