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): August 07, 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 2.02 Results of Operations and Financial Condition.

On August 7, 2023, Day One Biopharmaceuticals, Inc. (the "Company") issued a press release announcing its financial results for the quarter ended June 30, 2023. A copy of the press release is attached as Exhibit 99.1 to this report.

Item 7.01 Regulation FD Disclosure.

On August 7, 2023, the Company updated its corporate presentation. A copy of the updated presentation is attached as Exhibit 99.2 to this report.

The information in this Current Report on Form 8-K, including Exhibit 99.1 and Exhibit 99.2 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 and Exhibit 99.2 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 Number	Description
99.1	Press release issued by Day One Biopharmaceuticals, Inc. regarding its financial results for the quarter ended June 30, 2023, dated August 7, 2023.
99.2	Corporate 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, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

DAY ONE BIOPHARMACEUTICALS, INC.

Date: August 7, 2023

By: /s/ Charles N. York II, M.B.A.

Charles N. York II, M.B.A.
Chief Operating Officer and Chief Financial Officer

Day One Reports Second Quarter 2023 Financial Results and Corporate Progress

Results from FIREFLY-1 demonstrate overall response rate (ORR) of 67% and clinical benefit rate (CBR) of 93% in 69 heavily pretreated Response Assessment Neuro-Oncology High-Grade Glioma (RANO-HGG) evaluable patients presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting

Initiated rolling submission of the tovorafenib New Drug Application (NDA) in relapsed or progressive pediatric low-grade glioma (pLGG) in May 2023

The Company expects to complete the rolling submission of the tovorafenib NDA by October 2023

Completed $172.5 million public offering, strengthening balance sheet and extending cash runway into 2026

BRISBANE, Calif., Aug. 7, 2023 – Day One Biopharmaceuticals (Nasdaq: DAWN) ("Day One" or the "Company"), a clinical-stage biopharmaceutical company dedicated to developing and commercializing targeted therapies for people of all ages with life-threatening diseases, today announced its second quarter 2023 financial results and highlighted recent corporate achievements.

"Day One had a remarkable second quarter, with the initiation of the rolling submission of the tovorafenib NDA, followed by an oral presentation at ASCO with updated data that we anticipate will support our regulatory application to the FDA," said Jeremy Bender, Ph.D., chief executive officer of Day One. "The majority of children with relapsed or progressive pLGG need new treatment options. With a strong balance sheet, we believe we are well positioned to achieve our key milestones while working towards expanding our pipeline with other innovative therapies."

Program Highlights

- On June 4, 2023, Day One announced new clinical data from the registrational Phase 2 FIREFLY-1 trial evaluating the investigational agent tovorafenib in relapsed or progressive pLGG in an oral presentation at the 2023 ASCO Annual Meeting. These new data, with a data cutoff of December 22, 2022, included:

  RANO-HGG (n=69) data:
  - 67% (n=46) ORR by RANO-HGG, the primary endpoint of the trial
  - 93% CBR (complete response (CR) + partial response (PR)/unconfirmed partial response (uPR) + stable disease (SD))
    - 6% (n=4) CR
    - 61% (n=42) PR, including 3 uPR
    - 26% (n=18) SD
  - At the time of data cutoff, the median duration of response (DOR) based on RANO-HGG criteria was not yet reached (95% CI: 9.0 months, not estimable)

Among a total of 77 treated patients:

- The median duration of tovorafenib treatment was 10.8 months, with 74% (n=57) of patients on treatment at the time of data cutoff

Safety data, based on the 136 patients treated in both Arm 1 and Arm 2 of FIREFLY-1, indicated monotherapy tovorafenib to be generally well-tolerated. The vast majority of adverse events were Grade 1 or Grade 2, with most common side effects reported related to tovorafenib being change in hair color (71%), fatigue (50%), vomiting (43%), maculopapular rash (41%) and headache (39%). The most commonly reported lab abnormalities were CPK elevation, anemia, hypophosphatemia and AST elevation. Nearly all of the lab abnormalities had no clinical manifestations and did not require clinical intervention or change in study treatment.

