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 22, 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 Society for Laboratory Automation and Screening Digital International Conference and Exhibition (SLAS) to be held virtually from January 25-27, 2021. The Company will be presenting a poster presentation entitled, "*A Mass Spectrometry Proteomics-Based Approach to Identify Target Receptors for Novel Extracellular tRNA Synthetase Fragments*," via a prerecorded audio recording on the SLAS website. 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 22, 2021
99.2	Poster Presentation titled "A Mass Spectrometry Proteomics-Based Approach to Identify Target Receptors for Novel Extracellular tRNA Synthetase Fragments."

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 22, 2021

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

aTyr Pharma to Present Poster Highlighting Research Approach for Identifying Receptor Targets for Extracellular tRNA Synthetases

Poster to be presented at the 2021 Society for Laboratory Automation and Screening Digital International Conference and Exhibition.

Research approach led to the identification of target receptors for two tRNA synthetases and further validates company's biology platform.

SAN DIEGO – January 22, 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 audio presentation at the upcoming Society for Laboratory Automation and Screening Digital International Conference and Exhibition (SLAS) to be held virtually January 25-27, 2021. The abstract and poster are available on the SLAS website.

The poster describes a mass spectrometry proteomics-based approach to identify target receptors for two distinct extracellular tRNA synthetase fragments. The utilization of this workflow, which included recombinant protein expression, flow cytometry, and receptor screening in living cells using the ligand-receptor capture TriCEPS technology, resulted in the identification of receptor targets for fragments of the tRNA synthetases AARS and DARS as well as insights into their potential biological activity in immunology, cancer and fibrosis. Furthermore, this approach can be applied more broadly to identify receptor targets of extracellular proteins and other ligands such as peptides, antibodies or viruses.

Details of the abstract and poster presentation are as follows:

Title: A mass spectrometry proteomics-based approach to identify target receptors for novel extracellular tRNA synthetase fragments
Authors: Blythe C. Dillingham, Jennifer Brasseit, Björn Hegemann, Ann L. Menefee, Justin Rahman, Zhiwen Xu, Paul Helbling, Leslie A. Nangle, Ryan A. Adams. aTyr Pharma, San Diego, CA, CSL Behring, Dualsystems Biotech.
Track: Assay Development and Screening
Date: January 25 – 27, 2021

The poster is also available on the aTyr website.

“We are pleased to present our findings utilizing a novel approach for identifying receptor targets of extracellular proteins, and for the first time provide insight into the potential biological function of extracellular tRNA synthetases AARS and DARS,” said Sanjay S. Shukla, M.D., M.S., President and Chief Executive Officer of aTyr. “These findings further validate the relevance of our tRNA synthetase biology platform to important disease pathways and demonstrate its ability to generate new drug targets. Identifying receptor targets for these two tRNA synthetases, which are relevant to immunology, cancer and fibrosis, will help guide the development of potential new therapies in these areas of high unmet need.”

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 further research and development activities related to, and potential utility of, the newly identified receptor targets, the potential therapeutic benefits and applications of our current and future product candidates; 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.

A Mass Spectrometry Proteomics-E
Extracellular tRNA Synthetase Frag

Blythe C. Dillingham[1], Jennifer Brasseit[2], Björn Hegemann[2], Ann L. Menefee[1], Justin Ra

1. aTyr Pharma, 2. CSL Behring, 3. Dualsystems Biotech *Contact: radams@atyrpharma.com

Overview

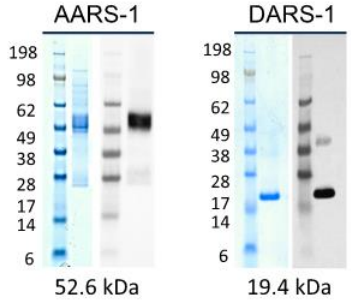
- **Purpose:** To identify target receptors and determine the biological functions of novel extracellular tRNA synthetase fragmen
- **Methods:** tRNA synthetase fragments were expressed recombinantly, and their binding to various human cell lines was asse was completed in three cell-lines using the ligand-receptor capture technology LRC-TriCEPS followed by mass spectrometry p completed by siRNA knock-down and flow cytometry, and biological function was determined using a FRET-based enzyme-in
- **Results:** Utilizing this workflow, we successfully identified target cell-surface receptors for tRNA synthetase fragments and ha unknown biological functions. In doing so, we have also created a novel approach which can be applied more broadly to iden proteins in an endogenous system.

