

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): May 19, 2019

ATYR PHARMA, INC.

(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction  
of incorporation)

3545 John Hopkins Court, Suite #250  
San Diego

(Address of Principal Executive Offices)

001-37378

(Commission File Number)

20-3435077  
(IRS Employer  
Identification No.)

92121  
(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 2019 American Thoracic Society (ATS) Annual Meeting held in Dallas, Texas from May 17 – 22, 2019. During the ATS Annual Meeting, the Company is presenting a poster presentation entitled, "ATYR1923 Modulates the Inflammatory Response in Experimental Models of Interstitial Lung Disease." 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.

(d) Exhibits.

99.1 [Poster presentation titled "ATYR1923 Modulates the Inflammatory Response in Experimental Models of Interstitial Lung Disease"](#)

**SIGNATURE**

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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 20, 2019

#10533

# ATYR1923 Modulates Lung Disease

C. Burkart, M. Seikkula, L. Eide, S. Paz, D. Ch...  
aTyr Pharma, San Diego, CA

## Abstract

**Rationale:** ATYR1923 is a novel immunomodulatory therapeutic protein that consists of the histidyl-tRNA synthetase (HARS) N-terminal immunomodulatory (iMod) domain fused to human IgG1 Fc which extends the circulating half-life of the molecule resulting in a longer pharmacological duration of action. We have previously shown that secreted forms of the HARS iMod domain reduce bleomycin-induced lung fibrosis in rodents and reduce activation of human T cells *in vitro*. Based on this knowledge, we hypothesized that ATYR1923 might also modulate inflammatory and fibrotic processes in other rodent models of interstitial lung disease (ILD).

**Methods:** ATYR1923 was evaluated in the following murine models of ILD: Sclerodermatous chronic graft-versus-host disease (scl cGVHD), *Saccharopolyspora rectivirgula*-induced chronic hypersensitivity pneumonitis (CHP), *Propionibacterium acnes*-induced pulmonary fibrosis (sarcoidosis) and SKG mice [rheumatoid arthritis-associated interstitial lung disease, (RA-ILD)]. ATYR1923 was given intravenously once a week at 0.4 - 3 mg/kg. At study termination, lung tissue was collected for protein and histopathological analysis. Lung homogenates were analyzed for cytokines and chemokines implicated in lung fibrosis using a multiplex immunoassay platform (Luminex). Lung-derived single cell suspensions were immunophenotyped by flow cytometry.

**Results:** In the scl cGVHD model, low-dose ATYR1923 determined by histopathological and biochemical analysis significantly lower numbers of lymphocytes in ATYR1923 compared to vehicle groups. ATYR1923 also significantly reduced fibrosis-related cytokines or chemokines (e.g. IFN- $\gamma$ , IL-6, IL-17, IL-22, CXCL10, CXCL12, CXCL13, CXCL16, CXCL20, CXCL21, CXCL22, CXCL23, CXCL24, CXCL25, CXCL26, CXCL27, CXCL28, CXCL29, CXCL30, CXCL31, CXCL32, CXCL33, CXCL34, CXCL35, CXCL36, CXCL37, CXCL38, CXCL39, CXCL40, CXCL41, CXCL42, CXCL43, CXCL44, CXCL45, CXCL46, CXCL47, CXCL48, CXCL49, CXCL50, CXCL51, CXCL52, CXCL53, CXCL54, CXCL55, CXCL56, CXCL57, CXCL58, CXCL59, CXCL60, CXCL61, CXCL62, CXCL63, CXCL64, CXCL65, CXCL66, CXCL67, CXCL68, CXCL69, CXCL70, CXCL71, CXCL72, CXCL73, CXCL74, CXCL75, CXCL76, CXCL77, CXCL78, CXCL79, CXCL80, CXCL81, CXCL82, CXCL83, CXCL84, CXCL85, CXCL86, CXCL87, CXCL88, CXCL89, CXCL90, CXCL91, CXCL92, CXCL93, CXCL94, CXCL95, CXCL96, CXCL97, CXCL98, CXCL99, CXCL100).

**Conclusions:** ATYR1923 has pharmacological activity in the inflammatory phase of the model. Furthermore, proteomic analysis demonstrated immunomodulatory activity in other animal models of highly inflammatory or T cell driven. These data are consistent with the inflammatory responses that may lead to subsequent fibrosis in the bleomycin model. In a recently completed Phase I study in healthy subjects, ATYR1923 was well tolerated and supported further evaluation of this potential therapy.

