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

May 7, 2018
Date of Report (Date of earliest event reported)

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, California 92121

(Address of principal executive offices, including zip code)

(858) 731-8389

(Registrant's telephone number, including area code)

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))

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 2018 American Association of Immunologists (AAI) Annual Meeting held in Austin, Texas from May 4 – 8, 2018. During the AAI Annual Meeting, the Company is presenting a poster presentation entitled, "Identification of a T Cell Immunomodulatory Domain in Histidyl-tRNA Synthetase." The poster presentation has been posted on the Company's website and is attached hereto as Exhibit 99.1.

The information under this Item 7.01, including Exhibit 99.1 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 Exhibits.

(d) Exhibits.

99.1	Poster presentation titled “Identification of a T Cell Immunomodulatory Domain in Histidyl-tRNA Synthetase.”

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/ Sanjay S. Shukla
Sanjay S. Shukla, M.D., M.S.
President and Chief Executive Officer

Date: May 7, 2018

Identification of a T Cell Immunomodulatory Dom

Elisabeth Mertsching, Jeanette Ampudia, Ryan Adams, Sanna Rosengren, Leslie Nangle, John Me David King

aTyr Pharma, San Diego, CA, USA

Abstract

Histidyl-tRNA synthetase (HARS) is the autoantigen target of Jo-1 antibodies, which occur in the major form of anti-synthetase syndrome. These patients are characterized by an autoimmune myositis and interstitial lung disease. Circulating extracellular HARS is detected in healthy individuals, but is reduced or undetectable in Jo-1-positive individuals. Administration of ATYR1940, a recombinant form of HARS, ameliorates lung fibrosis and reduces T cell cytokine production in the bleomycin-induced lung injury model. Similar effects were observed with the N-terminal domain of HARS (the iMod domain) conjugated to IgG Fc, suggesting that this domain confers the immunomodulatory activity of HARS.

To confirm primary immune effects of ATYR1940 and ATYR1923 (iMod.Fc), human T cells were isolated from PBMC from healthy individuals and stimulated with anti-CD3/anti-CD28. Proteins containing the HARS iMod domain reduced *in vitro* activation of human CD4⁺ and CD8⁺ T cells, as evidenced by reduced secretion of IL-2, IFNγ, TNFα, IL-17, IL-13, and granzyme B, as well as decreased upregulation of activation markers such as CD69 and CD40L. ATYR1940 and ATYR1923 also inhibited cytokine release after *ex vivo* stimulation of human memory T cells in a NSG mouse xenogeneic GVHD model. T cell inhibition by ATYR1940 was dependent on its iMod domain, as demonstrated using an iMod-specific blocking monoclonal antibody. The ATYR1940-induced T cell gene signature reflected a general inhibitory effect on activation as well as on cell cycle protein expression. These results suggest that circulating levels of HARS may act to control the threshold stimulatory signal required to activate T cells. We propose circulating HARS as a soluble immune set-point modulator.

Introduction

- A number of non-canonical functions of proteins generated from tRNA synthetase genes have been reported, demonstrating diverse roles for these proteins outside of protein synthesis (Wakasugi & Schimmel, 1999; Park et al., 2008; Arif et al., 2017).
- Proteins derived from the histidyl-tRNA synthetase (HARS) gene are found extracellularly and are detected in the serum of all healthy donors.
- Patients with anti-synthetase syndrome that are positive for anti-HARS (Jo-1) antibodies are often characterized by inflammatory infiltrates in skeletal muscle and lung.
- In these individuals, circulating HARS is reduced or undetectable (unpublished results).

Hypothesis: Extracellular HARS may exert immunomodulatory functions

Material and Methods

Cell Culture:

- Peripheral blood mononuclear cells (PBMC) were isolated from the blood of healthy donors and T cells, CD4⁺ T cells and CD8⁺ T cells were purified by negative selection using magnetic beads.
- T cells were incubated in medium alone (unstimulated) or were stimulated with plate-bound anti-CD3 antibodies at 1.25 – 5 µg/mL and with soluble anti-CD28 antibodies at 1 µg/mL in the presence of ATYR1940, iMod-Fc, iMod or vehicle.
- After 24 hours of stimulation, cytokine and granzyme B release was measured in the supernatant by ELISA, Luminex Milliplex and/or MSD immunoassays and cells were analyzed for expression of surface activation markers by flow cytometry.