The Company also shared the evaluation of responses by Response Assessment in Pediatric Neuro-Oncology Low-Grade Glioma (RAPNO-LGG) and Response Assessment Neuro-Oncology Low-Grade Glioma (RANO-LGG). Those results include:

*RAPNO-LGG data (n=69):

- 51% (n=35) ORR by RAPNO-LGG
  - 25% (n=17) PR including 4 uPR
  - 26% (n=18) minor response (MR) including 4 unconfirmed MR (uMR)
  - 36% (n=25) patients with SD
- The median time to response was 5.5 months for confirmed responses
- At the time of data cutoff, Independent Review Committee (IRC)-assessed median DOR based on confirmed RAPNO-LGG responses is 12 months (95% CI: 11.2, not estimable)

**Pending adjudication*

RANO-LGG (n=76) data:

- 49% (n=37) ORR by RANO-LGG
  - 26% (n= 20) PR including 8 uPR
  - 22% (n= 17) MR including 2 uMR
  - 34% (n=26) patients with SD
- The median time to response was 4.2 months for confirmed responses
- At the time of data cutoff, the IRC-assessed median DOR based on confirmed RANO-LGG responses is 14.4 months (95% CI: 8.4, not estimable)

- Two additional posters were presented on June 5, 2023 during the ASCO Pediatric Oncology session, including a trial-in-progress poster for the FIREFLY-2 trial and a poster describing a healthcare resource utilization study conducted for pLGG patients.

- Day One presented two posters at the 2023 American Society of Pediatric Oncology/Hematology Conference on May 10, 2023, focused on the pLGG burden of illness and healthcare utilization data.

- The pivotal Phase 3 FIREFLY-2/LOGGIC clinical trial evaluating tovorafenib as a front-line therapy in patients aged 6 months to 25 years with pLGG continues to enroll in the United States, Canada, Europe, Australia and Asia, with approximately 100 sites planned.

- Patient enrollment continues in the Phase 1b/2 FIRELIGHT-1 trials evaluating tovorafenib as a monotherapy and as a combination with the Company's investigational MEK inhibitor, pimasertib, in adults and adolescents with relapsed, progressive, or refractory solid tumors harboring MAPK pathway aberrations.

Corporate Highlights and Upcoming Milestones

- In June 2023, Day One announced the successful closing of a public offering including the full exercise of the underwriters' option to purchase additional shares, raising gross proceeds of $172.5 million which strengthens the Company's balance sheet and extends cash runway into 2026.

- The Company anticipates completing the rolling submission of the tovorafenib NDA by October 2023, following submission of an amended clinical study report (CSR) that will include safety and efficacy data from a planned June 2023 data cutoff.

Second Quarter 2023 Financial Highlights

- **Cash Position:** Cash, cash equivalents and short-term investments totaled $442.9 million on June 30, 2023. Based on Day One's current operating plan, management believes it has sufficient capital resources to fund anticipated operations into 2026.

- **R&D Expenses:** Research and development expenses were $32.2 million for the second quarter of 2023 compared to $22.6 million for the second quarter of 2022. The increase was primarily due to additional employee compensation costs, as well as clinical trial and manufacturing activities related to Day One's lead product candidate, tovorafenib.

- **G&A Expenses:** General and administrative expenses were $17.1 million for the second quarter of 2023 compared to $14.2 million for the second quarter of 2022. The increase was primarily due to additional employee compensation costs, as well as the ongoing build-out of commercial capabilities.

- **Net Loss:** Net loss totaled $45.9 million for the second quarter of 2023 with non-cash stock compensation expense of $9.5 million, compared to $36.5 million for the second quarter of 2022 with non-cash stock compensation expense of $5.6 million.

