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): September 16, 2019

Synthorx, Inc.
(Exact name of registrant as specified in its charter)

Delaware	001-38756	46-4709185
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

11099 N. Torrey Pines Road, Suite 190 La Jolla, California	92037
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (858) 750-4789

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	**THOR**	**The Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

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 8.01 Other Matters.

On September 17, 2019, certain members of the management team of Synthorx, Inc. (the "Company") will be presenting a poster (the "Poster") at the 14th World Congress on Inflammation 2019 conference. A copy of the Poster is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) *Exhibits*.

Exhibit No.	Description
99.1	Poster, dated September 17, 2019.

Forward-Looking Statements

Certain statements contained in this report are forward-looking statements that involve a number of risks and uncertainties. Words such as "believe," "may," "will," "estimate," "promise," "plan", "continue," "anticipate," "intend," "expect," "potential" and similar expressions (including the negative thereof) are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identifying words. For such statements, the Company claims the protection of the Private Securities Litigation Reform Act of 1995. Actual events or results may differ materially from the Company's expectations. Factors that could cause actual results to differ materially from those stated or implied by the Company's forward-looking statements are disclosed in the Company's filings with the Securities and Exchange Commission, including in the section captioned "Risk Factors" in the Company's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2019. These forward-looking statements represent the Company's judgment as of the time of this report. The Company disclaims any intent or obligation to update these forward-looking statements, other than as may be required under applicable law.

SIGNATURES

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.

Synthorx, Inc.

Dated: September 16, 2019

By: /s/ Laura Shawver
Laura Shawver, Ph.D.
President and Chief Executive Officer

THOR-809: An IL-2 Engineered From an Expanded Genetic Alphabet for the Potential Treatment of Autoimmune Disorders

Marcos E. Milla, Carolina E. Caffaro, Lina Ma, Ingrid B. Joseph, David B. Chen, Taylor Ismaili, Kristine M. San Jose, Yelena Pavlova, Namit Singh, Lilia K. Koriazova, Hans R. Aerni, Michael J. Pena, Jerod L. Ptacin

INTRODUCTION

- CD4+ regulatory T cells (Tregs) play a crucial role in maintaining immune homeostasis. Treg dysfunction is associated with multi-organ autoimmune (AI) and inflammatory-related diseases[1]. At high doses, recombinant interleukin-2 is approved to treat melanoma and renal cell carcinoma. At low doses, IL-2 selectively induces proliferation of Tregs through activation of the high-affinity alpha-beta-gamma IL-2 receptor (IL-2Rαβγ), resulting in immune suppression, without activating the beta-gamma IL-2 receptor (IL-2Rβγ) expressed on CD8+ T effector cells (Teffs) and natural killer (NK) cells. Therapeutic benefit of low dose IL-2 has been demonstrated in chronic graft-versus-host disease and HCV-induced vasculitis[2,3]. Treg-mediated downmodulation by IL-2 of the immune effector function that prevents antigen recall may reset immune tolerance in select AI disorders.
- We applied our expanded genetic alphabet platform using a novel, fully-synthetic DNA base pair, to create optimized biologics with enhanced pharmacological properties. Using this platform, we developed a site-specific, covalently bound mono-pegylated IL-2 that selectively expands peripheral Tregs in mice and non-human primates (NHP).
- THOR-809 was identified as an IL-2 variant that maximized proliferation of peripheral Tregs, with an optimal PK/PD profile and a strong preference for Treg proliferation relative to Teffs (no expansion) and NK cells (minimal expansion). These properties correlated with extended half-life and sustained exposure. In NHPs, subcutaneous dosing of THOR-809 demonstrated dose-dependent proliferation of peripheral Tregs with no detectable proliferation of Teffs or NK cells up to 200 mcg/kg.
- Our results support continued investigation of THOR-809 as a treatment for AI disorders.

Synthorx Expanded Genetic Code Platform: A Synthetic DNA Base Pair Encodes Novel Amino Acids to Create Optimized Biologics

X-Y Base Pair creates new codons that specifically encode novel amino acid chemistry into proteins

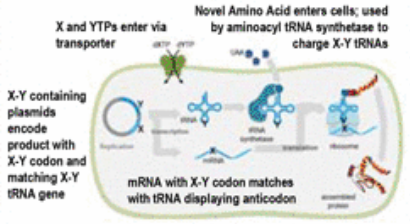
Site-Specific Bioconjugation
- Novel amino acid installation creates a dedicated, specific and stable chemical attachment site
- Designed to bioconjugate moieties for improved properties: e.g. PEG

Specificity
- Improved target selectivity through altered receptor binding

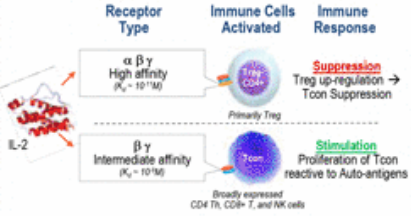
Polymer-Conjugates
- Increased half-life
- Epitope shielding through covalent and stable PEG attachment via bio-orthogonal chemistry

