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): November 8, 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 November 8, 2019, certain members of the management team of Synthorx, Inc. (the "Company") will be presenting a poster (the "Poster") at the Society for Immunotherapy of Cancer 2019 Annual Meeting & Pre-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 November 8, 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 September 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: November 8, 2019

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

Exhibit 99.1

Discovery of Pharmacologically Differentiated Interleukin 15 (IL-15) Agonists Employing a Synthetic Biology Platform

Carolina E. Caffaro; Jerod L. Ptacin; Rob W. Herman; Lina Ma; David B. Chen; Nicole Acuff; Kristine M. San Jose; Kelsea Loescher; Jill Mooney; Ingrid B. Joseph; Marcos E. Milla Synthorx, Inc., La Jolla, CA

INTRODUCTION

Synthorx Expanded Genetic Code Platform for 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 pharmacological properties through altered receptor binding

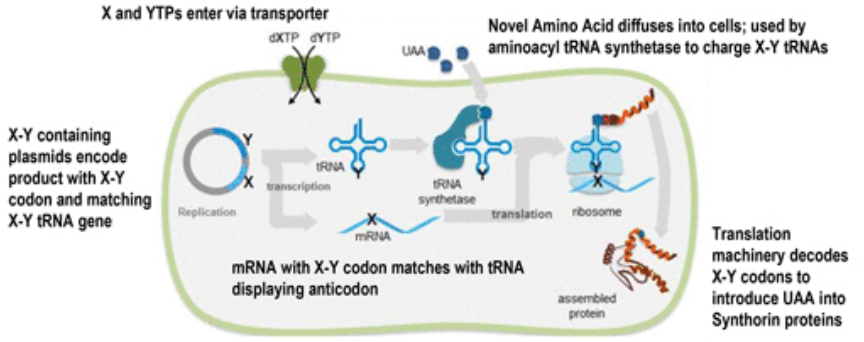
Pharmacokinetics

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

1. doi:10.1038/nature13314. 2. doi:10.1038/nature24659

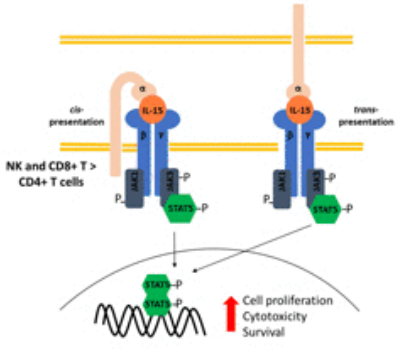
An X-Y Base Pair Directs the Introduction of Novel Amino Acids to Produce Therapeutic Proteins in Engineered Cells

Production System for Synthorins in *E. coli*



IL-15 Possesses Distinct Properties in Immuno Oncology

IL-15 Cis- and Trans-presentation



Key Differentiators

IL-15 induces proliferation and survival of CD8+ T memory (Tmem) cells, activates natural killer (NK) cells, and enhances antibody-driven cellular toxicity (ADCC) without expanding immunosuppressive regulatory CD4+ T cells (Treg). IL-15 agonistic activity can occur via cis or trans presentation.

IL-15 Liabilities

The high potency and resulting toxicity of IL-15, combined with its short half-life, has limited its potential as an immunotherapeutic agent.

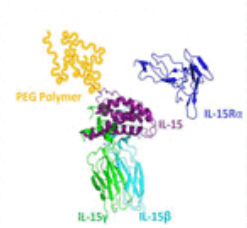
Synthorx THOR-900 Compounds

We hypothesize that extension of the half-life of IL-15 could provide persistence of signaling for CD8+ Tmem expansion. Modulation of the interaction with specific receptor chains (IL-15Rα and/or IL-2/15Rβγ) by pegylation may enable preferential stimulation of target cell subsets for enhanced pharmacodynamic responses.

