

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

| OMB APPROVAL | |
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Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Check this box to indicate that a transaction was made pursuant to a contract, instruction or written plan for the purchase or sale of equity securities of the issuer that is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c). See Instruction 10.

| | | |
|---|---|---|
| 1. Name and Address of Reporting Person* <u>Burrows Scott L</u> (Last) (First) (Middle) 221 CRESCENT STREET, BUILDING 23, SUITE 105 (Street) WALTHAM MA 02453 (City) (State) (Zip) | 2. Issuer Name and Ticker or Trading Symbol <u>Spyre Therapeutics, Inc. [SYRE]</u> | 5. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) Chief Financial Officer |
| | 3. Date of Earliest Transaction (Month/Day/Year) 03/03/2026 | |
| 4. If Amendment, Date of Original Filed (Month/Day/Year) | | |

Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned

| 1. Title of Security (Instr. 3) | 2. Transaction Date (Month/Day/Year) | 2A. Deemed Execution Date, if any (Month/Day/Year) | 3. Transaction Code (Instr. 8) | | 4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5) | | | 5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4) | 6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 7. Nature of Indirect Beneficial Ownership (Instr. 4) |
|---------------------------------|--------------------------------------|--|--------------------------------|---|---|------------|------------------------|---|--|---|
| | | | Code | V | Amount | (A) or (D) | Price | | | |
| Common Stock | 03/03/2026 | | M ⁽¹⁾ | | 2,500 | A | \$14.5 | 100,494 | D | |
| Common Stock | 03/03/2026 | | s ⁽¹⁾ | | 2,300 | D | \$40.56 ⁽²⁾ | 98,194 | D | |
| Common Stock | 03/03/2026 | | s ⁽¹⁾ | | 200 | D | \$41.66 ⁽³⁾ | 97,994 ⁽⁴⁾ | D | |

Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

| 1. Title of Derivative Security (Instr. 3) | 2. Conversion or Exercise Price of Derivative Security | 3. Transaction Date (Month/Day/Year) | 3A. Deemed Execution Date, if any (Month/Day/Year) | 4. Transaction Code (Instr. 8) | | 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) | | 6. Date Exercisable and Expiration Date (Month/Day/Year) | | 7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4) | 8. Price of Derivative Security (Instr. 5) | 9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4) | 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) | |
|--|--|--------------------------------------|--|--------------------------------|---|--|-------|--|-----------------|---|--|--|---|--|-------|
| | | | | Code | V | (A) | (D) | Date Exercisable | Expiration Date | | | | | | Title |
| Stock Option (Right to Buy) | \$14.5 | 03/03/2026 | | M ⁽¹⁾ | | | 2,500 | (5) | 09/01/2033 | Common Stock | 2,500 | \$0 | 402,357 | D | |

Explanation of Responses:

- This transaction was executed pursuant to a Rule 10b5-1 trading plan adopted on November 10, 2025.
- The price reported above is a weighted average price. The shares were sold in multiple transactions at prices ranging from \$40.17 to \$41.11, inclusive. The Reporting Person undertakes to provide to the Issuer, any security holder of the Issuer, or the staff of the Securities and Exchange Commission (the "SEC"), upon request, full information regarding the number of shares sold at each separate price within the range.
- The price reported above is a weighted average price. The shares were sold in multiple transactions at prices ranging from \$41.55 to \$41.76, inclusive. The Reporting Person undertakes to provide to the Issuer, any security holder of the Issuer, or the staff of the SEC, upon request, full information regarding the number of shares sold at each separate price within the range.
- Includes 67,476 restricted stock units ("RSUs"). Each RSU represents a contingent right to receive, upon vesting, one share of Common Stock. The RSUs vest in two equal installments on each of September 1, 2026 and 2027, subject to the Reporting Person's continued employment with the Issuer.
- This option represents a right to purchase 404,857 shares of the Issuer's common stock (which have been adjusted to reflect the Issuer's 1-for-25 reverse stock split on September 8, 2023), one quarter of which vested and became exercisable on September 1, 2024, with the remaining three quarters vesting in monthly installments over the following three years, subject to the Reporting Person's continued employment with the Issuer.

Remarks:

/s/ Heidi King-Jones, as 03/03/2026
Attorney-in-Fact

** Signature of Reporting Person Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.