

---

**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

February 27, 2019  
Date of Report (Date of earliest event reported)

---

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

---

**Delaware**  
(State or other jurisdiction  
of incorporation)

001-37378  
(Commission  
File Number)

20-3435077  
(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 Keystone Symposia 2019 Conference in Santa Fe, New Mexico from February 24-28, 2019. During the conference, the Company will be presenting a poster presentation entitled, “*ATYR1923 Reduces Neutrophil Infiltration in an Acute Lipopolysaccharide (LPS) Lung Injury Model.*” 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.

**Forward-Looking Statements**

This Current Report on Form 8-K contains forward-looking statements within the meaning of the Private Litigation Reform Act. 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, including statements regarding the potential therapeutic benefits and applications of our product candidates; our ability to successfully advance our pipeline or product candidates, undertake certain development activities (such as the initiation of clinical trials, clinical trial enrollment, the conduct of clinical trials and the announcement of top-line results) and accomplish certain development goals, and the timing of such events; and the scope and strength of our intellectual property portfolio. 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. 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, risks associated with the discovery, development and regulation of our product candidates, the risk that we 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), 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.

**Item 9.01 Exhibits.**

(d) Exhibits.

99.1 [Press Release of aTyr Pharma, Inc. dated February 27, 2019.](#)

99.2 [Poster presentation titled "ATYR1923 Reduces Neutrophil Infiltration in an Acute Lipopolysaccharide \(LPS\) Lung Injury Model."](#)

**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: February 27, 2019

**IMMEDIATE RELEASE****Contact:**

Joyce Allaire  
Managing Director, LifeSci Advisors, LLC  
jallaire@lifesciadvisors.com

**aTyr Pharma Presents Compelling Preclinical Data Highlighting Potential of ATYR1923 to Regulate Myeloid Cell Biology During Lung Inflammation**

*Poster presentation at the Keystone Symposia 2019 Conference: Myeloid Cells (B7)*

SAN DIEGO, February 27, 2019 -- aTyr Pharma, Inc. (Nasdaq: LIFE), a biotherapeutics company engaged in the discovery and development of innovative medicines based on novel immunological pathways, today announced a poster presentation at the Keystone Symposia 2019 Conference in Santa Fe, New Mexico from February 24-28, 2019.

"We are pleased to present these important preclinical findings at Keystone Symposia 2019, the first evidence of ATYR1923's ability to bind to NRP-2 and down-regulate myeloid cells, specifically neutrophils," said Dr. Sanjay Shukla, President and Chief Executive Officer of aTyr. "With ATYR1923 currently being evaluated in a Phase 1b/2a clinical study in patients suffering from pulmonary sarcoidosis, these findings help support our belief in the mechanism of action of ATYR1923 to suppress immune engagement in this and other serious and potentially debilitating interstitial lung diseases."

**Poster Presentation: Wednesday, February 27, 2019 from 1:30-3:00pm (MST)**

**Title:** "ATYR1923 Reduces Neutrophil Infiltration in an Acute Lipopolysaccharide (LPS) Lung Injury Model"

**Presenter:** Suzanne Paz, Ph.D., aTyr Pharma, Inc.

This poster describes a preclinical study to determine if aTyr Pharma's lead clinical candidate, ATYR1923, can influence myeloid cell migration. ATYR1923 was administered intravenously to C57BL/6 mice 24 hours prior to LPS challenge by airway administration to generate acute lung inflammation.

Multi-color flow cytometry was used for immunophenotyping analysis and detection of NRP-2 levels on surfaces of various immune cell populations. *In vitro*, mouse bone-marrow derived macrophages (BMDM), human THP-1 monocytic cells, and primary human dendritic cells (DCs) were used to confirm induction of NRP-2 cell surface expression following activation.

**Conclusions:**

- This presentation highlights how ATYR1923 binds to both human and mouse NRP-2.
-

- NRP-2 is detected on the cell surface of myeloid cells both *in vitro* and *in vivo*.
- NRP-2 was induced following activation of TLR found on the cell surface (mainly TLR1, 2, 4, 5 & 6), but not endosomal TLR ligands (TLR3, 7/8, & 9).
- ATYR1923 significantly decreased the CD11b+ population following LPS installation in the lung, which was ascribed to an inhibitory effect on neutrophil infiltration.
- These findings highlight the potential of ATYR1923 to regulate myeloid cell biology during lung inflammation.

A copy of the poster can be found here: [ATYR1923 Poster](#)

#### **About aTyr**

aTyr is a biotherapeutics company engaged in the discovery and development of innovative medicines based on novel immunological pathways. aTyr's research and development efforts are concentrated on a newly discovered area of biology, the extracellular functionality 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. aTyr is focused on the therapeutic translation of the Resokine pathway, comprised of extracellular proteins derived from the histidyl tRNA synthetase gene family. ATYR1923 is a clinical-stage product candidate which binds to the neuropilin-2 receptor and is designed to down-regulate immune engagement in interstitial lung diseases and other immune-mediated 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 Litigation Reform Act. 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, including statements regarding the potential therapeutic benefits and applications of our product candidates; our ability to successfully advance our product candidates, undertake certain development activities (such as the initiation of clinical trials, clinical trial enrollment, the conduct of clinical trials and the announcement of top-line results) and accomplish certain development goals, and the timing of such events; and the scope and strength of our intellectual property portfolio. 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. 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, risks associated with the discovery, development and regulation of our product candidates, the risk that we 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), 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.