Upcoming Events

- 2023 Wedbush PacGrow Healthcare Conference, August 8-9, 2023

- Morgan Stanley 21st Annual Global Healthcare Conference, September 11-13, 2023

About Tovorafenib

Tovorafenib is an investigational, oral, brain-penetrant, highly-selective type II pan-RAF kinase inhibitor designed to target a key enzyme in the MAPK signaling pathway, which is being investigated in primary brain tumors or brain metastases of solid tumors. Tovorafenib has been studied in over 325 patients to date. Currently tovorafenib is under evaluation in a pivotal Phase 2 clinical trial (FIREFLY-1) among pediatric, adolescent and young adult patients with relapsed or progressive pLGG, which is an area of considerable unmet need with no approved therapies for the vast majority of patients. The pivotal Phase 3 FIREFLY-2/LOGGIC clinical trial is evaluating tovorafenib as a front-line therapy versus standard of care chemotherapy. Tovorafenib is also being evaluated alone or as a combination therapy for adolescent and adult patient populations with relapsed or progressive solid tumors with MAPK pathway aberrations (FIRELIGHT-1).

Tovorafenib has been granted Breakthrough Therapy and Rare Pediatric Disease designations by the U.S. Food and Drug Administration (FDA) for the treatment of patients with pLGG harboring an activating RAF alteration. Tovorafenib has also received Orphan Drug designation from the FDA for the treatment of malignant glioma, and from the European Commission for the treatment of glioma.

About Day One Biopharmaceuticals

Day One Biopharmaceuticals is a clinical-stage biopharmaceutical company that believes when it comes to pediatric cancer, we can do better. We put kids first and are developing targeted therapies that deliver to their needs. Day One was founded to address a critical unmet need: the dire lack of therapeutic development in pediatric cancer. The Company's name was inspired by "The Day One Talk" that physicians have with patients and their families about an initial cancer diagnosis and treatment plan. Day One aims to re-envision cancer drug development and redefine what's possible for all people living with cancer—regardless of age—starting from Day One.

Day One partners with leading clinical oncologists, families, and scientists to identify, acquire, and develop important emerging cancer treatments. The Company's lead product candidate, tovorafenib, is an investigational, oral, brain-penetrant, highly-selective type II pan-RAF kinase inhibitor. The Company's pipeline also includes pimasertib, an investigational, oral, highly-selective small molecule inhibitor of mitogen-activated protein kinases 1 and 2 (MEK-1/-2). Day One is based in Brisbane, California. For more information, please visit www.dayonebio.com or find the Company on LinkedIn or Twitter.

Cautionary Note Regarding Forward-Looking Statements

This press release contains "forward-looking" statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to: Day One's plans to develop cancer therapies, expectations from current clinical trials, the execution of the Phase 2 and Phase 3 clinical trial for tovorafenib as designed, any expectations about safety, efficacy, timing and ability to complete clinical trials, release data results and to obtain regulatory approvals for tovorafenib and other candidates in development, and the ability of tovorafenib to treat pLGG or related indications.

Statements including words such as "believe," "plan," "continue," "expect," "will," "develop," "signal," "potential," or "ongoing" and statements in the future tense are forward-looking statements. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they do not fully materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements.

Forward-looking statements are subject to risks and uncertainties that may cause Day One's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties in this press release and other risks set forth in our filings with the Securities and Exchange Commission, including Day One's ability to develop, obtain regulatory approval for or commercialize any product candidate, Day One's ability to protect intellectual property, the potential impact of global business or macroeconomic conditions, including as a result of inflation, rising interest rates, instability in the global banking system, geopolitical conflicts and the sufficiency of Day One's cash, cash equivalents and investments to fund its operations. These forward-looking statements speak only as of the date hereof and Day One specifically disclaims any obligation to update these forward-looking statements or reasons why actual results might differ, whether as a result of new information, future events or otherwise, except as required by law.

