# 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 20, 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 Thoracic Society (ATS) Annual Meeting held in San Diego, CA from May 18 – 23, 2018. During the ATS Annual Meeting, the Company is presenting a poster presentation entitled, "Preclinical Characterization of ATYR1923 (iMod.Fc), an Immune-Modulatory Therapeutic With Potentially Broad Application in Interstitial Lung Diseases." 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 “Preclinical Characterization of ATYR1923 (iMod.Fc), an Immune-Modulatory Therapeutic With Potentially Broad Application in Interstitial Lung Diseases.” |

**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 21, 2018

A1064/917

# Preclinical Characterization o With Potentially Broad Applic

K. Ogilvie, Q. Xu, M. T. Do, R. A. Adams, K. Chiang, D. Lee, M. Thoma

aTyr Pharma, San Diego, CA

## Abstract

**INTRODUCTION:** During the evolution of complex organisms, aminoacyl-tRNA synthetase genes evolved to incorporate new sequences and generate multiple splice variants, which lose their tRNA synthetase activity and take on novel functions (Lo et al. *Science*. 2014;345(6194):328-32). Histidyl-tRNA synthetase (HARS) and its splice variants are secreted and exhibit extracellular activity, which we have termed the Resokine pathway. Based on the overexpression in the lung of a splice variant encoding the N-terminal domain of Resokine, we hypothesized that it modulates the activity of immune cells in interstitial lung diseases (ILDs) and consequently ameliorates disease.

**RATIONALE:** In previous work, we showed that administration of Resokine proteins containing the N-terminal immunomodulatory (iMod) domain reduced bleomycin-induced lung fibrosis in mice, demonstrating the functional significance of the Resokine pathway in the lung. Based on these observations, we sought to engineer and characterize a clinical candidate with appropriate pharmaceutical properties for clinical study in ILD. Specifically, we sought to extend the duration of action of the iMod by fusion to the fragment crystallizable region (Fc) of human immunoglobulin G1 (IgG1 Fc).

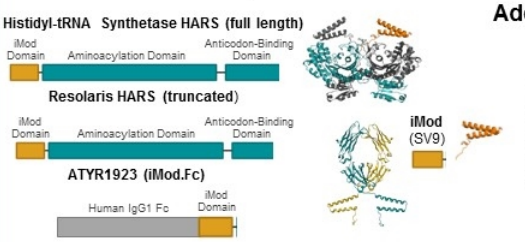
**METHODS:** ATYR1923 (iMod.Fc), a Resokine N-terminal domain fused to human Fc, was expressed in *Escherichia coli* and purified to homogeneity, confirming low endotoxin (limulus amebocyte lysate [LAL] assay) and pathogen-associated molecular pattern signals by a novel cell-based method. A rat model of bleomycin-induced lung fibrosis was employed to explore the effects ATYR1923 *in vivo*, including who plethysmography and histological disease scoring on day 22. Pharmacokinetic studies and Good Labo Practice (GLP)-compliant 1- and 3-month toxicology studies were conducted in rats and nonhuman pri (NHPs).

**RESULTS:** ATYR1923 exhibited the therapeutic potential of the iMod domain while having a long *in viv* ATYR1923 had a terminal half-life of ~3 days in rats and ~4.5 days in NHPs, in contrast to the isolated domain that had a terminal half-life of ~20 minutes in rats. In rat bleomycin-induced lung fibrosis, ATYR 0.1–3 mg/kg weekly beginning on day 9 exerted therapeutic activity as revealed by reversal of bleomyc changes in respiratory parameters and decreased histological fibrosis (Ashcroft score) and immune inf One- and 3-month GLP-compliant studies found no adverse test article–related findings. The no-observed-adverse-effect level was 60 mg/kg in both species.

**CONCLUSIONS:** ATYR1923 has been engineered to have a long duration of action and is efficacious bleomycin-induced lung fibrosis preclinical models when administered weekly. Based on the preclinica clinical testing is planned.

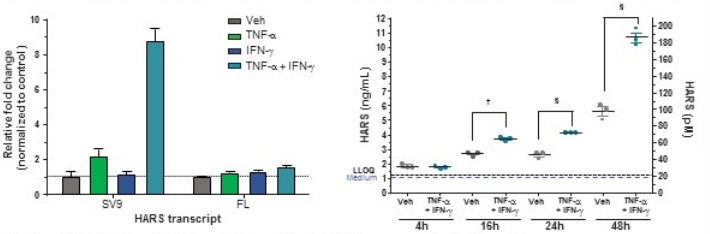
## Introduction

### Resokine Family of Molecules



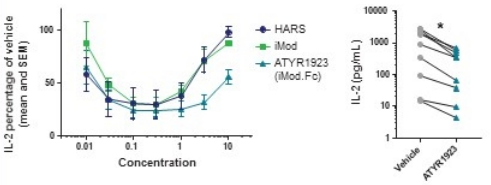

HARS, histidyl-tRNA synthetase; IgG1 Fc, fragment crystallizable region of human immunoglobulin G1; ATYR1923 (iMod.Fc), a Resokine N-terminal domain fused to human Fc; SV9, splice variant species 9.

