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

April 17, 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 for Cancer Research (AACR) Annual Meeting held April 14-18, 2018 in Chicago, Illinois. During the AACR Annual Meeting, the Company is presenting two preclinical poster presentations for its immuno-oncology program based on the Resokine pathway. The poster presentations are entitled, "Circulating levels of Resokine, a soluble modulator of the immune system, are upregulated in both experimental cancer models and in patients across multiple tumor types," and "Antibodies targeting Resokine, a soluble immune modulator, inhibit tumor growth in syngeneic mouse models." The poster presentations have been posted on the Company's website and are attached hereto as Exhibits 99.1 and 99.2.

The information under this Item 7.01, including Exhibits 99.1 and 99.2 hereto, are 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 “Circulating levels of Resokine, a soluble modulator of the immune system, are upregulated in both experimental cancer models and in patients across multiple tumor types.”
99.2	Poster presentation titled “Antibodies targeting Resokine, a soluble immune modulator, inhibit tumor growth in syngeneic mouse models.”

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: April 17, 2018

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Circulating levels of Res experimental cancer mo

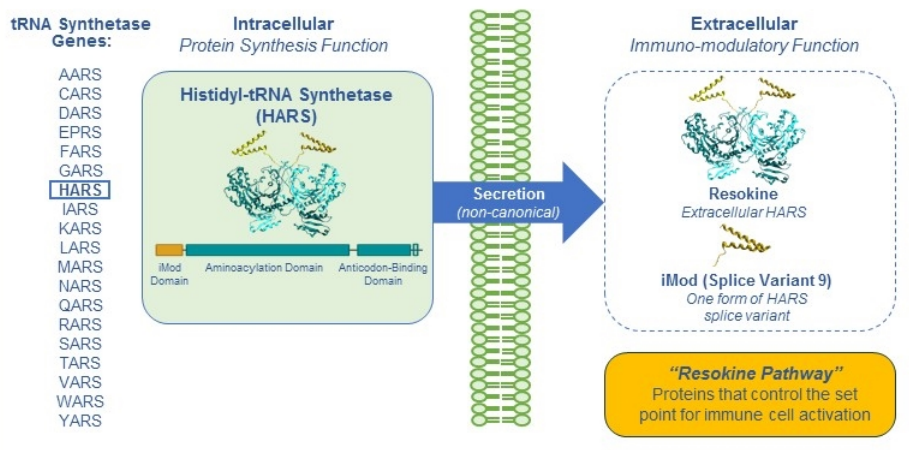
Ryan Adams, Elisabeth Mertsching, Leslie Nangle,

aTyr Pharma, San Diego, CA

Abstract

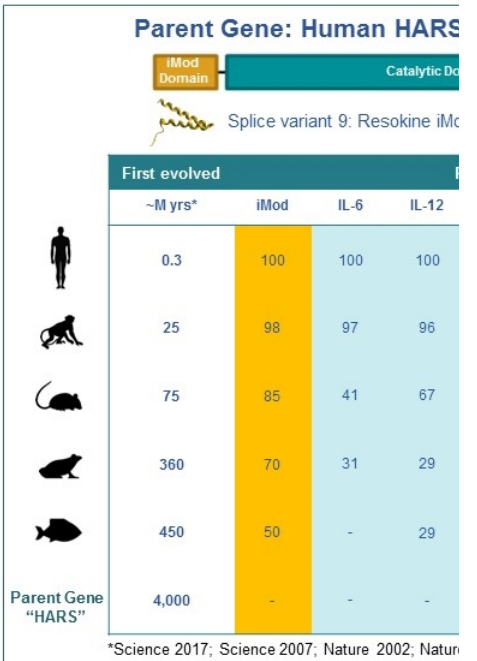
The Resokine family of proteins are derived from the histidyl tRNA synthetase gene (HARS) via proteolysis or alternative splicing and appear to be important as extracellular modulators of cellular activity. Resokine is a newly identified regulator of immune cell activity, and circulating levels of Resokine in normal individuals may represent a soluble set-point control to modulate T cell activity. Resokine activity is a non-canonical function arising from the tRNA synthetase gene family, and the activity is effected by a 60 amino acid N-terminal domain arising from the gene for histidyl-tRNA synthetase. This domain is present in the full-length protein as well as multiple splice variants that have lost their original tRNA synthetase functionality. Resokine is secreted from cells, including tumor cell lines, and *in vitro* studies have demonstrated that Resokine can inhibit the activation of immune cells. *In vitro*, for example, Resokine addition during T cell activation induced by antibodies to CD3 and CD28, can result in reduced levels of inflammatory cytokines, such as IL-2, interferon gamma, and TNF alpha; inhibition of the up-regulation of cell-surface activation markers, such as CD69, CD40L, and 4-1BB; and inhibition of release of the cytotoxic mediator granzyme B. We have tested levels of circulating Resokine in both mice with syngeneic tumors as well as >300 cancer patients across multiple tumor types. In normal C57BL/6 mice serum levels of Resokine ranged from 70-250pM (n=10) whereas in mice bearing B16F10 tumors, levels were significantly higher (450-3000pM, $p<0.001$) and correlated with tumor size. Resokine levels in normal human volunteers exhibit a more variable range, from 8pM to >2333pM (n=148), with 18% of individuals having levels <30pM, which was set as the active threshold level based on the concentration required to inhibit T cell activation *in vitro*. In contrast, samples across >300 cancer patients with different tumor types exhibited higher circulating levels with only 4% of individuals having levels below the activity threshold of 30pM. This data is consistent with the hypothesis that tumors secrete Resokine as an additional mechanism to down-regulate immune activity, and suggests further investigation of the utility of Resokine levels as a new biomarker of immune activity in patients.