Day One Biopharmaceuticals, Inc.
Consolidated Statements of Operations
(unaudited)
(in thousands, except shares)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	**2022**	**2023**	**2022**
Operating expenses:				
Research and development	$ 32,182	$ 22,560	$ 60,010	$ 37,563
General and administrative	17,072	14,159	35,099	26,904
Total operating expenses	49,254	36,719	95,109	64,467
Loss from operations	(49,254)	(36,719)	(95,109)	(64,467)
Investment income, net	3,406	189	6,872	191
Other expense, net	(15)	—	(19)	(1)
Net loss attributable to common stockholders	(45,863)	(36,530)	(88,256)	(64,277)
Net loss per share, basic and diluted	$ (0.61)	$ (0.60)	$ (1.20)	$ (1.08)
Weighted-average number of common shares used in computing net loss per share, basic and diluted	74,964,878	60,760,527	73,478,567	59,586,529

Day One Biopharmaceuticals, Inc.
Selected Consolidated Balance Sheet Data
(unaudited)
(in thousands)

	June 30, 2023	December 31, 2022
Cash, cash equivalents and short-term investments	$ 442,882	$ 342,269
Total assets	450,756	349,062
Total liabilities	24,702	17,023
Accumulated deficit	(357,924)	(269,668)
Total stockholders' equity	426,054	332,039

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Day One Biopharmaceuticals

Targeted Therapies for People of All Ages

August 2023

Disclaimer

This presentation and the accompanying oral commentary contain forward-looking statements that are based on our management's beliefs and assumptions and on information currently available to our management. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "could," "expect," "plan," anticipate," "believe," "estimate," "predict," "intend," "potential," "would," "continue," "ongoing" or the negative of these terms or other comparable terminology. Forward-looking statements include all statements other than statements of historical fact contained in this presentation, including information concerning our future financial performance, including the sufficiency of our cash, cash equivalents and short-term investments to fund our operations, business plans and objectives, timing and success of our planned nonclinical and clinical development activities, timing and results of nonclinical studies and clinical trials, efficacy and safety profiles of our product candidates, execution of the Phase 2 and Phase 3 clinical trials for tovorafenib and the Phase 1b/2 clinical trial for tovorafenib and pimasertib as designed, any expectations about safety, efficacy, timing and ability to complete clinical trials and to obtain regulatory approvals for tovorafenib and other candidates in development, the ability of tovorafenib to treat pediatric low-grade glioma (pLGG) or related indications, the potential therapeutic benefits and economic value of our product candidates, potential growth opportunities, competitive position, industry environment and potential market opportunities, our ability to protect intellectual property and the impact of global business or macroeconomic conditions, including as a result of inflation, rising interest rates, instability in the global banking system, and geopolitical conflicts, including the war in Ukraine, on our business and operations.

Forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. These factors, together with those that are described under the heading "Risk Factors" contained in our most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission ("SEC") and other documents we file from time to time with the SEC, may cause our actual results, performance or achievements to differ materially and adversely from those anticipated or implied by our forward-looking statements.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Cancer Drug Development For People Of All Ages

Mission That Creates Value

- Day One's mission is to help children with cancer, from day one and every day after
- Develop medicines for genomically-defined cancers
- Establish first-in-class position through rapid pediatric registration
- Expand to adolescent and adult populations in parallel and pursue those opportunities with the same commitment we do for children

Tovorafenib (DAY101) Lead Program

- Investigational, oral, CNS-penetrant Type II RAF inhibitor
- Being developed as tablets and pediatric-friendly liquid suspension
- Breakthrough Therapy Designation
- Rare Pediatric Disease Designation
- Orphan Drug Designation (US/EU)

Growing Portfolio and Runway Beyond Clinical Milestones

- Two clinical-stage MEKi assets, in-licensed for combination trials
- Projected cash runway into 2026
- Key FIREFLY-1 milestones
  - Initiated rolling NDA in May 2023[1]
  - New clinical data presented in June 2023
  - Expected completion of rolling NDA by October 2023 following submission of an amended clinical study report[2]

[1]NDA data set will include analysis of primary (ORR by RANO-HGG) and secondary (ORR by RAPNO-LGG, PFS) efficacy endpoints, safety, and exploratory analyses (including ORR by RANO-LGG).[2]Amended clinical study report will include safety and efficacy data from a planned June 2023 data cutoff.