Graft-versus-Host Disease (GvHD) model:

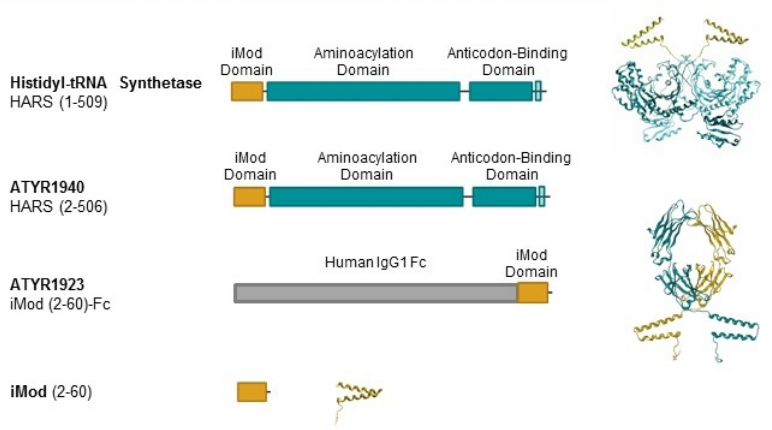
- Human PBMC were injected into NSG (NOD *scid* gamma) mice and spleens collected 11 days later.
- Splenocytes were analyzed by flow cytometry to confirm effector/memory phenotype, and cultured with anti-human CD3 antibodies at 2.5 µg/mL and anti-human CD28 antibodies at 1 µg/mL in the presence of vehicle or ATYR1940.
- Cytokine release was measured using Luminex Milliplex immunoassays.

Gene profiling:

- Gene profiling was performed on unstimulated T cells and on T cells stimulated with 2.5 µg/mL of anti-CD3 antibodies and 1 µg/mL of anti-CD28 antibodies in presence of ATYR1940, ATYR1923 or vehicle for 24 hours. RNA sequencing was done by GENEWIZ. Gene expression was also measured using QuantiGene Plex assays (Thermo Fisher Scientific).

Statistics: One-way ANOVA (Dunnett's post-hoc test) was used to compare each condition to the stimulated vehicle control. ****p < 0.0001; ***p <0.001; **p < 0.01; *p <0.05.

Figure 1. Generation of HARS-Derived Proteins



The N-terminal domain of HARS, the iMod domain, consisting of the first 59 amino acids, is sometimes referred to as the WHEP domain, a specialized version of the helix-turn-helix motif, that is responsible for forming complexes with other proteins (Rho et al., 1999).