INTRODUCTION

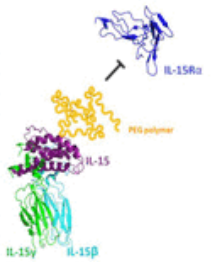
Site-Specific Pegylation Allows Fine-tuning of IL-15Rα and β Engagement. Three Differential IL-15 Synthorin Profiles were Sought, to Investigate their Potential for Improved Pharmacodynamics and Safety

Half-Life Extension Only (THOR-924)



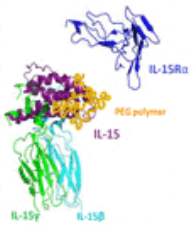
- Intact IL-15 pharmacology with extended half-life

Reduced ∝, Normal β (THOR-908)



- Reduced engagement of IL-15R∝, normal at IL-2Rβ
- Extended half-life

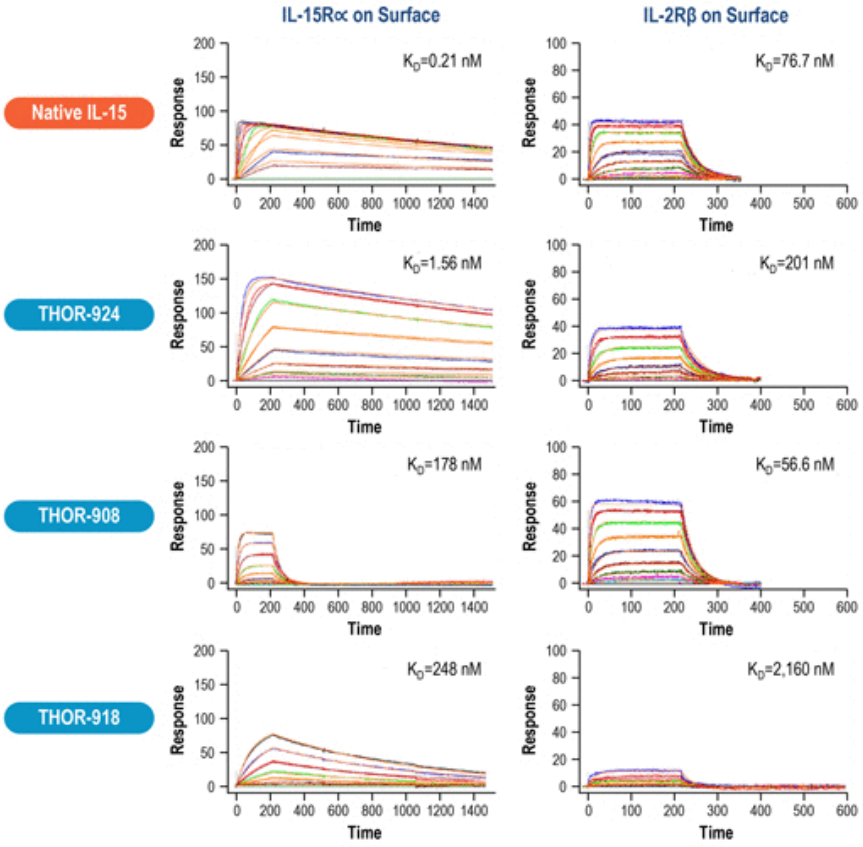
Reduced ∝ & β (THOR-918)



- Reduced engagement of both IL-15R∝ and β
- 10-30-fold decrease in binding to IL-2Rβ, potential for decreased receptor internalization
- Extended half-life