Our Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Recent & Anticipated Milestones
Tovorafenib (DAY101) Type II Pan-RAF Inhibitor • FDA Breakthrough Therapy Designation for relapsed pLGG • FDA Rare Pediatric Disease Designation (PRV Eligible) for pLGG • FDA Orphan Drug Designation for malignant glioma • EC Orphan Designation for glioma	Relapsed pLGG	FIREFLY-1[1] (pivotal)				**Initiated rolling NDA:** May 2023 **New clinical data presented:** June 2023 **Expected rolling NDA complete:** October 2023
	Frontline pLGG	FIREFLY-2 (pivotal)				**First patient dosed:** March 2023
	RAF-altered solid tumors[2] (monotherapy)	FIRELIGHT-1*				**First patient dosed:** November 2021 **Poster presented:** April 2023
Pimasertib MEK 1/2 Inhibitor	MAPK-altered solid tumors[3] (Combo w/tovorafenib)	FIRELIGHT-1*				**First patient dosed:** May 2022

*Includes patients ≥12 years of age. [1] FIREFLY-1 Arm 1 expected to support registration. [2] DAY101 adult monotherapy Phase 1 dose escalation and expansion trial previously completed. [3] Pimasertib Phase 1 dose escalation and expansion trial previously completed. pLGG, pediatric low-grade glioma. Tovorafenib and Pimasertib are investigational products. Safety and efficacy have not been established by any health authority.

Tovorafenib (DAY101)

Type II RAF Inhibitor

Pediatric Low-Grade Glioma (pLGG): The Most Common Type Of Brain Tumor In Children

PLGGs are chronic and relentless, with patients suffering profound tumor and treatment-associated morbidity that can impact their life trajectory over the long term[6]

A Serious and Life-Threatening Disease

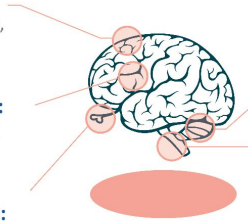
- An estimated 26,000 children/young adults are living with *BRAF*-altered pLGGs in the U.S. today[1,2]
- Surgery plays a significant role in treatment, but 70% of patients require systemic therapy[3,4]
- For the majority of patients in the relapse setting, there is no standard of care and no approved therapies
- ~70% of pLGGs have *BRAF* alterations, of these ~85% are *BRAF* fusions and ~15% are *BRAF* V600E mutations[5]
- Majority of patients have many years of treatment until the tumors typically senesce by their mid-20s

Disease Symptoms[7]

Cerebral gliomas:
Seizures, muscle weakness, behavioral changes

Hypothalamic gliomas:
Endocrine dysfunction and visual deficits

Optic pathway gliomas:
Decreased vision (acuity and/or fields), bulging or misalignment of eyes



Cerebellar gliomas:
Impaired balance, coordination or depth perception

Brain stem gliomas:
Difficulty swallowing or with speech, abnormal breathing

[1] CBTRUS, Qaddoumi et al 2009, Schreck et al 2019, ClearView Analysis; [2] SEER US complete prevalence counts of patients aged under 25 with Brain and Other Nervous Systems tumors as of January 1, 2017. Estimated prevalence are Day One calculations based on publicly available data. [3] Ostrum QT et al., Neuro Oncol. 2015; 16(Suppl 10):x1-x36; [4] De Blank P. et al., Curr Opin Pediatr. 2019 Feb; 31(1):21-27. [5] Jones DTW et al., Cancer Res. 2008; 68:8673–77. [6] Traunwieser T et al., Neurooncol Adv. 2020; 2:vdaa094. [7] Sievert AJ, Fisher MJ. Pediatric low-grade gliomas.*J Child Neurol.* 2009;24(11):1397-1408. doi:10.1177/0883073809342005 .

