UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 25, 2021

ATYR PHARMA, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-37378**	**20-3435077**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

3545 John Hopkins Court, Suite #250	
San Diego	**92121**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's telephone number, including area code: (858) 731-8389

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligations of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	LIFE	The Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 or Rule 12b-2 of the Securities Exchange Act of 1934.

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 7.01 Regulation FD Disclosure.

aTyr Pharma, Inc. (the "Company") is participating at the Virtual Keystone Symposia: Tumor Metabolism and the Microenvironment to be held January 25-28, 2021. On January 27, 2021, the Company will present a poster entitled, "*Neuropilin-2 is Expressed on Immune Cells Present in the Tumor Microenvironment, and May Contribute to the Suppression of Immune Regulation Leading to Progression and Metastasis of Cancer*," and participate in a live Q&A session. The press release announcing the poster presentation is attached as Exhibit 99.1. The poster presentation has been posted on the Company's website and is attached hereto as Exhibit 99.2.

The information under this Item 7.01, including Exhibits 99.1 and 99.2 hereto, is being furnished herewith and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall such information be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release of aTyr Pharma, Inc. dated January 25, 2021
99.2	Poster Presentation titled "Neuropilin-2 is Expressed on Immune Cells Present in the Tumor Microenvironment, and May Contribute to the Suppression of Immune Regulation Leading to Progression and Metastasis of Cancer."

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ATYR PHARMA, INC.

By: /s/ Jill M. Broadfoot
Jill M. Broadfoot
Chief Financial Officer

Date: January 25, 2021

IMMEDIATE RELEASE
Contact:
Ashlee Dunston
Director, Investor Relations and Corporate Communications
adunston@atyrpharma.com

aTyr Pharma Presents Findings Further Validating NRP2 as a Potential Regulator of Solid Tumor Progression

Poster highlights NRP2 expression on immune cells in the tumor microenvironment.

Company's lead NRP2 antibody, ATYR2810, is in development for oncology.

SAN DIEGO – January 25, 2021 – aTyr Pharma, Inc. (Nasdaq: LIFE), a biotherapeutics company engaged in the discovery and development of innovative medicines based on novel biological pathways, today announced that it will present a poster and participate in a live Q&A session at the Virtual Keystone Symposia: Tumor Metabolism and the Microenvironment, which is being held January 25 – 28, 2021. The abstract and poster are available on the Keystone Symposia website.

The poster presents preclinical findings demonstrating that Neuropilin-2 (NRP2) was highly expressed on key immune cells implicated in regulating cancer progression, including myeloid derived suppressor cells (MDSCs), tumor associated macrophages (TAMs) generated from triple negative breast cancer cell lines, mature dendritic cells (DCs), and inducible T regulatory cells (Tregs). Further research showed that MDSCs and TAMs suppressed T cell proliferation and activation.

Details of the abstract and poster presentation are as follows:

Title: Neuropilin-2 is Expressed on Immune Cells Present in the Tumor Microenvironment, and May Contribute to the Suppression of Immune Regulation Leading to Progression and Metastasis of Cancer
Authors: Samantha Tyler, Michaela Ferrer, Clara Polizzi, Rodrigo Da Silva, Lisa Eide, Kendall Walwick, Matt Seikkula, Christoph Burkart, Suzanne Paz, Leslie Nangle. aTyr Pharma, San Diego, CA.
Session: Poster Session 2
Live Q&A Date and Time: January 27, 2021, 4:00 – 5:00PM EST

The poster is also available on the aTyr website.

“As we continue to explore the role of NRP2 in the progression of certain aggressive tumors, we are pleased to demonstrate for the first time that NRP2 is highly expressed on key immune cells in the tumor microenvironment that are implicated in regulating the progression of tumors and their metastasis,” said Sanjay S. Shukla, M.D., M.S., President and Chief Executive Officer of aTyr. “These findings support the potential of NRP2 as a target for cancer therapeutics, possibly through the immune regulation of the tumor microenvironment. Our panel of highly specific antibodies selectively targeting

NRP2, such as our lead IND candidate ATYR2810, may present differentiated approaches to treating certain aggressive cancers where NRP2 is implicated."

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 aTyr

aTyr is a biotherapeutics company engaged in the discovery and development of innovative medicines based on novel biological 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 potential therapeutic benefits and applications of NRP2 antibodies, including ATYR2810; timelines and plans with respect to certain development activities (such as the timing of data from clinical trials); 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, uncertainty regarding the COVID-19 pandemic, risks associated with the discovery, development and regulation of our product candidates, the risk that we or our partners 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 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.

