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): June 15, 2026

SPYRE THERAPEUTICS, INC.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-37722**	**46-4312787**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

221 Crescent Street Building 23 Suite 105 Waltham, MA	**02453**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: 617 651-5940

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 obligation 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, $0.0001 Par Value Per Share	SYRE	The Nasdaq Stock Market LLC (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 7.01 Regulation FD Disclosure.

SPY002 SKYLINE Part A Induction Topline Results

On June 15, 2026, Spyre Therapeutics, Inc. ("Spyre" or the "Company") issued a press release announcing positive initial 12-week induction topline data from Part A of the Phase 2 SKYLINE trial of SPY002 for the treatment of moderately-to-severely active ulcerative colitis ("UC").

A copy of the press release is attached hereto as Exhibit 99.1. The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1 attached hereto, is intended to be furnished and shall not be deemed "filed" for 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 it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or under the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On June 15, 2026, the Company announced positive initial 12-week induction topline data from Part A of the Phase 2 SKYLINE trial of SPY002 for the treatment of moderately-to-severely active UC.

SPY002 SKYLINE Part A Induction Topline Results

Initial 12-week findings from SKYLINE Part A demonstrated that SPY002 met all key objectives. The study population consisted of 35% advanced therapy-exposed participants with a mean disease duration of 7.0 years, a mean baseline Robarts Histopathology Index ("RHI") score of 16.9 ± 8.5 (SD), a mean modified Mayo Score ("mMS") of 6.9 ± 1.0 (SD), and 56% of whom had a baseline endoscopy score of 3.

Efficacy: SPY002 achieved the primary endpoint, demonstrating a statistically significant 10.7-point reduction in RHI score ($p<0.0001$), robust rates of clinical remission and endoscopic improvement, and a meaningful change in mMS, results that are among the highest reported in UC.

Endpoint (Week 12)	**SPY002**
Change in RHI from baseline *Primary endpoint*	-10.7 *($p<0.0001$)*
Clinical remission rate	33%
Endoscopic improvement rate	42%
Change in modified Mayo Score	-3.7

Safety: SPY002 was well tolerated with a safety profile consistent with the TL1A class. There were twenty subjects with treatment-emergent adverse events ("TEAEs") during the induction treatment period. Two serious adverse

events (“SAEs”) were reported, both deemed not drug-related. One case was for hospitalization for exacerbation of UC, the other case was for worsening of heart failure in a subject with a history of heart failure. The most common adverse events (“AEs”) (occurring in ≥ 2 patients) were arthralgia (n=2), hypertension (n=3), nausea (n=2), UC (n=2), and viral respiratory tract infection (n=2).

	SPY002 (n=48)
Subjects with any AE (n, %)	20 (41.7%)
Severe (Grade ≥ 3) AE	2 (4.2%)[1,2]
Drug-related AE	3 (6.3%)[3]
AE leading to drug discontinuation	2 (4.2%)[2,4]
SAE	2 (4.2%)[1,2]
Drug-related SAE	0
AEs of special interest	0
Death	0

[1]*Hospitalization for exacerbation of UC in one subject, deemed not drug-related.*

[2]*Hospitalization for worsening heart failure in one subject with history of heart failure and atrial fibrillation, who was subsequently diagnosed with worsening of aortic stenosis; deemed not drug-related.*

[3]*One case each of nausea, hypertension, and arthralgia.*

[4]*Exacerbation of UC, deemed not drug-related.*

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press release issued by Spyre Therapeutics, Inc. regarding Data, dated June 15, 2026.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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.

SPYRE THERAPEUTICS, INC.

Date: June 15, 2026

By: /s/ Cameron Turtle

Cameron Turtle
Chief Executive Officer

Spyre Announces Potential Best-in-Class SPY002 (anti-TL1A) Part A Induction Results from SKYLINE Trial in Moderate-to-Severe Ulcerative Colitis Patients

SPY002 met its primary endpoint with a statistically significant reduction of 10.7 points (p<0.0001) from baseline at Week 12 in Robart's Histopathology Index (RHI) score

Secondary endpoints included clinical remission by modified Mayo Score of 33% and endoscopic improvement of 42%

SPY002 was well tolerated with a safety profile consistent with the TL1A class

SPY002 Phase 2 results delivered within one year of Phase 1 results, highlighting continued operational excellence; on track for multiple additional readouts this year

WALTHAM, Mass., June 15, 2026 (GLOBE NEWSWIRE) – Spyre Therapeutics, Inc. (NASDAQ: SYRE), a clinical-stage biotechnology company committed to developing next-generation therapies that elevate the standard in immunology by delivering more complete disease control, greater durability, and a simpler treatment experience for patients**,** today announced positive 12-week induction data from Part A of the Phase 2 SKYLINE trial of SPY002, a potential best-in-class anti-TL1A being investigated for the treatment of moderately-to-severely active ulcerative colitis (UC).