## Introduction

### Resokine Family of Molecules

#### Histidyl-tRNA Synthetase HARS (full length)

iMod Domain Aminoacylation Domain Anticodon-Binding Domain



#### iMod (SV9)

iMod Domain



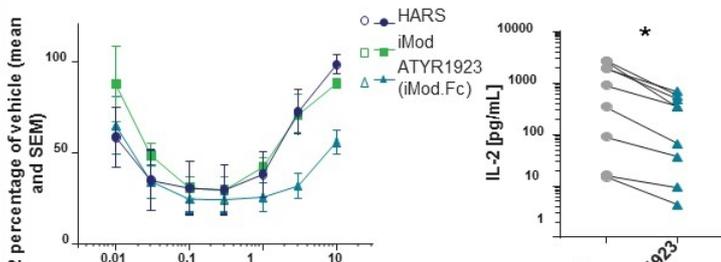
#### ATYR1923 (iMod.Fc)

Human IgG1 Fc iMod Domain

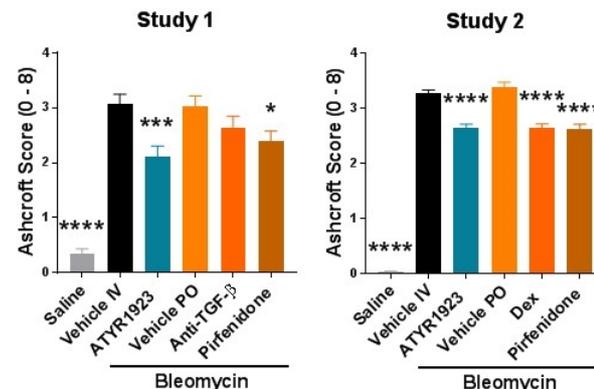


HARS, histidyl-tRNA synthetase; iMod (SV9), splice variant species 9; ATYR1923 (iMod.Fc), a Resokine N-terminal domain (iMod) fused to human Fc

### iMod-Containing Proteins Decrease Activation of Human T Cells<sup>1</sup>



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



One-Way ANOVA with Dunn's multiple comparisons test (BLM + Vehicle)

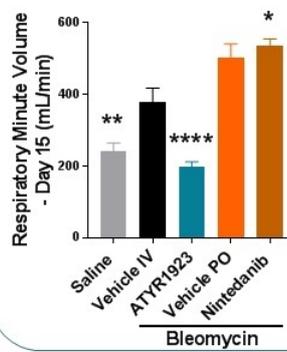
- ATYR1923 administered therapeutically at 0.4 mg/kg (IV QW D8 and D15)
- Anti-TGF- $\beta$  antibody 3 mg/kg (QOD D0 - 21), Pirfenidone 100 or 200 mg/kg (BID D8 - D21), Dexamethasone 0.25 mg/kg (PO QD D0 - D21)
- ATYR1923 drives efficacy as determined by Ashcroft score comparable to vehicle, greater than pirfenidone, anti-TGF- $\beta$  antibody and dexamethasone in separate studies

### Early Intervention With ATYR1923 Improves Respiratory Function in a Rat Bleomycin Model

IL-2 Concentration [pM]

Vehicle  
ATYR1923  
Paired Student's t-test.

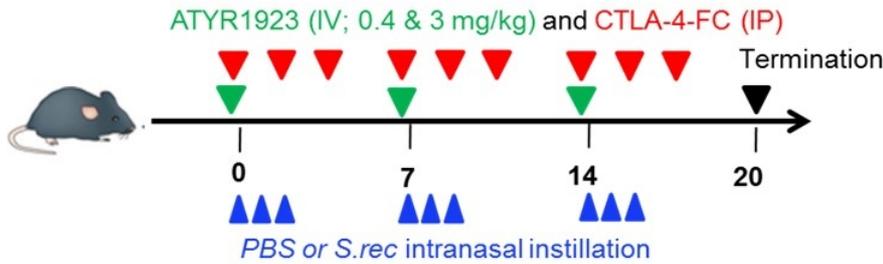
- IL-2 measured 24 hours after stimulation with anti-CD3 and anti-CD28 antibodies of human T cells isolated from healthy donor peripheral blood mononuclear cells
- Similar findings with other cytokines (TNF $\alpha$ , IL13, CCL20, IL10) and granzyme B as well as surface activation markers (CD69, CD40L, ICOS, 4-1BB, OX40).