Neuropilin-2 is Expressed on Immune Cells Pres the Suppression of Immune Regulation leading

Samantha Tyler[1], Michaela Ferrer[1], Clara Polizzi[1], Rodrigo Da Silva[1], Lisa Nangle[1*]

[1]aTyr Pharma, San Diego California

*Corresponding author

Abstract

Neuropilin-2 (NRP2) is a single transmembrane pleiotropic receptor, known to utilize VEGF receptors and plexins for signal transductic recently been described to play a role in the progression of tumors and their metastasis. Studies have shown the importance of NRP2 in c antigen presentation, phagocytosis and cell-cell interaction within immune cells, however, the contribution of NRP2 to the progression ar of cancer and immune regulation in the tumor microenvironment is still unknown. Our experiments aimed to identify which immune cell NRP2 receptor, and to elucidate the role of NRP2 in the suppression of T cells by myeloid cells that contribute to the progression of tumors show that NRP2 is highly expressed on key immune cells implicated in cancer progression including tumor-associated macrophages (TAM from triple-negative breast cancer cell lines, and myeloid-derived suppressor cells (MDSCs). We show that both cell types suppress T cell and activation via flow cytometry by proliferation modelling and by decreased CD25 and CD69 expression in the myeloid cell/T cell respectively. In addition, cytokines in the suppression supernatants were measured utilizing the Meso Scale Discovery platform. A reductio 2, IL-4 and IL-17A is seen in the T cell co-cultures, confirming a reduction in T cell activation. We also show an increase in NRP2 expressior dendritic cells (DCs), and that MDA-MB-231 differentiated TAMs prevent their maturation. We demonstrate this with the suppression of th of anti-tumor IL-12, and by a decrease in CD83, CD86 and HLA-DR expression on DCs in TAM/DC co-cultures utilizing the Meso Scale Discov and flow cytometry respectively. We also demonstrate that inducible T regulatory cells (Tregs) generated *in vitro* express high levels of N variety of *in vivo* syngeneic models, we confirm that NRP2 is expressed on a variety of immune cells such as TAMS, DCs, MDSCs demonstrating that our therapeutic target is expressed on important immune suppressive cells in both human and mouse systems. We first time that NRP2 is highly expressed on the immune suppressive cells of the tumor microenvironment. These are key cells implicated the progression of tumors and their metastasis. These findings indicate the potential of NRP2 as a target for anti-cancer therapeutics, pos immune regulation of the tumor microenvironment.

Introduction

- NRP2 is a single transmembrane receptor, known to utilize VEGF receptors and plexins for signal transduction
- NRP2 has been described to play a role in the progression of tumors and their metastasis (Caunt et al, 2008)
- NRP2 has been shown to play a role in cell migration, antigen presentation, phagocytosis and cell-cell interaction within immune cells (Schellenburg et al, 2017)
- NRP2s contribution to the progression and metastasis of cancer and immune regulation in the tumor microenvironment is still unknown
- We aim to determine expression of NRP2 on a variety of immune cells in the tumor microenvironment, and ultimately its role on each of those cells

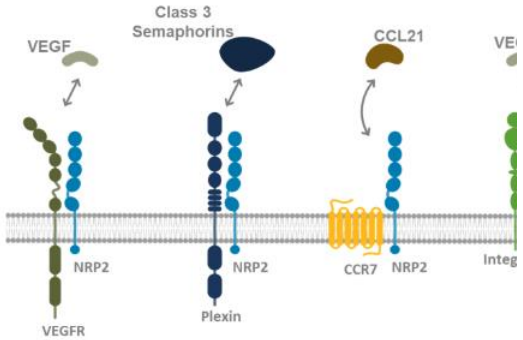


Fig 1. Schematic of NRP2 and its co-receptors and binding par with VEGF variants, Plexin with class 3 Semaphorins, CCR7 w Integrin with VEGF variants and the extracellular matrix (ECM)