RESULTS

IL-15 Synthorins Show Differential Engagement of the IL-15R∝ and β

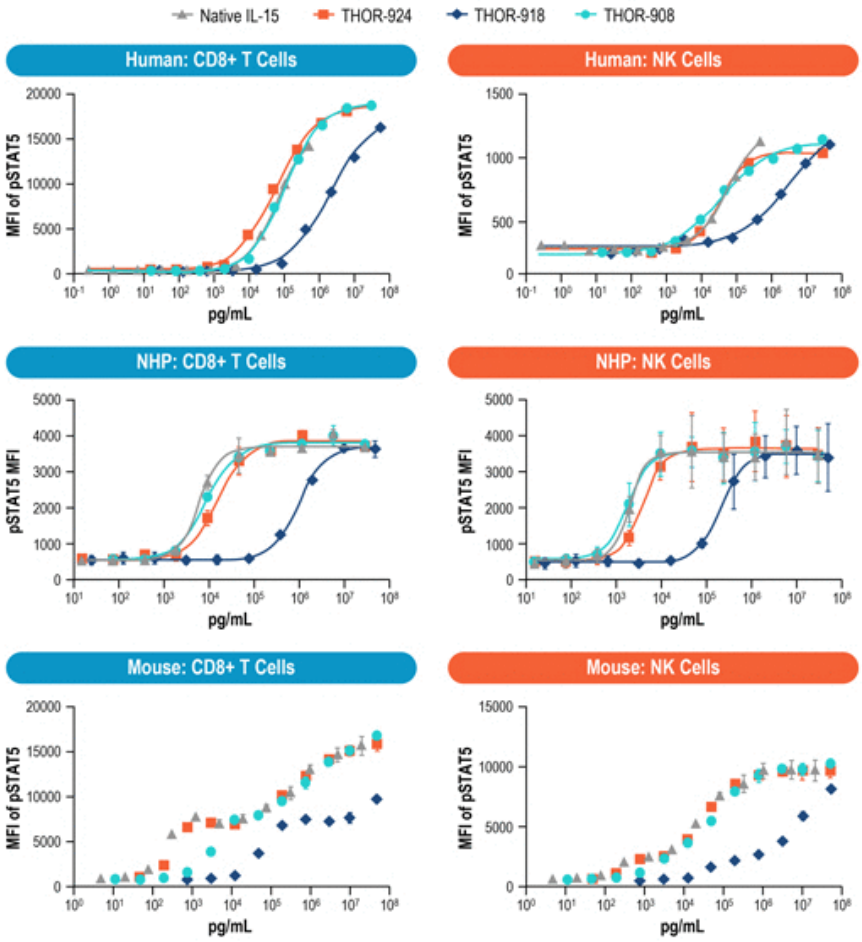


- The half-life extended lead candidate **THOR-924** shows binding kinetics and potency to native IL-15 for engagement of IL-2/15Rβ, with only a 7-fold decrease in binding to IL-15R∝ mainly stemming from a decrease in the on-rate of receptor engagement
- Reduced ∝ hits THOR-908 and THOR-918 display >500-fold decrease in binding to IL-15R∝ and differential IL-15R∝ and β engagement:
  - THOR-908 displays fast on- and off rates at IL15R∝; THOR-918 shows slow on and off-rates

RESULTS

IL-15 Synthorins Exhibit Differential Receptor Activation of Primary Immune Cells

pSTAT5 Profiling of Human LRS, NHP and Mouse Whole Blood Upon Stimulation With Native or Pegylated IL-15



Ex-vivo Multi-species pSTAT5 Profiling Confirms Differential Engagement of IL-15Rα and β

THOR-924:

- Induces STAT5 phosphorylation in CD8+ T and NK cells with <3-fold difference in potency relative to native IL-15 across species
- Bimodal curve for mouse CD8+ T cells (splenocytes) suggests native engagement of IL-15Rα

THOR-908:

- Shows normal potency in human LRS and NHP whole blood assays monitoring pSTAT5 induction, suggesting engagement of IL-2Rβ similar to unmodified IL-15
- Dose-response in mouse splenocytes indicates a decrease in potency at IL-15Rα yet normal binding to IL-2Rβ compared to native IL-15

THOR-918:

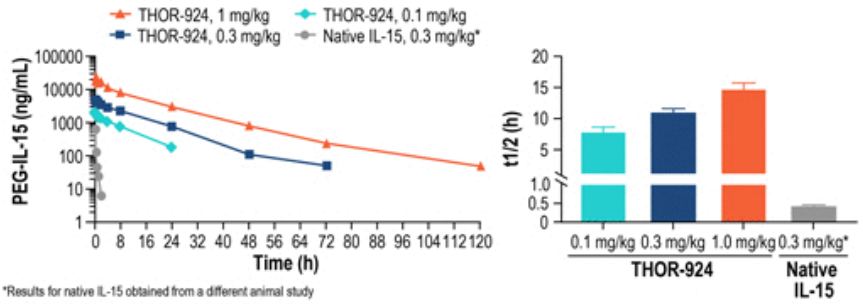
- 50 to >1,000-fold decrease in potency at CD8+ T and NK cells, depending on species: human > NHP > mouse