Resokine: Extracellular Proteins Derived From HARS Gene



- Resokine (the extracellular proteins derived from the HARS gene) is secreted from

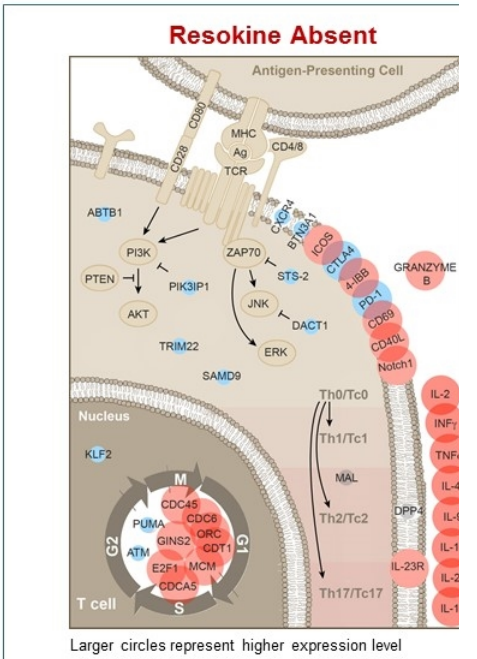
iMod Domain: Conserv



*Science 2017; Science 2007; Nature 2002; Natur

- Comparison of sequence alignments bet shown a high level of evolutionary conse This type of species conservation is simil cytokines, growth factors, and checkpoin

Resokine Sets Level pM Conc



Larger circles represent higher expression level

Cartoon compiled from RNAseq, flow cyt

- Resokine (the extracellular proteins derived from the HARS gene) is secreted from cells via a non-canonical pathway and circulates naturally in all individuals tested. The N-terminal "iMod" domain consists of amino acids 2-60 from HARS and has structural similarity to 4 alpha–helical bundle cytokines.

- The presence of Resokine attenuates the against CD3/CD28. Analysis of gene exp revealed lowered levels of many immune treated with picomolar amounts of Resok

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Antibodies Targeting Re
Mouse Models

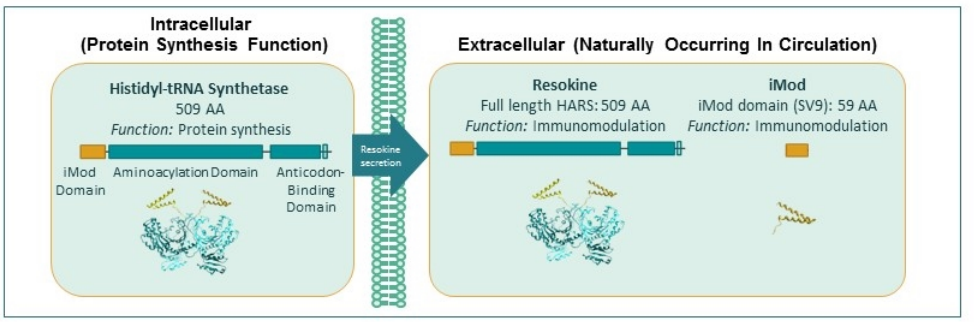
Kathy Ogilvie[1], Cherie Ng[1], Leslie Nangle[1], Jeanette

