

Number of Shares Beneficially Owned by Each Reporting Person With:	5	Sole Voting Power
	0.00	
		Shared Voting Power
	6	
	4,251,996.00	
		Sole Dispositive Power
	7	
	0.00	
		Shared Dispositive Power
	8	
	4,251,996.00	
9	Aggregate Amount Beneficially Owned by Each Reporting Person	
	4,251,996.00	
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)	
	4.8 %	
12	Type of Reporting Person (See Instructions)	
	IA, PN	

SCHEDULE 13G

CUSIP No.

1	Names of Reporting Persons	
	Roderick Wong	
	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	
	UNITED STATES	
		Sole Voting Power
	5	
	0.00	
Number of Shares Beneficially Owned by Each Reporting Person With:		Shared Voting Power
	6	
	4,251,996.00	
		Sole Dispositive Power
	7	
	0.00	
		Shared Dispositive Power
	8	
	4,251,996.00	
9	Aggregate Amount Beneficially Owned by Each Reporting Person	
	4,251,996.00	
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)
4.8 %
Type of Reporting Person (See Instructions)

12 HC, IN

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:

(a)

This statement is filed by: (i) RTW Investments, LP ("RTW Investments"), a Delaware limited partnership and the investment adviser to certain funds (the "RTW Funds"), with respect to shares of Common Stock, par value \$0.0001 per share (the "Shares") of Spyre Therapeutics, Inc. (the "Company") directly held by the RTW Funds; and (ii) Roderick Wong, M.D. ("Dr. Wong"), the Managing Partner and Chief Investment Officer of RTW Investments, with respect to the Shares directly held by the RTW Funds. The foregoing persons are hereinafter sometimes collectively referred to as the "Reporting Persons." The filing of this statement should not be construed as an admission that any of the foregoing persons or any Reporting Person is, for the purposes of Section 13 of the Securities Exchange Act of 1934, as amended, the beneficial owner of the Shares reported herein.

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

(b)

The address of the business office of each of the Reporting Persons is 40 10th Avenue, Floor 7, New York, New York 10014.

Citizenship:

(c)

RTW Investments is a Delaware limited partnership. Dr. Wong is a citizen of the United States.

Title of class of securities:

(d)

Common Stock, \$0.0001 par value

(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

(a)

Amount beneficially owned:

The information required by Item 4(a) is set forth in Rows 5 - 9 of the cover page for each of the Reporting Persons and is incorporated herein by reference. The percentages set forth in Row 11 of the cover pages are calculated based upon 87,936,477 Shares outstanding as of June 24, 2026, as reported in the Issuer's Registration Statement on Form S-3ASR filed with the Securities and Exchange Commission (the "SEC") on June 26, 2026.

Percent of class:

(b)

RTW Investments: 4.8% Dr. Wong: 4.8% %

(c)

Number of shares as to which the person has:

(i) Sole power to vote or to direct the vote:

RTW Investments: 0 Dr. Wong: 0

(ii) Shared power to vote or to direct the vote:

RTW Investments: 4,251,996 Shares Dr. Wong: 4,251,996 Shares

(iii) Sole power to dispose or to direct the disposition of:

RTW Investments: 0 Dr. Wong: 0

(iv) Shared power to dispose or to direct the disposition of:

RTW Investments: 4,251,996 Shares Dr. Wong: 4,251,996 Shares

Item 5. Ownership of 5 Percent or Less of a Class.

☒ Ownership of 5 percent or less of a class

Item 6. Ownership of more than 5 Percent on Behalf of Another Person.

If any other person is known to have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, such securities, a statement to that effect should be included in response to this item and, if such interest relates to more than 5 percent of the class, such person should be identified. A listing of the shareholders of an investment company registered under the Investment Company Act of 1940 or the beneficiaries of employee benefit plan, pension fund or endowment fund is not required.

See Item 2. The RTW Funds have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the Shares reported herein.

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 acquired and are held in the ordinary course of business and 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.

RTW Investments, LP

Signature: /s/ Roderick Wong, M.D.

Name/Title: Roderick Wong, M.D., Managing Partner

Date: 08/14/2026

Roderick Wong

Signature: /s/ Roderick Wong, M.D.

Name/Title: Roderick Wong, M.D.

Date: 08/14/2026

Exhibit Information

Exhibit 99.1 Joint Filing Agreement (incorporated by reference to Exhibit 99.1 to the Reporting Persons' Schedule 13G filed with the SEC on February 14, 2024).