

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

SCHEDULE 13G

UNDER THE SECURITIES EXCHANGE ACT OF 1934

Spyre Therapeutics, Inc.

(Name of Issuer)

Common Stock, \$0.0001 par value per share

(Title of Class of Securities)

(CUSIP Number)

09/24/2026

(Date of Event Which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

- ☐ Rule 13d-1(b)
- ☒ Rule 13d-1(c)
- ☐ Rule 13d-1(d)

SCHEDULE 13G

CUSIP No.

	Names of Reporting Persons
1	Paradigm BioCapital Advisors LP
	Check the appropriate box if a member of a Group (see instructions)
2	☐ (a) ☒ (b)
3	Sec Use Only
	Citizenship or Place of Organization
4	DELAWARE
Number of Shares Beneficially	Sole Voting Power 5 4,457,450.00

Owned by Each Reporting Person With:	6	Shared Voting Power
		0.00
		Sole Dispositive Power
	7	4,457,450.00
		Shared Dispositive Power
	8	0.00
	Aggregate Amount Beneficially Owned by Each Reporting Person	
9		4,457,450.00
10	Check box if the aggregate amount in row (9) excludes certain shares (See Instructions)	
		☐
11	Percent of class represented by amount in row (9)	
		5.1 %
12	Type of Reporting Person (See Instructions)	
		PN

SCHEDULE 13G

CUSIP No.

Names of Reporting Persons		
1	Paradigm BioCapital Advisors GP LLC	
	Check the appropriate box if a member of a Group (see instructions)	
2	☐ (a)	
	☒ (b)	
3	Sec Use Only	
4	Citizenship or Place of Organization	
	DELAWARE	
	Sole Voting Power	
	5	4,457,450.00
Number of Shares Beneficially Owned by Each Reporting Person With:	6	Shared Voting Power
		0.00
		Sole Dispositive Power
	7	4,457,450.00
		Shared Dispositive Power
	8	0.00
	Aggregate Amount Beneficially Owned by Each Reporting Person	
9		4,457,450.00
10	Check box if the aggregate amount in row (9) excludes certain shares (See Instructions)	
		☐
11	Percent of class represented by amount in row (9)	
		5.1 %

12 Type of Reporting Person (See Instructions)

OO

Comment for Type of Reporting Person: limited liability company

SCHEDULE 13G

CUSIP No.

Names of Reporting Persons

1 Senai Asefaw, M.D.

Check the appropriate box if a member of a Group (see instructions)

2 ☐ (a)
☒ (b)

3 Sec Use Only

Citizenship or Place of Organization

4 UNITED STATES

Sole Voting Power

5 4,457,450.00

Number of
Shares Shared Voting Power

Beneficially 6 0.00

Owned by Sole Dispositive Power

Each 7 4,457,450.00

Reporting Shared Dispositive

Person 8 Power

0.00

Aggregate Amount Beneficially Owned by Each Reporting Person

9 4,457,450.00

Check box if the aggregate amount in row (9) excludes certain shares (See Instructions)

10 ☐

Percent of class represented by amount in row (9)

11 5.1 %

Type of Reporting Person (See Instructions)

12 IN

SCHEDULE 13G

CUSIP No.

Names of Reporting Persons

1 Paradigm BioCapital International Fund Ltd.

2 Check the appropriate box if a member of a Group (see instructions)

☐ (a)

☒ (b)

3 Sec Use Only
Citizenship or Place of Organization

4 CAYMAN ISLANDS

Sole Voting Power

5

3,928,646.00

Number of
Shares Beneficially

Shared Voting Power

6

0.00

Owned by
Each

Sole Dispositive Power

7

3,928,646.00

Reporting
Person

Shared Dispositive

With:

Power

8

0.00

Aggregate Amount Beneficially Owned by Each Reporting Person

9

3,928,646.00

Check box if the aggregate amount in row (9) excludes certain shares (See Instructions)

10

☐

Percent of class represented by amount in row (9)

11

4.5 %

Type of Reporting Person (See Instructions)

12

CO

SCHEDULE 13G

Item 1.

Name of issuer:

(a)

Spyre Therapeutics, Inc.

Address of issuer's principal executive offices:

(b)

221 Crescent Street, Building 23, Suite 105, Waltham, MA 02453

Item 2.

Name of person filing:

This Schedule 13G is filed by the following (the "Reporting Persons"): (1) Paradigm BioCapital Advisors LP (the "Adviser"); (2) Paradigm BioCapital Advisors GP LLC (the "Adviser GP"); (3) Senai Asefaw, M.D. ("Senai Asefaw"); and (4) Paradigm BioCapital International Fund Ltd. (the "Fund"). The Fund is a private investment

(a)

vehicle. The Fund and one or more separately managed accounts managed by the Adviser (the "Account") directly beneficially own the Common Stock reported in this statement. The Adviser is the investment manager of the Fund and the Account. The Adviser GP is the general partner of the Adviser. Senai Asefaw is the managing member of the Adviser GP. The Adviser, the Adviser GP and Senai Asefaw may be deemed to beneficially own the Common Stock directly beneficially owned by the Fund and the Account. Each Reporting Person disclaims beneficial ownership with respect to any Common Stock other than the Common Stock directly beneficially owned by such Reporting Person.