"SPY002 demonstrated an indication-leading 10.7-point reduction in RHI and meaningful clinical remission and endoscopic outcomes in line with the anti-TL1A class and among the highest across therapeutic classes," said Deanna Nguyen, M.D., SVP of Clinical Development and SKYLINE study lead. "Together with its target Q3-6M sub-cutaneous maintenance profile, these data build upon our impressive SPY001 results and reinforce our thesis that optimized monotherapy components are the foundation for potentially best-in-class combinations. We remain on track to report Part A data for SPY003 (anti-IL-23) in Q3, which, if successful, would complete proof-of-concept for our investigational monotherapy components. We are now enrolling Part B of the SKYLINE trial, which includes three combination arms with the potential to deliver best-in-disease efficacy, safety, and treatment experience."

SPY002 SKYLINE Part A Induction Topline Results

SKYLINE is a two-part induction and maintenance platform trial of SPY001, SPY002, SPY003, as well as pairwise combinations thereof (six investigational agents total) in patients with moderately-to-severely active ulcerative colitis. Part A is an open-label assessment of the safety and efficacy of a single dose level of each investigational monotherapy, and Part B is a randomized and placebo-controlled assessment of the safety and efficacy of investigational monotherapies (two dose levels) and combinations.

SPY002 is an extended half-life investigational antibody targeting TL1A, an upstream cytokine implicated in chronic inflammation and fibrosis in IBD. Initial 12-week findings from SKYLINE Part A demonstrated that SPY002 met all key objectives. The study population consisted of 35% advanced therapy-exposed participants with a mean disease duration of 7.0 years, a mean baseline RHI score of 16.9 ± 8.5 (SD), a mean modified Mayo Score of 6.9 ± 1.0 (SD), and 56% of whom had a baseline endoscopy score of 3.

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[3]One case each of nausea, hypertension, and arthralgia.

[4]Exacerbation of UC, deemed not drug-related.

About Spyre Therapeutics

Spyre Therapeutics is a clinical-stage biotechnology company committed to developing next-generation therapies that elevate the standard in immunology by delivering more complete disease control, greater durability, and a simpler treatment experience for patients. Spyre's pipeline includes investigational extended half-life antibodies targeting α4β7, TL1A, and IL-23.

For more information, visit Spyre's website at www.spyre.com.

Forward-Looking Statements

Certain statements in this press release, other than purely historical information, may constitute "forward-looking statements" within the meaning of the federal securities laws, including for purposes of the safe harbor provisions under the United States Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements regarding: Spyre’s ability to achieve the expected benefits or opportunities with respect to its product candidates, including their potential commercialization and its ability to develop next-generation therapies that elevate the standard in immunology by delivering more complete disease control, greater durability,

and a simpler treatment experience for patients; the potential for the three combination arms to deliver best-in-disease efficacy, safety, and treatment experiences; Spyre's ongoing and future clinical development activities, including Spyre's plans for data readouts for the ongoing SKYLINE trial. The words "opportunity," "potential," "milestones," "pipeline," "strategy," "anticipate," "believe," "could," "estimate," "expect," "may," "might," "plan," "possible," "predict," "should," "will," "would," and similar expressions (including the negatives of these terms) may identify forward-looking statements, but the absence of these words does not mean that a statement is not forward-looking. These forward-looking statements are based on current expectations and beliefs and involve a number of risks and uncertainties, many of which are beyond Spyre's control, and other assumptions that may cause actual results or performance to be materially different from those expressed or implied by these forward-looking statements. These risks and uncertainties include, but are not limited to, uncertainties and risks arising from regulatory feedback, including potential disagreement by regulatory authorities with the Company's interpretation of data and the Company's clinical trials for its product candidates; the potential for interim data not being delivered within expected time frames or final data not being consistent with or different than the topline or interim data reported for our programs; the potential impact of Trump Administration policies and changes in law on our business; and those uncertainties and factors described in Spyre's most recent Annual Report on Form 10-K, as supplemented and updated by subsequent Quarterly Reports on Form 10-Q and any other filings that Spyre has made or may make with the SEC from time to time. You should not place undue reliance on forward-looking statements in this press release, which speak only as of the date they are made and are qualified in their entirety by reference to the cautionary statements herein. Spyre does not undertake or accept any duty to make any updates or revisions to any forward-looking statements.

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