Engineered Cells Install a Novel Amino Acid Utilizing X-Y to Produce Therapeutic Proteins with Optimized Properties

Production system for Synthorins in *E. coli*



Dual Pharmacology of IL-2 is Mediated by αβγ and βγ Receptor Sub-Types

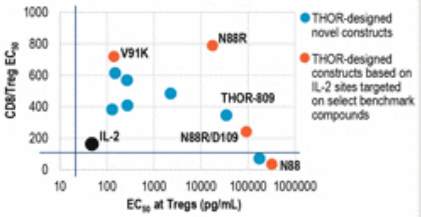


THOR-809 is Designed to Activate Tregs Without

RESULTS

Screening in Mice Identified Multiple IL-2 Synthorins With Differentiated *Ex Vivo* Pharmacology

- Analysis of pSTAT5 activation in freshly isolated human PBMCs identified Synthorins with diverse potency profiles
- Multiple Synthorins covering a broad Treg potency range and CD8/Treg ratios were selected for mouse PK/PD profiling



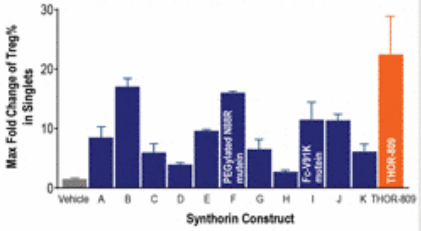
Key Findings

The pSTAT5 signal reports on receptor engagement and activation. We observed loose coupling between pSTAT5 and readouts of cell proliferation, including Ki67 and Treg counts. As a result, compound profiling for Treg expansion and activation in vivo (mouse) was required to select candidates with superior pharmacodynamic properties.

Functional Screen For Treg Expansion in Mice Identified THOR-809

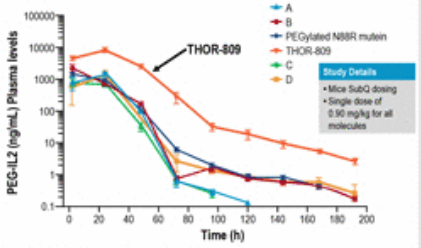
Maximum Fold Increase in Treg % in Total Blood Cells

A single subcutaneous dose (~0.9mg/kg) of the indicated Synthorin variant was administered to C57/Bl6 mice. Flow cytometry was used to quantitate Treg (CD4+ CD25+ FoxP3+) expansion in peripheral blood.



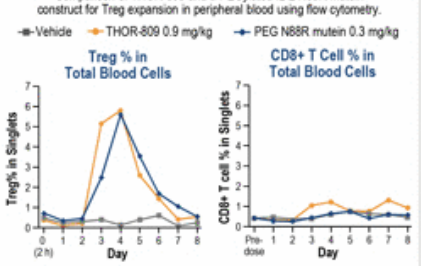
THOR-809 Shows Increased Exposure in Mice

A-D represent other IL-2 AI constructs made by Synthorx



THOR-809 Expands Tregs in Mice

Comparison of THOR-809 and a PEGylated IL-2 N88R mutein construct for Treg expansion in peripheral blood using flow cytometry.



THOR-809 Induces Treg Activation and Biomarkers of Suppressive Function in Mice

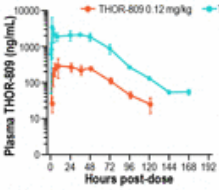
Comparison of THOR-809 and a PEGylated IL-2 N88R mutein construct for Treg

RESULTS

THOR-809 Pharmacokinetics in NHP

Single subcutaneous dose of THOR-809 administered at t=0

THOR-809 Pharmacokinetic Parameters in Non-human Primates

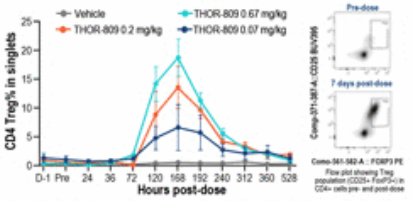


Test Article Dose	Unit	Parameter	Mean value
THOR-809 0.12mg/kg	h	$t_{1/2}$	17.2
	h*ng/mL	AUC last	18,349
	ng/mL	Cmax	361
THOR-809 0.67mg/kg	h	$t_{1/2}$	18.0
	h*ng/mL	AUC last	71,940
	ng/mL	Cmax	1,358

THOR-809 Induces Treg Expansion in NHP

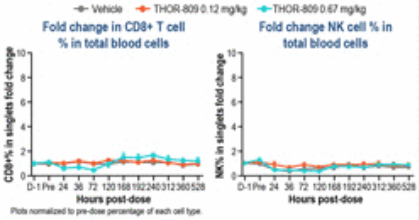
THOR-809 induced large-scale expansion of peripheral Tregs in blood

