UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 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): April 20, 2023

DAY ONE BIOPHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-40431**	**83-2415215**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

2000 Sierra Point Parkway, Suite 501
Brisbane, California **94005**
(Address of principal executive offices) **(Zip Code)**

Registrant's telephone number, including area code: (650) 484-0899

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:

☐ Written communications 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 $0.0001 per share	DAWN	Nasdaq Global Select Market

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 7.01 Regulation FD Disclosure.

On April 20, 2023, Day One Biopharmaceuticals, Inc. (the "Company") released a poster presentation entitled "Clinical Activity of the Type II pan-RAF Inhibitor Tovorafenib in BRAF-fusion Melanoma" (the "Poster Presentation"). The Poster Presentation will be provided at the Company's previously announced presentation at the 19th European Association of Dermato-Oncology (EADO) Congress held on April 20, 2023 at 8:45 a.m. Eastern Time.

A copy of the Poster Presentation is furnished as Exhibit 99.1 and is incorporated herein by reference.

The information in this Current Report on Form 8-K, including Exhibit 99.1 to this report, shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended (the "Securities Act"). The information contained in this Current Report on Form 8-K and in the accompanying Exhibit 99.1 shall not be incorporated by reference into any other filing under the Exchange Act or under the Securities Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Poster Presentation
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

DAY ONE BIOPHARMACEUTICALS, INC.

Date: April 20, 2023

By: /s/ Charles N. York II, M.B.A.
Charles N. York II, M.B.A.
Chief Operating Officer and Chief Financial Officer

Clinical activity of the type II pan-RAF inhibitor tovorafenib in *BRAF*-fusion melanoma

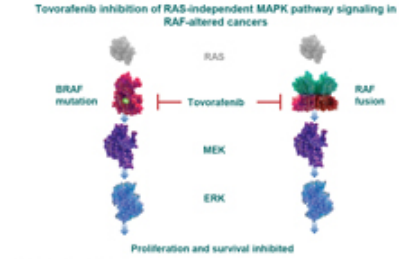
Jeeyun Lee, MD,[1] Natraj R. Ammakkanavar, MD,[2] Aprajita Saini, MS,[3] Mark W. Kieran MD, PhD,[3] Lisa M. Kopp, DO, MPH,[3] Bert H. O'Neil, MD[2]

[1]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [2]Community North Cancer Center, Indianapolis, IN, United States of America; [3]Day One Biopharmaceuticals, Brisbane, CA, United States of America

Background

- A distinct molecular subset of melanoma with no other known driver mutations harbors *BRAF* fusions:[1]
  - *BRAF* fusions occur in 2.6-6.7% of all melanomas[2]
- Tovorafenib is an investigational, oral, selective, CNS-penetrant, type II pan-RAF inhibitor targeting both monomeric and dimeric forms of RAF[3] (**Figure 1**)
- Preclinical and clinical data have indicated that tovorafenib is not associated with paradoxical activation of the mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK) pathway as has been reported for type I *BRAF* inhibitors[3-5]
- Single-agent tovorafenib activity has been observed in *BRAF*- and *NRAS*-mutated melanoma, low-grade gliomas harboring *RAF*-fusions, and a patient with a novel *SNX8-BRAF* fusion spindle cell sarcoma[4-7]

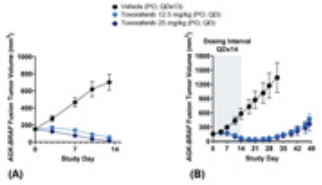
Figure 1. Tovorafenib mechanism of action



MAPK, mitogen-activated protein kinase.