# ATYR1923 Reduces Neutrophil Infiltration

Suzanne Paz, Clara Polizzi, Dalena Chu, Lauren Guy  
aTyr Pharma, San Diego, CA, USA

## Abstract

A number of aminoacyl tRNA-synthetases have evolved non-canonical functions including the tRNA synthetase HARS. HARS downregulates immune responses via its N-terminal domain, which we have termed the iMod (immunomodulatory domain). We fused HARS to human IgG1 Fc to generate ATYR1923, which is currently in clinical evaluation for pulmonary disease. NRP-2 (Neuropilin-2), a pleiotropic co-receptor participating in several pathways including class III semaphorins/plexins, is a known ligand of NRP-2. We investigated the role of NRP-2 in immune regulation, although growing evidence indicates that NRP-2 is involved in neutrophil activation and recruitment to inflammatory sites. For instance, NRP-2 expression on alveolar macrophages is upregulated by inhaled LPS (Immormino *et al.* 2018). To determine whether ATYR1923 was able to influence myeloid cells, iMod construct, iMod-COMP, were administered intravenously to C57BL/6 mice 24h prior to LPS challenge. We evaluated whether ATYR1923 induce a systemic inflammatory response or by airway administration to generate acute lung inflammation. We performed immunophenotyping analysis and detection of NRP-2 levels on surfaces of various immune cell populations including macrophages (BMDM), human THP-1 monocytic cells, and primary human dendritic cells (DCs) were used. Results indicated that LPS stimulation *in vitro* or *in vivo* upregulated NRP-2 on a variety of myeloid cells including DCs and neutrophils. Notably, prophylactic administration of ATYR1923 or iMod.COMP led to a significant reduction in LPS-induced neutrophil infiltration into the bronchoalveolar space. This finding appeared to be specific to neutrophils as infiltration of monocytes, alveolar macrophages, or other myeloid cells was not altered. Altogether, these results suggest that ATYR1923 inhibition of neutrophil migration to inhibit lung inflammation.

## 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 thought to play a role in regulating key cells in the immune system to ensure appropriate control of immune responses.
- ATYR1923 is a clinical stage immunomodulatory protein.
- ATYR1923 comprises the iMod domain of HARS fused to Human IgG Fc (Fig 1.) to extend plasma half-life.
- NRP-2 was identified to be a binding partner of ATY1923.
- ATYR1923 exerts some of its immunomodulatory functions by affecting T cell activation & cytokine release (data presented at AAI 2018 by E. Mertcsching).
- NRP-2 was shown to play a role in airway inflammatory responses to inhaled LPS (Immormino *et al.* 2018)

### Fig 1. Gen

Histidyl-tRNA Synthetase  
HARS (1-509)

iMod (2-60)

ATYR1923  
iMod (2-60)-Fc

iMod-COMP

Fig. 1 Schematic of  
ATYR1923 & iMod

In vivo Experimental Procedure

In vitro Ex



Group	Test Article (TA)	Dose (mg/kg)	TA Route	LPS Treatment (µg)	Time Point (hrs)
1	NA				24
2	Vehicle	0	IV	0	24
3	Vehicle	0	IV	10	24
4	ATYR1923	1	IV	10	24
5	ATYR1923	3	IV	10	24
6	ATYR1923	10	IV	10	24
7	iMod-comp	3	IV	10	24

**Table 1. In vivo study design**

- **Day -1:** Body weights (BW) for TA administration were recorded & animals were dosed with TA at 5ml/kg according to the table above
- **Day 0:** Mice in grps 3-7 were anesthetized at 2-4% Isoflurane (1L/min.) & dosed OP (oropharyngeally) with 10 ug LPS in 50 µL PBS. Grp 2 received 50 µL PBS only. Grp 1 mice were naïve to induction & treatment.
- **Day 1:** BWs were recorded and mice were euthanized with lethal ketamine/xylazine cocktail (~300/30 mg/kg) at 24 hours post LPS induction. Blood was collected from the abdominal vein, processed for serum for pathway analysis (cytokine, ATYR1923 &/or NRP2 levels). The lung and trachea were exposed & perfused for BALF (bronchoalveolar lavage) collection using 0.8 ml PBS through cannulated trachea. Collected BALF was placed on ice and volume recorded. BALF cells were collected by centrifugation and supernatant was retained for potential measurement of pathway analysis (HARS pathway proteins, cytokines and/or ATYR1923 etc.). RBC lysis was applied to BALF cells & stained for flow cytometry analysis. Results from flow analysis were analyzed using FlowJo & statistical analysis performed using Prism.