Experimental Procedures

Fig 2. Generation of Primary Human MDA-MB-231 TAMs

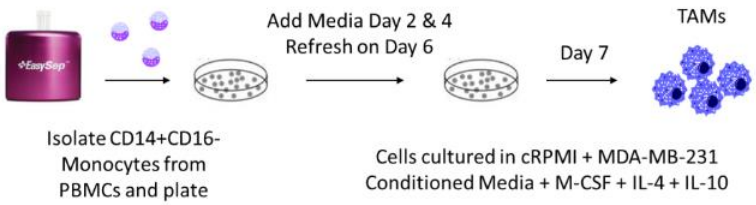


Fig 6. T cell Suppression Assay

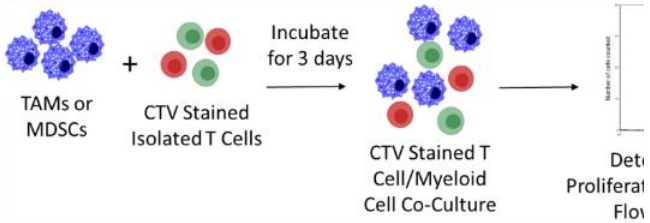


Fig 7. DC Suppression Assay

Fig 3. Generation of Primary MDSCs

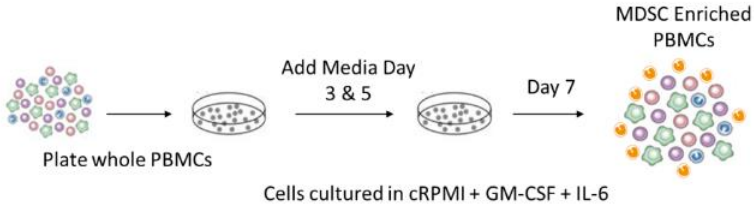


Fig 4. Generation of Primary Human Dendritic Cells

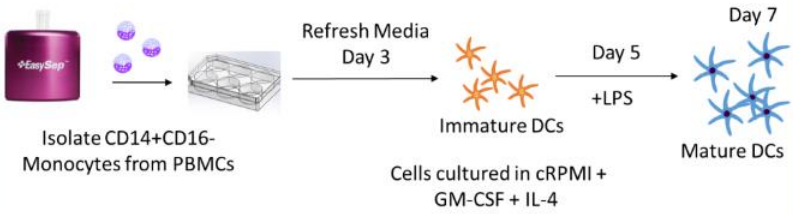
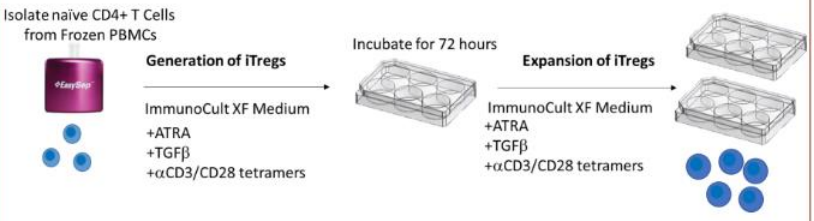
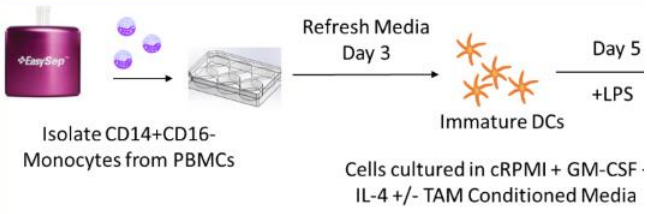


Fig 5. Generation of Primary Human inducible Tregs



Figs 2-5. Schematic representation showing the experimental procedures to generate: human TAMs from MDA-MB-231 conditioned media (Figure 2); human MDSCs (Figure 3); human dendritic cells (Figure 4) and human inducible Tregs (Figure 5). NRP2 levels were measured using flow cytometry and were analyzed using FlowJo and statistical analysis performed using Prism.



Figs 6-7. Schematic representation showing the experimental procedur suppression of T cells by TAMs or MDSCs (Figure 6) and suppression c conditioned media (Figure 7). Proliferation, activation and suppression using flow cytometry. Cytokines measured by Mesoscale Discovery statistical analysis performed using Prism.

In vivo Procedures

Table 1. Mouse Syngeneic Tumor Models

Tumor Model	Cell Line Name	Implantation Site	Organs Col Immunoph
Breast Cancer	4T1	Flank	Tumor,
Colorectal Carcinoma	CT26.WT	Flank	Tumor,
Renal Adenocarcinoma	RENCA	IV	Lungs,

Table 2. Mouse Syngeneic Tumor Models

Cell Types	Markers Utilized to Identify Cell Types
TAMs	CD45+CD4-CD8-CD19-CD11b+GR1-F4/80+
MDSCs	CD45+CD45+CD4-CD8-CD19-CD11b+GR1+
DCs	CD45+CD4-CD8-CD19-CD11b^{low}CD11c+
Tregs	CD45+CD11b-CD11c-CD3+CD4+CD25+ (GITR+ or Fc

Table 1-2. *In vivo* syngeneic models (Table 1) utilized to determine NRP isolated immune cells (Table 2) and the markers used to identify speci subsets. NRP2 levels were measured using flow cytometry and were FlowJo and statistical analysis performed using Prism.

- Caunt M, Mak J, Liang WC, Stawicki S, Pan Q, Tong RK, Kowalski J, Ho C, Reslan HB, R Tessier-Lavigne M, Bagri A. Blocking neuropilin-2 function inhibits tumor cell metast
- Schellenburg S, Schulz A, Poitz DM, Muders MH. Role of neuropilin-2 in the immune