[1]aTyr Pharma, San Diego, CA; [2]MedImmune, Gaithersburg, MD

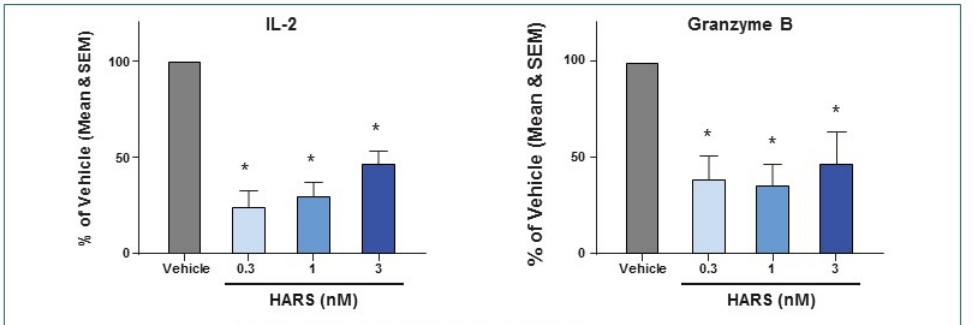
Abstract

A number of non-canonical functions have been established for proteins generated from the tRNA synthetase gene family. One of these, termed Resokine, is derived from histidyl-tRNA synthetase and plays an important role in controlling immune cell activation. Circulating levels are sufficient to down-regulate the extent of T cell activation that can be achieved in vitro. A panel of specific monoclonal antibodies has been generated and tested for their anti-tumor activity in mouse syngeneic tumor models. Antibodies to Resokine demonstrated anti-tumor activity across three different tumor models. Treatment of subcutaneous CT26 tumors resulted in improved efficacy compared to treatment with antibodies that block the PD-1/PD-L1 interaction. Significant efficacy was also observed in the difficult to treat subcutaneous B16F10 melanoma and 4T1 breast tumor models. In addition, anti-Resokine demonstrated significant activity in a tumor seeding model using B16F10 melanoma, which resulted in inhibition of tumor nodules in the lung, and was more efficacious than a combination of antibodies to PD-L1 and CTLA-4. Combinations of anti-Resokine antibody with either anti–PD-1 or anti–PD-L1 demonstrated at least additive, and potentially synergistic activity in these models. Animals with long-term tumor regressions were reimplanted with viable tumor cells, and demonstrated long-term immune memory with rejection of the newly implanted tumors. To understand the mechanism of anti-Resokine antibody therapy, cell depletion studies were carried out in the B16F10 tumor model. In these experiments, the activity of anti-Resokine antibodies was demonstrated to be dependent upon the presence of CD8 T cells and also NK cells, but independent of CD4 T cells. The immune-based mechanism of antibodies to Resokine was further demonstrated by rechallenge of mice that had regressed tumors upon treatment. Tumor regrowth was not observed even in the absence of further treatment whereas control mice grew tumors at the normal rate, suggesting that immune memory had been induced. Antibodies to Resokine offer an exciting new potential option for immunotherapy of cancer, which has significant activity as monotherapy and is compatible with more established modalities. Anti-Resokine antibodies are currently being developed to initiate clinical evaluation.

Resokine Proteins: Extracellular Histidyl-tRNA Synthetase Gene Products With Immune Modulation Activity



Resokine Reduces Cytokine and Granzyme B Release During T Cell Activation



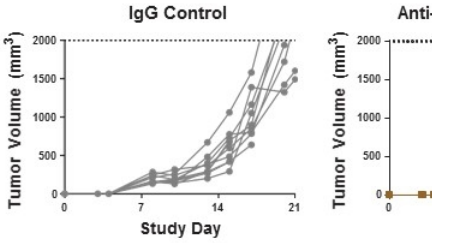
*p < 0.05

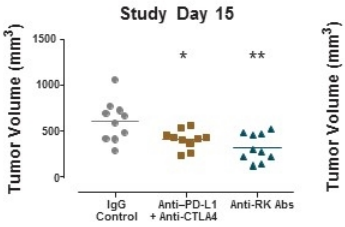
Similar for: IFNγ, TNF, TGFβ, IL-13, IL-4…

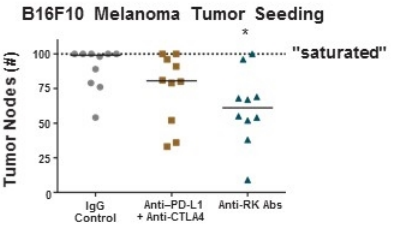
- Histidyl-tRNA synthetase is released from cells and is present in systemic circulation (Adams *et al.*, AACR 2018).
- Cancer patients have higher serum levels of Resokine compared to healthy subjects.

Antibodies

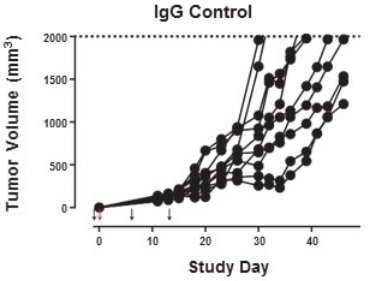
Efficacy in B16

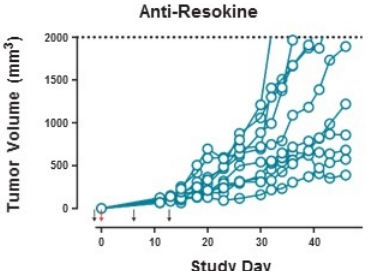






Efficacy in 4T1 B





- Resokine functions to inhibit T cell activation.

Hypothesis: Resokine restrains immune cell function in cancer and antibodies binding to Resokine will release the inhibition of the immune system leading to therapeutic benefit.

Red arrows indicate tumor cell implantation
Black arrows indicate antibody administration

Presented at the AACR Annual Meeting 2018; April 14–18, 2018; Chicago, IL