Figure 2. ATYR1940 Inhibits IL-2 and Granzyme B Release

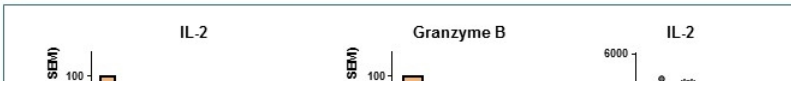


Figure 3. ATYR1940 Inhibits Upregulation of T Cell Activat

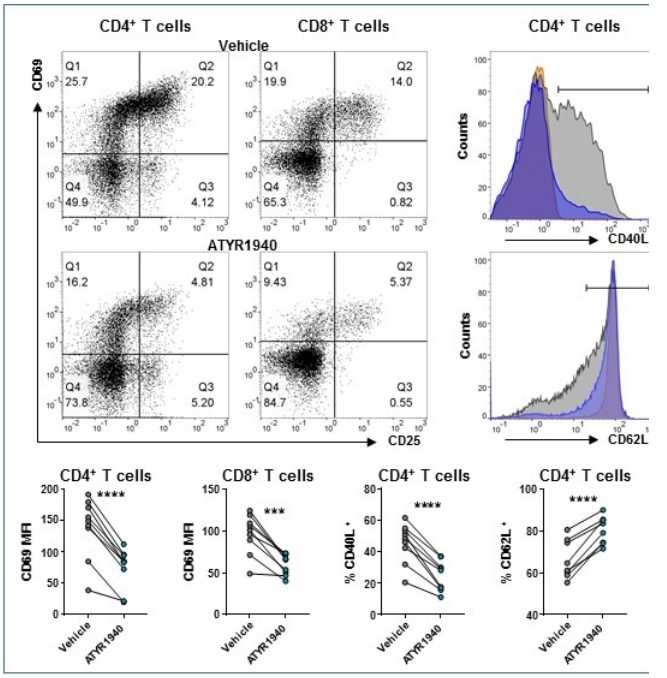


Figure 4. ATYR1940 Decreases Cytokine Release from Stim

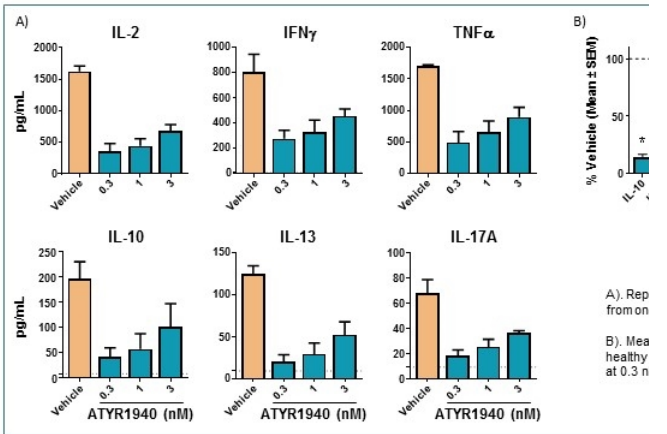


Figure 5. ATYR1940 Regulates Activation of CD4⁺ and C

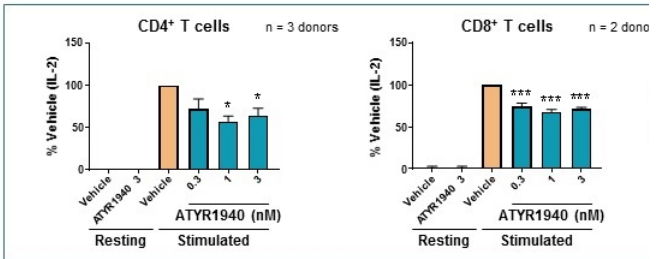
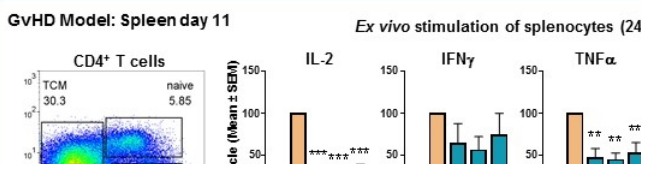
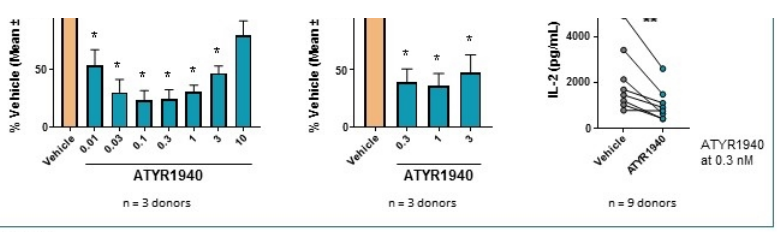


Figure 6. Memory T cells Respond to ATYR1940 Tre





References

- Arif A, Terenzi F, Potdar AA, Jia J, Sacks J, China A, Halawani D, Vasu K, Li X, Brown JM, Chen J, Kozma SC, Thomas G & Fox PL (2017) EPRS is a critical mTORC1-S6K1 effector that influences adiposity in mice. *Nature* 542, 357-361.
- Park SG, Schimmel P & Kim S (2008) Aminoacyl tRNA synthetases and their connections to disease. *Proc Natl. Acad. Sci.* 105, 11043-11048.
- Rho SB, Kim MJ, Lee JS, Seol W, Motegi H, Kim S & Shiba K (1999) Genetic dissection of protein–protein interactions in multi-tRNA synthetase complex. *Proc Natl. Acad. Sci.* 96, 4488-4493.
- Wakasugi K & Schimmel P (1999) Two distinct cytokines released from a human aminoacyl-tRNA synthetase. *Science* 284, 147-151.