In vivo proof of concept: antitumor efficacy

Figure 2. Antitumor activity of tovorafenib in *BRAF*-fusion melanoma PDX models



- Tovorafenib treatment of an *AGK-BRAF* fusion melanoma PDX model leads to regressions:
  - NOD SCID mice bearing melanoma PDX tumors with a confirmed *AGK-BRAF* fusion were treated with tovorafenib or vehicle control daily for 14 days (**Figure 2A**)
- Durable responses to tovorafenib were observed in *AGK-BRAF* fusion melanoma PDX:
  - NOD SCID mice bearing melanoma PDX tumors with a confirmed *AGK-BRAF* fusion were treated with tovorafenib or vehicle control for 14 days. Treatment was then stopped, and tumors monitored for regrowth. Tumor regrowth was not observed until 3 weeks post treatment (**Figure 2B**)

NOD SCID, nonobese diabetic severe combined immunodeficiency; PDX, patient-derived xenograft; PO, oral administration; QD, once daily.

FIRELIGHT-1

- FIRELIGHT-1 (NCT04985604) is an open-label, multicenter, phase (P) 1b/2 umbrella study of tovorafenib monotherapy or combination therapy in patients ≥12 years of age with recurrent, progressive or refractory solid tumors harboring molecularly defined alterations of components of the MAPK pathway (**Figure 3**)
- Substudy 1 (DAY101-102a) is investigating tovorafenib monotherapy in patients with a recurrent, progressive or refractory melanoma (cohort 1) or other solid tumor (cohort 2) harboring activating *BRAF* or *RAF1 (CRAF)* fusions or *RAF1* amplifications:
  - Primary endpoint: overall response rate per RECIST v1.1
  - Tovorafenib administered to adult patients (≥18 years of age) at 600 mg once weekly (QW) and for patients 12 to <18 years of age at 420 mg/m^2 QW (not to exceed 600 mg)

Figure 3. FIRELIGHT-1 trial design

*Projected enrollment: tovorafenib alone (n~43); melanoma cohort (n~18); tissue-agnostic cohort (n~25).
BM, biomarker; MAPK, mitogen-activated protein kinase; P, phase; RECIST, response evaluation criteria in solid tumors; RP2D, recommended P 2 dose; TBD, to be determined.

Results

- Preliminary clinical activity of tovorafenib monotherapy in the first 3 patients with *BRAF* fusion melanoma is reported (data cutoff Feb 8, 2023; **Table 1**)

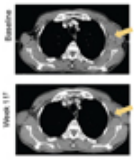
Table 1. Patient and disease characteristics

	Patient 1	Patient 2	Patient 3
Age (years)	53	38	71
Sex	M	M	M
ECOG status	0	1	0
Primary cancer	Cutaneous melanoma, non-Spitzoid	Malignant melanoma	Cutaneous melanoma, non-Spitzoid
BRAF fusion	*AGK-BRAF*	*TRIM33-BRAF*	*MKRN1-BRAF*
Stage at diagnosis	III	Unknown	II
Prior therapy:			
Surgery	Yes	No	No
Radiotherapy	No	Yes	Yes
Immune checkpoint inhibitor	Yes	Yes	Yes
Prior lines of targeted treatment	1	2	1
Tovorafenib dose	600 mg QW	600 mg QW	600 mg QW
TRAE D57	No	No	No
Dose modification/discontinuation due to AE*	No	No	No
Dose interruptions*	No	No	No
Treatment ongoing*	Yes	Yes	Yes
Current cycle*	5	5	3
Best RECIST response to tovorafenib*	CR	PR	PR†

*Data cutoff Feb 8, 2023. †Patient 3 is awaiting a confirmatory scan.
AE, adverse events; CR, complete response; ECOG, Eastern Cooperative Oncology Group; G, grade; M, male; PR, partial response; QW, once weekly; RECIST, response evaluation criteria in solid tumors; TRAE, treatment-related adverse event.