Introduction

- While canonically known for their intracellular role in protein synthesis, full-length and splice or proteolytic variants of tRNA synthetases have been found to exist in the extracellular space where they may play an immunomodulatory role.
- Full-length Histidyl-tRNA synthetase (HARS) has been established as a molecule present in circulation that modulates T-cell activity, and a HARS variant has been shown to bind to Neuropilin-2 and to inhibit proinflammatory chemokines and cytokines.
- Alanyl-tRNA Synthetase (AARS) and Aspartyl-tRNA Synthetase (DARS) are also present extracellularly and have links to immune modulation; however, their receptor targets and downstream biological function remain unknown:
  - Auto-antibodies targeting AARS and other synthetases are present in rare anti-synthetase syndromes associated with inflammatory phenotypes such as myositis and interstitial lung disease[3].
  - Full-length DARS protein and a DARS fragment are secreted from THP-1 Macrophages when stimulated with LPS (shown to the right).

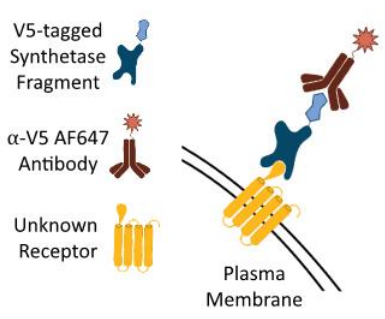
Materials and Methods

Recombinant Expression of AARS and DARS Fragments



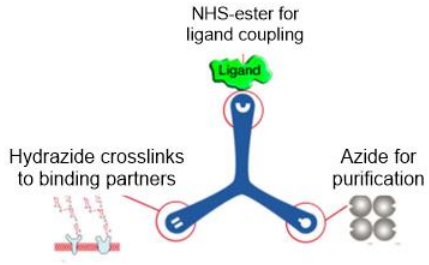
- V5-tagged extracellular tRNA synthetase fragments AARS-1 and DARS-1 were expressed recombinantly in Expi293 or ExpiCHO cells and purified for downstream *in vitro* assays.
- Shown to the left are SDS PAGE (blue) and anti-V5 Western blots (grey) detecting purified AARS-1 and DARS-1 under non-reduced conditions.

FACS Cell



LRC-TriCEPS Mass Spectrometry Proteomics Receptor Screen

TriCEPS 3.0 Reagent



- Ligand of interest is coupled to TriCEPS reagent.
- Upon ligand binding, TriCEPS cross-links to the receptor targets via the hydrazide functional group.
- Ligand-Receptor complexes are isolated using the azide group for purification.

LRC-TriCEPS Receptor Screen

Living cells

Control ligand (Transferrin)

Mild oxidant generates cell surface aldehydes

Ligand of interest (AARS-1 or DARS-1)

Cell-surface labeling

Cell lysis, pro
isolation a
digestior

Mass spectro
based analys
relative quant
(LC-MS/M

Experiments perf
Thresholds for significance: Log_{10} p-value > 2;

References

1. Frei, Andreas P et al. "Direct identification of ligand-receptor interactions on living cells and tissues." Nature Biotechnology vol. 30,10 (2012): 997-1001. doi:10.103
2. Sobotzki, Nadine et al. "HATRIC-based identification of receptors for orphan ligands" Nat Commun 9, 1519 (2018). https://doi.org/10.1038/s41467-018-03936-z
3. Witt, Leah J et al. "The Diagnosis and Treatment of Antisynthetase Syndrome." Clinical Pulmonary Medicine vol. 23,5 (2016): 218-226. doi:10.1097/CPM.00000000