```

# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**WASHINGTON, DC 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) **May 26, 2022**

# Oncternal Therapeutics, Inc.

(Exact Name of Registrant as Specified in Charter)

| **Delaware** | **000-50549** | **62-1715807** |
|---|---|---|
| (State or Other Jurisdiction of Incorporation) | (Commission File Number) | (IRS Employer Identification No.) |

**12230 El Camino Real**
**Suite 230**
**San Diego, CA 92130**
**(858) 434-1113**
(Address and zip code; telephone number, including area code, of registrant's principal executive offices)

**N/A**
(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 (*see* General Instruction A.2. below):

☐ Written communication 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, par value $0.001 per share | ONCT | The Nasdaq Stock Market, LLC |

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 8.01. Other Events

On May 26, 2022, Oncternal Therapeutics, Inc. ("Oncternal") disclosed updated interim clinical data from its ongoing Phase 1/2 CIRLL (Cirmtuzumab and Ibrutinib targeting ROR1 for Leukemia and Lymphoma) clinical trial evaluating zilovertamab, an investigational anti-ROR1 monoclonal antibody, in combination with ibrutinib in patients with mantle cell lymphoma ("MCL") and chronic lymphocytic leukemia ("CLL"). The updated interim data will be presented at the American Society of Clinical Oncology (ASCO) 2022 Annual Meeting.

As of the April 8, 2022 data cut-off date, 27 of the 33 patients with relapsed/refractory MCL enrolled in the dose-finding and dose-expansion cohorts of the CIRLL Phase 1/2 clinical trial were evaluable for efficacy. These patients had high-risk factors and were heavily pre-treated at study entry, 52% with a high Ki-67 proliferative index (≥30%) ("High Ki-67 Patients") and 46% with intermediate/high simplified MCL international (sMIPI) prognostic score. The objective response rate ("ORR") was 85% (23 of 27 evaluable patients), including recently enrolled patients with relatively short follow-up time. The complete response ("CR") rate was 41% (11 of 27 evaluable patients). CRs have remained durable for up to 35 months. The partial response ("PR") rate was 44% (12 of 27 evaluable patients), and the stable disease ("SD") rate was 7% (two patients). The total clinical best benefit rate (CR, PR and SD) was 93%.

The ORR and median duration of response ("DOR") were favorable in patients with high-risk features associated with difficult-to-treat disease. Patients with p53 mutations had an ORR of 83%, a median DOR of 13.8 months (95% confidence interval 11.9 months - not evaluable), a median progression-free survival ("PFS") of 17.3 months (95% confidence interval 2.9 months - not evaluable), and landmark PFS over 80% at 15 months. High Ki-67 Patients had an ORR of 86% and a median DOR that had not been reached (95% confidence interval 13.7 months - not estimable). Patients that had received more than one systemic prior therapy had an ORR of 83%. The median DOR had not been reached for patients with two prior lines of systemic therapy and was 34 months (95% confidence interval 13.8 months - 34.1 months) for patients with three or more prior lines of systemic therapy. Patients that received prior ibrutinib treatment had an ORR of 80% (four of five evaluable patients), with two CRs, two PRs and 1 SD. Median PFS was 35.9 months for all patients with MCL after a median follow-up of 14.4 months (95% confidence interval 11.4 months – 19.3 months), regardless of number of prior systemic therapies. Further, median PFS has not been reached for patients achieving a CR. Historical data published for single agent ibrutinib for 370 patients with relapsed/refractory MCL from three clinical trials showed an ORR of 66%, CR rate of 20% and median PFS of 12.8 months (Rule et al., 2017, British Journal of Haematology). Historical data in 20 patients with p53 mutation showed an ORR of 55% and median PFS of four months (Rule, 2019).

As of the April 8, 2022 data cut-off date, all 34 patients with CLL enrolled in the dose-finding and dose-confirming cohorts of this clinical trial were evaluable for efficacy. Patients had high-risk factors, and most were heavily pre-treated at study entry, with 71% having RAI staging II or higher and a median of two systemic prior therapies (range 1-9). The ORR was 91% (31 of 34 evaluable patients). The CR rate was 9% (3 of 34 evaluable patients). The clinical benefit rate was 100%, with 28 of 34 evaluable patients (82%) achieving a PR and three patients (9%) had SD. Median PFS had not been reached for all patients with CLL, whether treatment-naïve or those with relapsed refractory disease. Landmark PFS was 100% at 36 months for CLL patients with one or two prior lines of therapy, which compares favorably to historical ibrutinib monotherapy of approximately 75% (Byrd, 2019). Landmark PFS was over 85% and 70% at 24 and 36 months, respectively, for CLL patients who had previously received more than two prior lines of therapy compared favorably to historical ibrutinib monotherapy of approximately 65% and approximately 50%, respectively (Byrd, 2019).

Thirty-one patients with CLL have also been enrolled in the randomized efficacy cohort of the clinical trial, of which 23 were evaluable for efficacy. Data on this cohort are maturing, and median PFS had not been reached as of the April 8, 2022 cut-off date after following for 24 months.

The combination of zilovertamab plus ibrutinib has been well tolerated, with treatment emergent adverse events consistent with those reported for ibrutinib alone. There have been no dose-limiting toxicities and no serious adverse events attributed to zilovertamab alone. In patients with MCL, Grade 3-4 neutrophil decrease was documented in 9.1% of patients with zilovertamab plus ibrutinib, compared to 29% for ibrutinib alone from its registration study.

Oncternal has not conducted head-to-head studies of zilovertamab in combination with ibrutinib compared to ibrutinib monotherapy and data from separate studies may not be directly comparable due to the differences in study protocols, conditions, and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative safety or efficacy of zilovertamab in combination with ibrutinib compared to ibrutinib monotherapy. In addition, interim results of a clinical trial may not be predictive of final results, and one or more of the clinical outcomes may materially change as data matures.

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.

Oncternal Therapeutics, Inc.

Date: May 26, 2022

By: /s/ Richard G. Vincent

Name: Richard G. Vincent

Title: Chief Financial Officer