

| OMB APPROVAL                                 |           |
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| OMB Number:                                  | 3235-0287 |
| Estimated average burden hours per response: | 0.5       |

**STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP**

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 if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

|  |   |  |
|--|---|--|
| 1. Name and Address of Reporting Person*<br><u>RTW INVESTMENTS, LP</u><br><br>(Last) (First) (Middle)<br>40 10TH AVENUE,<br>FLOOR 7<br><br>(Street)<br>NEW YORK NY 10014<br><br>(City) (State) (Zip) | 2. Issuer Name and Ticker or Trading Symbol<br><u>Milestone Pharmaceuticals Inc. [ MIST ]</u> | 5. Relationship of Reporting Person(s) to Issuer<br>(Check all applicable)<br><br>Director <input checked="" type="checkbox"/> 10% Owner<br><br>Officer (give title below) Other (specify below)                   |
|  | 3. Date of Earliest Transaction (Month/Day/Year)<br>05/21/2021                                |  |
|  |   | 6. Individual or Joint/Group Filing (Check Applicable Line)<br><br><input checked="" type="checkbox"/> Form filed by One Reporting Person<br><input type="checkbox"/> Form filed by More than One Reporting Person |

**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 Beneficial Ownership (Instr. 4) |
|---------------------------------|--------------------------------------|--|--------------------------------|---|---|------------|-------|---|--|--|
|                                 |                                      |  | Code                           | V | Amount  | (A) or (D) | Price |   |  |  |

**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   | Amount or Number of Shares |  |  |   |  |
| Pre-Funded Warrant <sup>(2)</sup>          | \$0.01   | 05/21/2021                           |  | P                              |   | 910,746  |     | 05/21/2021   | (3)             | Common Stock  | 910,746                    | \$5.48                                     | 8,518,257  | I   | By RTW <sup>(1)</sup>                                  |

1. Name and Address of Reporting Person\*  
RTW INVESTMENTS, LP  
 (Last) (First) (Middle)  
 40 10TH AVENUE,  
 FLOOR 7  
 (Street)  
 NEW YORK NY 10014  
 (City) (State) (Zip)

1. Name and Address of Reporting Person\*  
WONG RODERICK  
 (Last) (First) (Middle)  
 C/O RTW INVESTMENTS, LP  
 40 10TH AVENUE, FLOOR 7  
 (Street)  
 NEW YORK NY 10014  
 (City) (State) (Zip)

**Explanation of Responses:**

- The securities reported herein may be deemed beneficially owned by each of: (i) RTW Investments, LP ("RTW"), which is deemed the beneficial owner of shares held by RTW Master Fund, Ltd., RTW Venture Fund Limited and RTW Innovation Master Fund, Ltd. (the "Funds"), which are investment funds managed by RTW, and (ii) Roderick Wong, M.D., who serves as the Managing Partner and Chief Investment Officer of RTW. Dr. Wong exercises voting and dispositive control over the securities held by RTW and is therefore deemed to be a beneficial owner of securities owned or controlled by RTW. Each of RTW and Dr. Wong disclaim beneficial ownership of the reported securities held by the Funds, except to the extent of its or his pecuniary interest therein.
- Each pre-funded warrant represents the right to acquire one share of common stock for an exercise price of \$0.01 per share. The ability of the holder to exercise the pre-funded warrant is subject to a beneficial ownership limitation initially set at 9.99% of the Company's issued and outstanding common stock. This beneficial ownership limitation may be increased or decreased at the election of the warrant holder, provided that any increase shall not be effective until the 61st day after notice of adjustment is provided to the Company.
- The warrants do not have an expiration date.

RTW Investments, LP; By: /s/ attorney-in-fact for RTW Investments, LP 05/24/2021  
/s/ Alice Lee, attorney-in-fact 05/24/2021

[for Roderick Wong](#)

\*\* 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.**