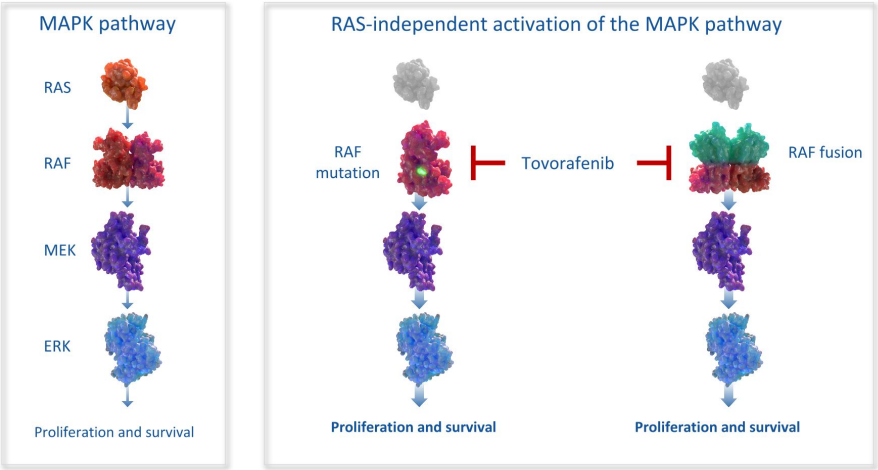
Current Treatments Can Be Disruptive To Childhood and Can Have Significant Long-Term Consequences

Surgery	Chemotherapy	Radiation	Targeted Therapies
• Significant recovery times • Risks of complications • Resection may be limited by location of tumor • Potential for functional deficits based on location of tumor and extend of resection	• Requirement for indwelling catheter and weekly infusions • Neutropenia • Hypersensitivity reactions • Nausea and vomiting • Peripheral neuropathy	• Risk of secondary malignancy • Risk of malignant transformation • Risk of vascular proliferation and stroke • Neurocognitive impact, depending on location of tumor and radiation field	• Rash • Fever • Vomiting • Fatigue • Anemia • Nail infections • Ophthalmologic toxicity • Cardiac toxicity

High unmet need for an effective therapy for the majority of pLGG relapsed or progressive patients that is minimally disruptive to their lives.

Source: 1. Heitzer AM, Raghubar K, Ris MD, et al. Neuropsychological functioning following surgery for pediatric low-grade glioma: a prospective longitudinal study. *J Neurosurg Pediatr.* 2019;1-9. doi:10.3171/2019.9.PEDS19357. 2. Bryant R. Managing side effects of childhood cancer treatment. *J Pediatr Nurs.* 2003;18(2):113-125. doi:10.1053/jpdn.2003.11. 3. Zahnreich S, Schmidberger H. Childhood cancer: occurrence, treatment and risk of second primary malignancies*Cancers (Basel).* 2021;13(11):2607. doi:10.3390/cancers/13112607. 4. National Cancer Institute. Fertility issues in girls and women with cancer. http://www.cancer.gov. Accessed June 13, 2022. 5. Alessi I., Caroleo A.M., de Palma L., Mastronuzzi A., Pro S., Colafati G.S., Boni A., Della Vecchia N., Velardi M., Evangelisti M., et al. Short and Long-Term Toxicity in Pediatric Cancer Treatment: Central Nervous System Damage. Cancers. 2022;14:1540. doi: 10.3390/cancers14061540.