Patient 1 with *AGK-BRAF* fusion cutaneous melanoma

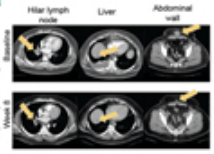
Parameter	Description/outcome
Prior therapies	• Multiple lymphadenectomies and skin lesion excision surgery • Pembrolizumab (11 weeks): – Best response: SD
Tovorafenib treatment to date in FL-1 102a (melanoma cohort)*	• 600 mg QW • 5 cycles with no dose interruption or modifications due to AEs
Antitumor activity results to date*	CR (11-week scan)†; confirmed at 16 weeks‡
Safety results to date*	TRAEs: transient rash (G1 and G2) anemia (G2) TEAE: neck pain (G1)



*Data cutoff Feb 8, 2023. †Out of window per protocol. ‡per RECIST v1.1.
AE, adverse event; CR, complete response; G, grade; FL-1, FIRELIGHT-1; QW, once weekly; RECIST, response evaluation criteria in solid tumors; SD, stable disease; TEAE, treatment-emergent adverse event; TRAEs, treatment-related adverse events.

Patient 2 with *TRIM33-BRAF* fusion malignant melanoma

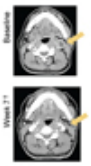
Parameter	Description/outcome
Prior therapies	• Radiation • Nivolumab (12 mo, adjuvant setting): – No best response, disease resected • Nivolumab + ipilimumab (3 cycles): – Best response: PD after 2 mo
Tovorafenib treatment to date in FL-1 102a (melanoma cohort)*	• 600 mg QW • 5 cycles with no dose interruption or modifications due to AEs
Antitumor activity results to date*	PR (8-week scan); confirmed at 16 weeks†
Safety results to date*	TRAEs: rash - maculopapular (G1) headache (G1) fatigue (G1)



*Data cutoff Feb 8, 2023. †per RECIST v1.1.
AE, adverse event; G, grade; FL-1, FIRELIGHT-1; mo, months; QW, once weekly; PD, progressive disease; PR, partial response; RECIST, response evaluation criteria in solid tumors; TRAEs, treatment-related adverse events.

Patient 3 with *MKRN1-BRAF* fusion cutaneous melanoma

Parameter	Description/outcome
Prior therapies	• Radiation • Pembrolizumab (2 mo): – Best response: SD
Tovorafenib treatment to date in FL-1 102a (melanoma cohort)*	• 600 mg QW • 3 cycles with no dose interruption or modifications due to AEs
Antitumor activity results to date*	PR (7-week scan)†‡; is awaiting a confirmatory scan
Safety results to date*	TRAEs: urticaria (G1) hand-foot syndrome (G1)



*Data cutoff Feb 8, 2023. †In window per protocol. ‡per RECIST v1.1.
AE, adverse event; G, grade; FL-1, FIRELIGHT-1; mo, months; QW, once weekly; PR, partial response; RECIST, response evaluation criteria in solid tumors; SD, stable disease; TRAEs, treatment-related adverse events.

Conclusions

- Early results from the first 3 patients of this ongoing trial showed that tovorafenib:
  - Displayed encouraging antitumor activity in *BRAF*-fusion melanoma
    - 2 PRs* and 1 CR per RECIST v1.1
  - Was generally well tolerated:
    - All TEAEs and TRAEs were G1 or G2
    - As of Feb 8, 2023, all 3 patients remained on tovorafenib with no dose reduction or treatment interruption

*Patient 3 is awaiting a confirmatory scan.
CR, complete response; G, grade; PR, partial response; TEAE, treatment-emergent adverse event; TRAEs, treatment-related adverse events.

References

1. Hutchinson KE, et al. Clin Cancer Res. 2013;19(24):6696-6702.
2. Botton, T. et al. Cell Rep. 2019;29(3):573-588.
3. Sun Y, et al. Neuro Oncol. 2017;19(6):774-785.
4. Okuyama, et al. Ann Oncol. 2017;28(suppl_5): abstr. 4583.
5. Kilburn L, et al. Neuro Oncol. 2022;24(Suppl_7):vii69 and presented poster.
6. Wright K, et al. Neuro Oncol. 2020;22(Suppl 2):i149, and associated presentation.
7. Offer K, et al. Poster P250 presented at: 2021 Connective Tissue Oncology Society Annual Meeting; November 10-13, 2021; Virtual Meeting.

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