EC_{50} (ng/mL)	NHP Whole Blood		Human LRS		Mouse Splenocytes			
	CD8+ T	NK	CD8+ T	NK	CD8+ T (bottom/top)		NK (bottom/top)	
IL-15	6.3	2.0	56.6	69.9	0.2	509	0.2	30.1
THOR-924	15.5	3.9	53.6	33.2	0.3	416	0.3	34.4
THOR-908	9.2	1.8	97.9	37.6	3.6	1,161	39.6	
THOR-918	1,028	207	1,970	2,808	69.3		114,681	

RESULTS

THOR-924 Shows Increased Plasma Exposure in Mice Compared to Native IL-15

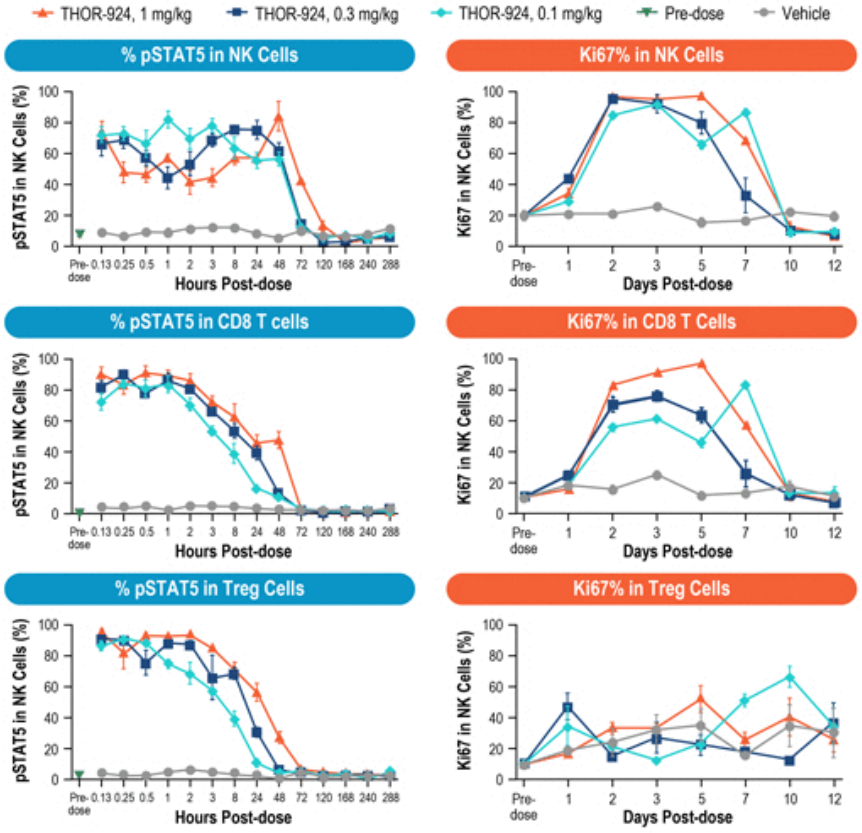
Mouse C57BL/6 IV Administration: THOR-924 Shows ~25-fold Longer Half-life for Compared to Native IL-15



*Results for native IL-15 obtained from a different animal study

THOR-924 Induces STAT5 Phosphorylation and Ki67 Upregulation in Mice

- A single IV dose of THOR-924 in C57BL/6 mice induces STAT5 phosphorylation in NK, CD8+ and Treg cells. Upregulation of Ki67 expression is limited to CD8+ T and NK cells (single IV dose 0.1, 0.3 and 1 mg/kg)