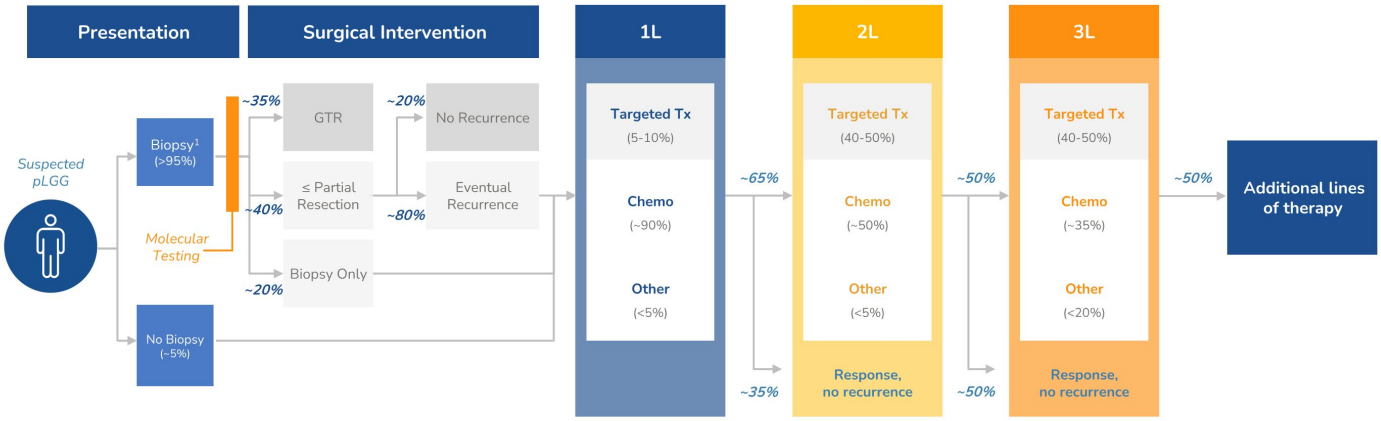
Tovorafenib (DAY101) Inhibits Both BRAF Fusions And BRAF V600 Mutations



- **Tovorafenib (DAY101) is an investigational, oral, selective, CNS-penetrant, type II pan-RAF inhibitor that was designed to inhibit both monomeric and dimeric RAF kinase**
  - Activity in tumors driven by both RAF fusions and BRAF V600E mutations
  - Tablet and pediatric-friendly liquid suspension
  - Once weekly dosing
- **Currently approved type I BRAFi are indicated for use in patients with tumors bearing BRAF V600E mutations**
  - Type I BRAF inhibitors cause paradoxical MAPK activation in the setting of wild-type RAF, increasing the risk of tumor growth in BRAF fusion-driven

Source: 1. Sun Y et al., Neuro Oncol. 2017; 19: 774–85; 2. Sievert AJ et al., PNAS. 2013; 110:5957-62; 3. Karajannis MA et al., Neuro Oncol 2014;16(10):1408-16

The Current pLGG Treatment Paradigm Reflects The Unrelenting Nature Of This Chronic Brain Tumor



Because many pLGGs undergo senescence when patients reach their 20s, the goal of therapy is to **maximize tumor control** while **minimizing treatment-associated toxicities** from surgery, chemotherapy, and radiation. As a result, a large number of pLGG patients will undergo **multiple lines of systemic therapy** over the course of their disease.