### SV9 Transcript and HARS Release From A549 Lung Adenocarcinoma Cells Are Upregulated by Inflammatory Cytokines




FL, full length; IFN, interferon; LLOQ, lower limit of quantification; TNF, tumor necrosis factor; Veh, vehicle.
*P≤0.05; †P≤0.01; ‡P≤0.001; §P≤0.0001.

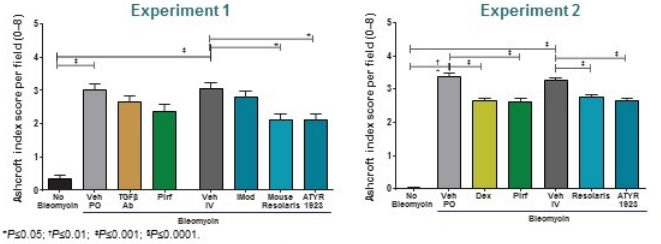
### iMod-Containing Proteins Decrease Activation of Human T Cells




IL, interleukin; SEM, standard error of the mean.
*P<0.05, paired Student's t-test.

- IL-2 measured 24 hours after stimulation with anti-CD3 and anti-CD28 antibodies of human T cells isolated from healthy donor peripheral blood mononuclear cells

### Weekly Therapeutic Dosing of ATYR1923 Ameliorates Fibrosis in Mouse Bleomycin-Induced Lung Injury



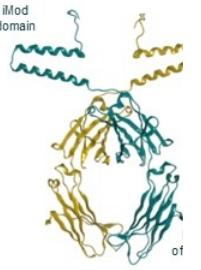

*P≤0.05; †P≤0.01; ‡P≤0.001; §P≤0.0001.

**Dosing information**

**Oral vehicle:** 1x PBS, BID D8-D21
**Intravenous (IV) vehicle:** 50 mM L-His, 140 mM NaCl, QD D8-D21
**Transforming growth factor (TGF)-β antibody:** clone 1D11, 3 mg/kg IP QOD D0-D21
**Pirfenidone (Pirf):** 100 mg/kg (Exp 1) or 200 mg/kg (Exp 2) PO BID D8-D21
**Dexamethasone (Dex):** 0.25 mg/kg PO QD D0-D21
**iMod:** 2.5 mg/kg IV QD D8-D21
**Resolaris™:** 3 mg/kg IV QD D8-D21
**ATYR1923:** 0.4 mg/kg IV QW D8, D15

- ATYR1923 administered therapeutically at 0.4 mg/kg once weekly (QW) drives efficacy comparable to or greater than pirfenidone, anti–TGF-β antibody, and dexamethasone

### ATYR1923




**iMod Domain**
- Encoded by a splice varian enriched in human lung
- Inhibits human T cell activ
- Exogenous administration fibrosis in mouse bleomyc lung fibrosis model
- Small protein readily clear

**Fc domain**
- Prolongs *in vivo* half-life

**ATYR1923 Therapeutic Rati**
- Retains ability of the isolat to inhibit human T cell acti
- T cells are pathogenic in i lung diseases (ILDs)
- Administration of ATYR19 therapeutic in rodent bleo induced lung fibrosis mode

## Methods

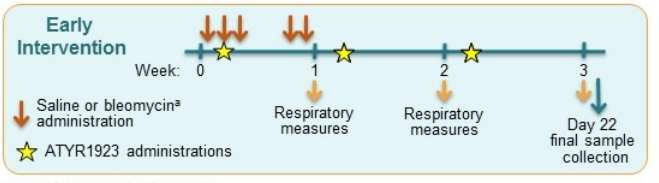
### Objectives

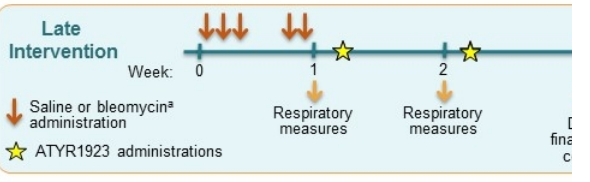
- Determine dose response when intervening on day 9
- Determine effects of intervention at day 2 vs day 9 (1 mg/kg)

**Dosing Information**

**Nintedanib:** 60 mg/kg PO QD (days 9–22)
**Vehicle PO:** QD (days 9–22)
**Vehicle IV:** QW (days 2, 9, and 16)
**ATYR1923:** 0.1–3 mg/kg (days 9 and 16)
**ATYR1923*:** 1 mg/kg (days 2, 9, and 16)

### In-Life Protocol




*Oropharyngeal (OP) dosing was skipped on days 4 and 5 due to animal welfare concerns.

**Presented at the ATS International Conference 2018; May 18–23, 2018; San Diego, California**