**Fig 2. Flow Cytometry Gating Strategy**

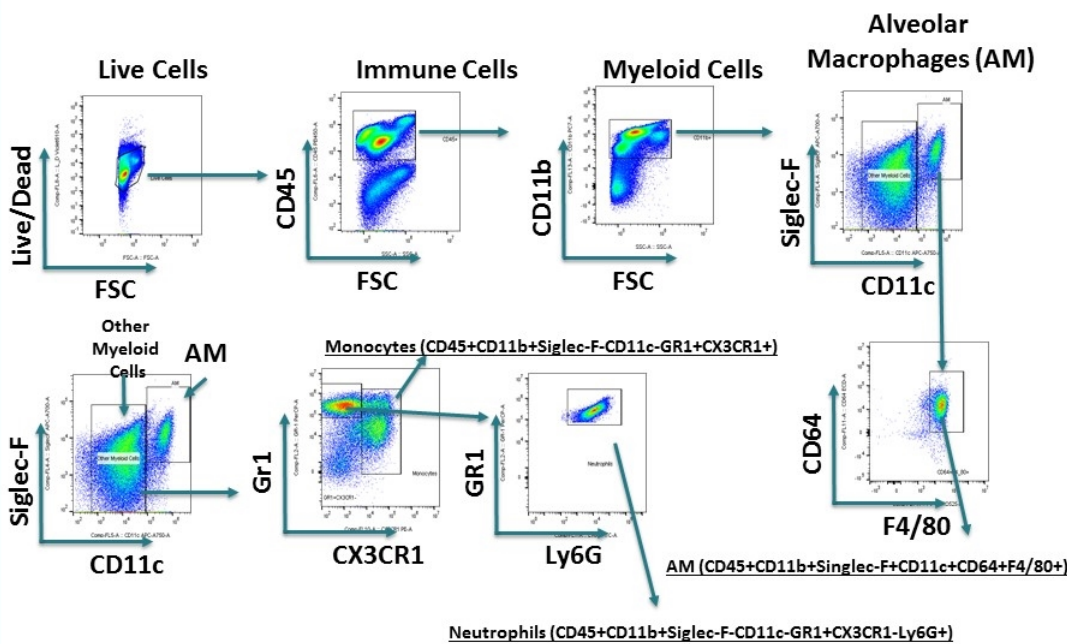
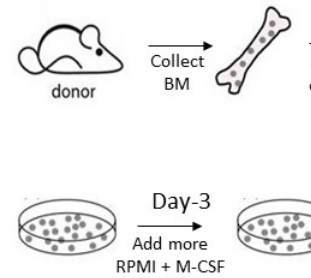


Fig. 2 Flow cytometry dot plots demonstrating the gating strategy utilized to identify immune cells, myeloid cells, alveolar macrophages (AM), monocytes and neutrophils.

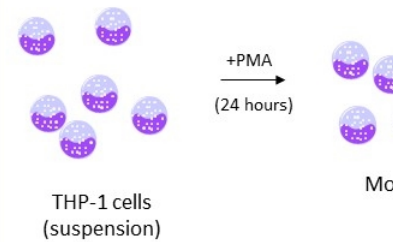
**References:**

- 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.
- Wakasugi K & Schimmel P (1999) Two distinct cytokines released from a human aminoacyl-tRNA synthetase. *Science* 284, 147-151.

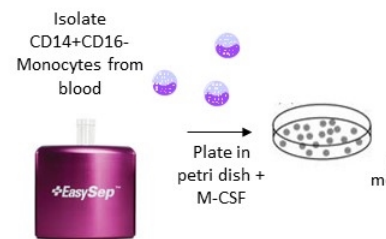
**Fig. 3 Gen**



**Fig 4. Generation of**



**Fig 5. Generation**



**Fig 6. Generation of**

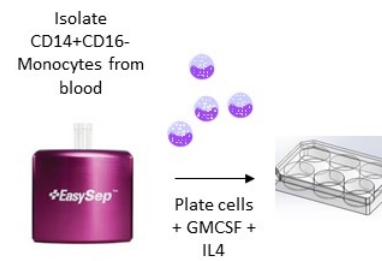


Fig.3-6 Schematic representat generate: mouse Bone Marro from THP1 cell line (Fig 4); h human primary dendritic cells (

- Guo HF, Vander Kooi CW. (2015) Neuropilin Function
- Rossignol M, Gagnon ML, Klagsbrun M. (2000) Gene of splice variants and soluble forms. *Genomics* 70: 2
- Roy S, Bag AK, Singh RK, Talmadge JE, Batra SK. Immunotherapy. *Front. Immunol.* 8:1228.

**Acknowledgements:**

- Irimamoto RW, Lauzier DC, Nakano N, Hernandez ML, Alexis NE, Gatto AJ, Hiley SL, Doerschuk CM, Feden LB, Cook DN & Moran TP. (2018) Neuropilin-2 regulates airway inflammatory responses to inhaled lipopolysaccharide. *Am J Physiol Lung Cell Mol Physiol.* 315 (2): L202-L211.111v

The authors would like to thank Jeanette Ampudia poster.

---