Treg Percentage in Total Blood Cells



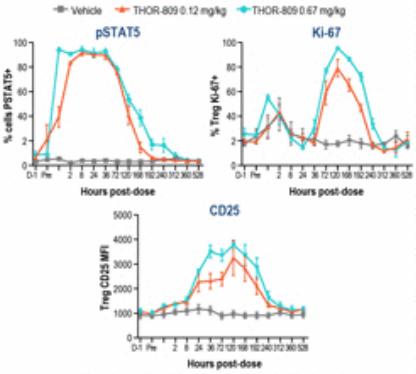
THOR-809 Does Not Expand CD8+ T or NK cells in NHP

Minimal change in peripheral CD8+ T cells and NK cells in blood post-dose



THOR-809 Induces Treg Biomarkers of Activation and Proliferation in NHP

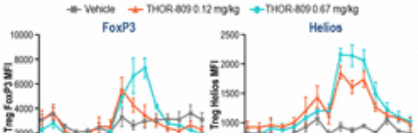
Quantitation of induction of biomarkers in peripheral blood Tregs using flow cytometry (pSTAT5, Ki-67, CD25)



THOR-809 Induces Treg Biomarkers of Differentiation and Suppressive Function in NHP

Quantitation of induction of biomarkers that correlate with Treg suppressive function in peripheral blood Tregs using flow cytometry.

FoxP3 and Helios are Treg transcription factors that control gene programs for Treg differentiation and suppressive activity.



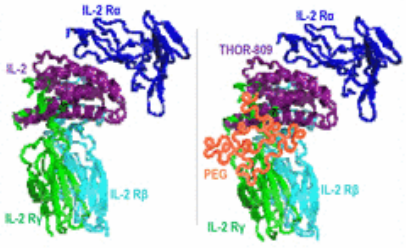
Stimulating Conventional T cells (Tcons)

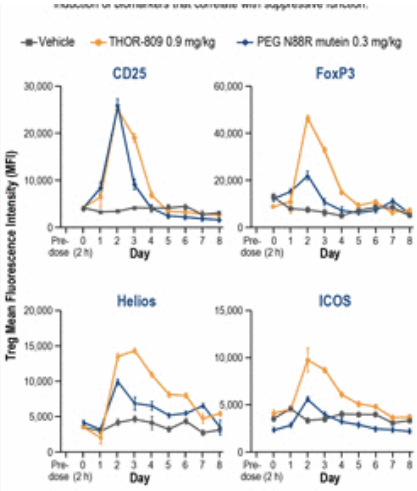
THOR-809's Key Differentiation

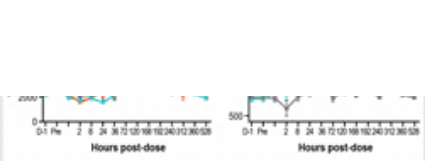
1. **IL-2 receptor αβγ complex bias** – Site-specific PEG tunes IL-2 pharmacology for preferential Treg activation and expansion over Tcon
2. **Ease of use** – pegylation allows for Q2W dosing and no more frequent
3. **Low risk for ADAs** – Sites targeted for pegylation have low risk of MHC-II binding and presentation. Covalent, stable PEG shields new amino acid

PEG-IL-2 Synthorin Properties

Stable PEG covalently attached to the novel amino acid installed where affinity at the IL-2 receptor βγ is reduced- **potency at the IL-2 receptor requires α**







CONCLUSIONS

- Ex vivo Screening for PEGylated, IL-2 Rαx biased IL-2 compounds
  - Structure Activity Relationship (SAR) screening identified multiple Synthorin IL-2 constructs biased for IL-2Rα
  - Identified compounds showed a broad range of Treg activation potency and Tcon:Treg ratios
- Screening in mice identified THOR-809 as a specific and effective Treg activator
- In mice, a single subcutaneous dose of THOR-809 induced:
  - Sustained pSTAT5 signaling in Treg cells
  - Specific expansion of Tregs, not Tcons
  - Increase in markers of Treg differentiation and suppressive function
  - FoxP3, CD25, Helios, and ICOS were up-regulated
- In cynomolgus monkey, a single subcutaneous dose of THOR-809 induced:
  - Dose-dependent expansion and activation of Tregs
  - No observed expansion of CD8+ T (Tcon) or NK cells
  - Increased Treg expression of biomarkers that correlate with differentiation and suppressive function

REFERENCES

1. Sakaguchi, S. et al. *Cell*. 2008;133:775–87. 2. Saadoun, D. et al. *N Engl J Med*. 2011;365:2067–77. 3. Rosenzwajg, M. et al. *J Autoimmun*. 2015;58, 48–58.