Address or principal business office or, if none, residence:

(b)

The principal business office of the Fund is c/o Walkers, 190 Elgin Avenue, George Town, Grand Cayman KY1-9001, Cayman Islands. The principal business office of the Adviser, the Adviser GP and Senai Asefaw is 520 Fifth Avenue, 23rd Floor, New York, NY 10036.

Citizenship:

(c)

For citizenship or place of organization see Item 4 of the cover page of each Reporting Person.

- (d) Title of class of securities:
Common Stock, \$0.0001 par value per share
- (e) CUSIP No.:
- Item 3. If this statement is filed pursuant to §§ 240.13d-1(b) or 240.13d-2(b) or (c), check whether the person filing is a:
- (a) ☐ Broker or dealer registered under section 15 of the Act (15 U.S.C. 78o);
 - (b) ☐ Bank as defined in section 3(a)(6) of the Act (15 U.S.C. 78c);
 - (c) ☐ Insurance company as defined in section 3(a)(19) of the Act (15 U.S.C. 78c);
 - (d) ☐ Investment company registered under section 8 of the Investment Company Act of 1940 (15 U.S.C. 80a-8);
 - (e) ☐ An investment adviser in accordance with § 240.13d-1(b)(1)(ii)(E);
 - (f) ☐ An employee benefit plan or endowment fund in accordance with § 240.13d-1(b)(1)(ii)(F);
 - (g) ☐ A parent holding company or control person in accordance with § 240.13d-1(b)(1)(ii)(G);
 - (h) ☐ A savings associations as defined in Section 3(b) of the Federal Deposit Insurance Act (12 U.S.C. 1813);
 - (i) ☐ A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment Company Act of 1940 (15 U.S.C. 80a-3);
 - (j) ☐ A non-U.S. institution in accordance with § 240.13d-1(b)(1)(ii)(J). If filing as a non-U.S. institution in accordance with § 240.13d-1(b)(1)(ii)(J), please specify the type of institution:
 - (k) ☐ Group, in accordance with Rule 240.13d-1(b)(1)(ii)(K).
- Item 4. Ownership
- Amount beneficially owned:
- (a) See Item 9 on the cover page for each Reporting Person, and Item 2, which information is given as of the close of business on September 24, 2026, the Date of Event which requires the filing of this Schedule 13G.
Percent of class:
 - (b) See Item 11 on the cover page for each Reporting Person. The percentages of beneficial ownership contained herein are based on 88,173,762 shares of Common Stock outstanding as of July 28, 2026, as reported by the Issuer in its Form 10-Q filed with the SEC on August 4, 2026. %
 - (c) Number of shares as to which the person has:
 - (i) Sole power to vote or to direct the vote:

See Item 5 on the cover page for each Reporting Person.
 - (ii) Shared power to vote or to direct the vote:

See Item 6 on the cover page for each Reporting Person.
 - (iii) Sole power to dispose or to direct the disposition of:

See Item 7 on the cover page for each Reporting Person.
 - (iv) Shared power to dispose or to direct the disposition of:

See Item 8 on the cover page for each Reporting Person.
- Item 5. Ownership of 5 Percent or Less of a Class.
- Item 6. Ownership of more than 5 Percent on Behalf of Another Person.
Not Applicable
- Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on by the Parent Holding Company or Control Person.
Not Applicable
- Item 8. Identification and Classification of Members of the Group.
Not Applicable
- Item 9. Notice of Dissolution of Group.
Not Applicable

Item 10. Certifications:

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect, other than activities solely in connection with a nomination under § 240.14a-11.

SIGNATURE

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Paradigm BioCapital Advisors LP

Signature: /s/ David K. Kim

Name/Title: David K. Kim / Authorized Signatory

Date: 10/01/2026

Paradigm BioCapital Advisors GP LLC

Signature: /s/ David K. Kim

Name/Title: David K. Kim / Authorized Signatory

Date: 10/01/2026

Senai Asefaw, M.D.

Signature: /s/ Senai Asefaw, M.D.

Name/Title: N/A

Date: 10/01/2026

Paradigm BioCapital International Fund Ltd.

Signature: /s/ David K. Kim

Name/Title: David K. Kim / Authorized Signatory

Date: 10/01/2026

Exhibit Information

Exhibit 99.1 - Joint Filing Agreement

JOINT FILING AGREEMENT

In accordance with Rule 13d-1(k) under the Securities Exchange Act of 1934, as amended, the persons named below agree to the joint filing on behalf of each of them of a statement on Schedule 13G (including amendments thereto) with respect to the Common Shares, par value \$0.0001 per share, of Spyre Therapeutics, Inc., and further agree that this Joint Filing Agreement be included as an Exhibit to such joint filing. In evidence thereof, the undersigned hereby execute this Agreement.

Dated: October 1, 2026

Paradigm BioCapital Advisors LP
Paradigm BioCapital Advisors GP LLC
Paradigm BioCapital International Fund Ltd.

By: /s/ David K. Kim
Name: David K. Kim
Title: Authorized Signatory

/s/ Senai Asefaw, M.D.
Senai Asefaw, M.D.