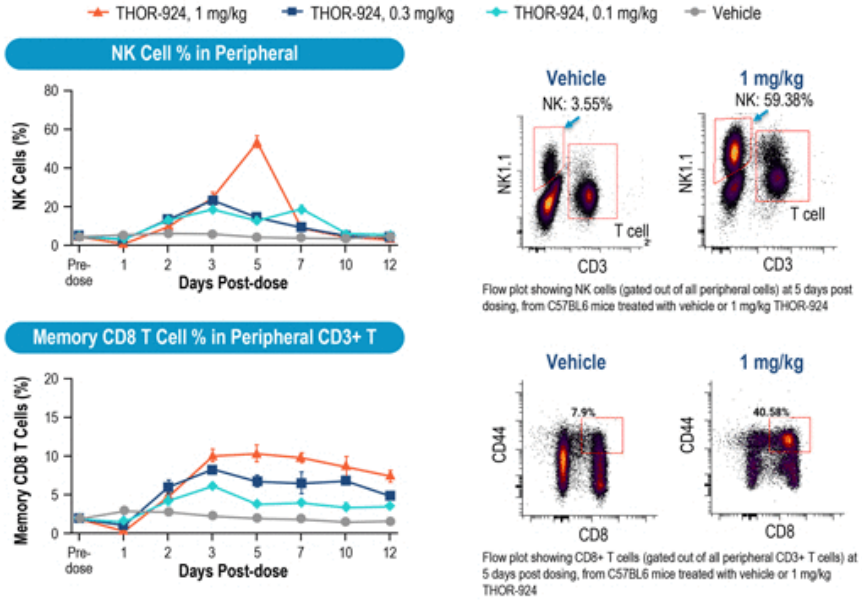


RESULTS

THOR-924 Expands Peripheral NK and CD8+ Tmem Cells in Mice in a Dose-Dependent Fashion

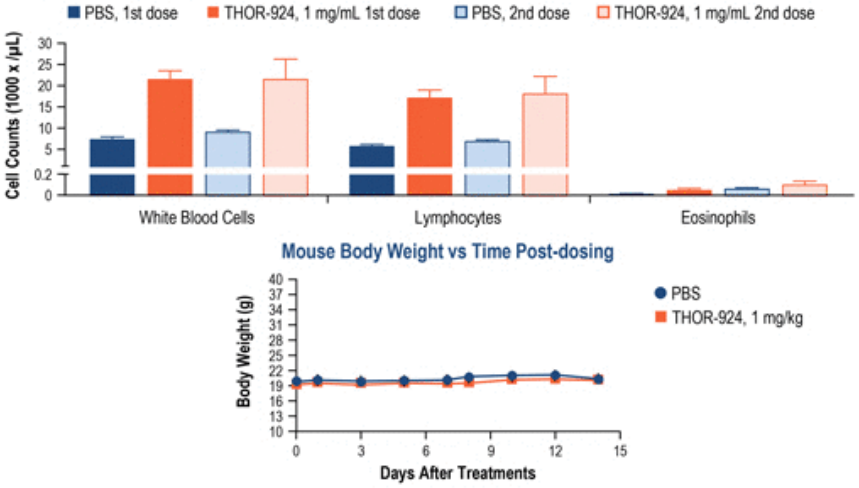
A Single IV Dose of THOR-924 Induced the Expansion of Memory CD8+ T and NK Cells in Mouse Blood

- Maximal expansion at 1 mg/kg



THOR-924 Does Not Induce Gross Toxicities After Two 1 mg/kg IV Doses in Mice

- Consistent WBC and lymphocyte expansion after the first and second dose of THOR-924 with no increase in eosinophils or weight loss



CONCLUSIONS

- *In vitro* and *Ex vivo* screening of site-specific, singly pegylated IL-15 Synthorins yielded hits with differentiated profiles for IL-15 receptors ∝ and β engagement
  - SAR analysis identified IL-15 constructs with differential engagement of the IL-15R:
    - THOR-924: similar to unmodified IL-15
    - THOR-908: normal engagement of IL-15R∝, normal at IL-2Rβ
    - THOR-918: normal engagement of both IL-15R∝ and β
  - IL-15 Synthorins differentially modulated of IL-15 receptors *Ex vivo*, as determined by monitoring pSTAT5 induction in mouse, NHP and human primary immune cells
- In mice, a single intravenous dose of THOR-924 induced:
  - Sustained pSTAT5 signaling in CD8 T, NK and Treg cells, with upregulation of Ki67 expression limited to CD8+ T and NK cells

- Selective expansion of peripheral CD8 Tmem and NK cells, but not Tregs
- Maximal expansion observed at 1 mg/kg

- Repeat dose study in mice showed:
  - WBC and lymphocyte expansion after the first and second dose
  - No changes in body weight, and no eosinophilia
- We conclude that THOR-924 shows an appropriate profile for a half-life extended IL-15 as a potent inducer of CD8+ T and NK cells without gross toxicity based on no eosinophilia or weight loss
- Future mouse PK/PD studies will evaluate whether THOR-908 and THOR-918 cause preferential stimulation of target cell subsets