- ATYR1923 administered therapeutically 2 post BLM at 1 mg/kg once weekly (IV)
  - Nintedanib dosed at 50 mg/kg starting day 2 post BLM (PO QD)
  - Administered ATYR1923 improved respiratory function on day 15 post BLM insult back to baseline (Saline - No BLM)
  - No significant effect of ATYR1923 on inflamed Ashcroft score at termination on day 22
- One-Way ANOVA with Dunn's multiple comparison (BLM + Vehicle IV)

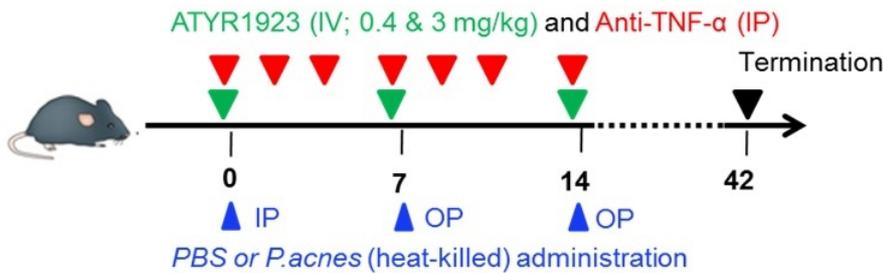
## Methods: Four Experimental Models of ILD

### S. rectivirgula



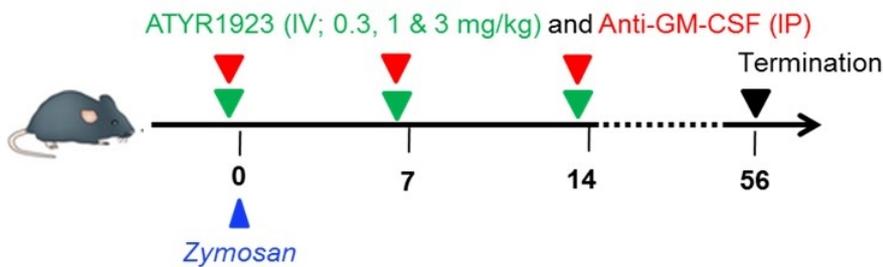
- Repeated challenges with *S. rectivirgula* experimental chronic hypersensitivity
- In humans a common form of CHP is aerolized *S. rectivirgula*.
- Test articles dosed until study termination

### P. acnes



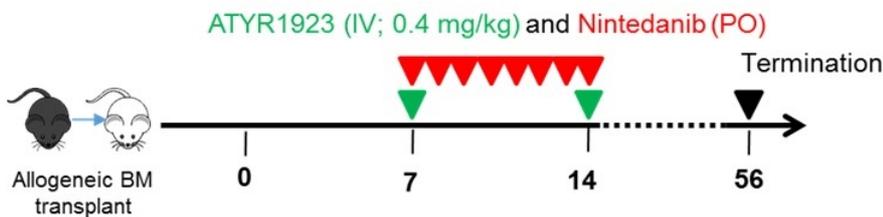
- P. acnes* has been implicated as the cause of chronic hypersensitivity pneumonitis
- Repeated *P. acnes* challenges induce chronic hypersensitivity pneumonitis
- Test articles dosed until study termination

### SKG



- SKG mice are genetically prone to develop chronic hypersensitivity pneumonitis
- Following zymosan administration, SKG mice develop chronic hypersensitivity pneumonitis (100%) and lung disease (20%)
- Test articles dosed until study termination

### cGvHD



- Murine graft vs host disease (cGvHD) is a murine model of chronic hypersensitivity pneumonitis
- B10.D2(H-2<sup>d</sup>) $\rightarrow$ Balb/c(H-2<sup>d</sup>) minor histocompatibility antigen mismatch model used to induce cGvHD
- Test articles dosed until study termination

All data are shown as mean  $\pm$  SEM. \* p < 0.05; \*\* p < 0.01; \*\*\* p < 0.001; \*\*\*\* p < 0.0001