Source: Physician Interviews, Bandopadhayay et al. Pediatric Blood Cancer. 2014; Sievert and Fischer. J Child Neurol. 2009; ClearView Analysis. GTR: Gross Total Resection[1]Molecular testing of biopsied samples occurs in all patients. Kandels et. al. Retrospective analysis of comprehensive SIOP registry; Hargrave et. al. Phase I/II;Fangusaro et. al. Phase II

Pivotal Phase 2 Trial Of Monotherapy Tovorafenib (DAY101) In Relapsed Or Progressive pLGG (FIREFLY-1)

Trial Design

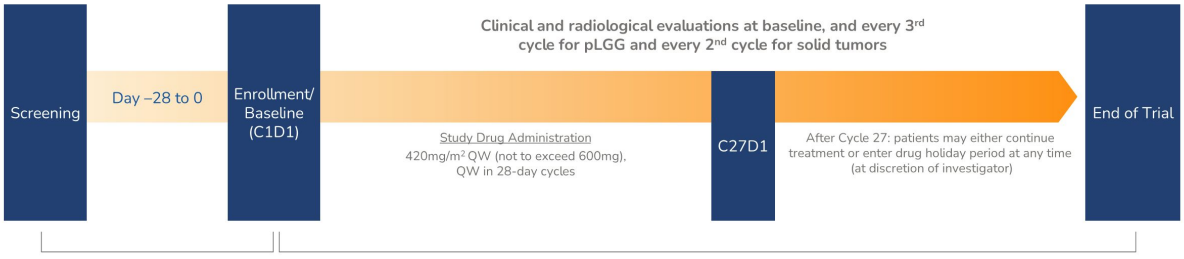
- Three arm, open-label, global registrational phase 2 trial
- **Pivotal Arm 1 (recurrent/progressive pLGG, n=77): harboring a *KIAA1549-BRAF* fusion or *BRAF* V600E mutation**
- Arm 2 (expanded access recurrent/progressive LGG, n=59): harboring an activating *RAF* alteration
- Arm 3 (extracranial solid tumors): harboring an activating *RAF* fusion

Endpoints (Pivotal Arm 1)

- **Primary endpoint: ORR based on RANO-HGG[1], assessed by blinded independent central review**
- Secondary endpoints: ORR by RAPNO-LGG[2] assessed by blinded independent central review; PFS, DoR; TTR, CBR; safety
- Exploratory analyses: ORR and CBR by RANO-LGG[3] assessed by blinded independent central review

Key Inclusion Criteria

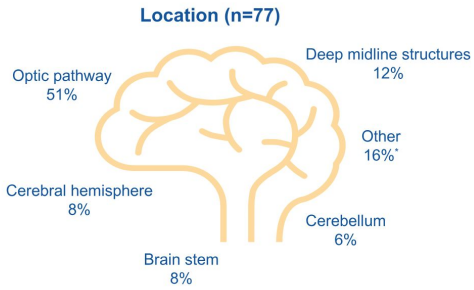
- 6 months – 25 years of age
- *RAF*-altered tumor
- ≥1 prior line of systemic therapy with radiographic progression
- Prior use of MAPK pathway targeted therapy was permitted

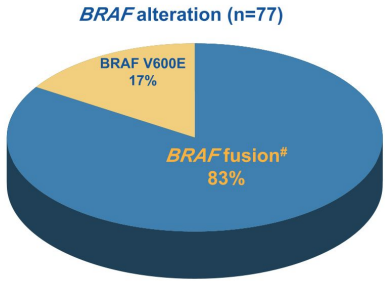


Dec 22, 2022 data cutoff. [1] Wen PY, et al. *J Clin Oncol.* 2010;28(11):1963-1972. [2] Fangusaro J, et al. Lancet Oncol. 2020;21(6):e305–316. [3] van den Bent MJ, et al. Lancet Oncol. 2011;12(6):583-593. Abbreviations: CBR, clinical benefit rate; IRC, independent review committee; C, cycle; D, day; LGG, low-grade glioma; ORR, objective response rate; PFS, progression-free survival; DoR, duration of response; QW, once weekly; TTR, time to response; RANO, Response Assessment in Neuro-Oncology; RAPNO, Response Assessment in Pediatric Neuro-Oncology; MAPK, mitogen-activated protein kinase. For more information, please refer to NCT05475485

FIREFLY-1 Baseline Patient Characteristics

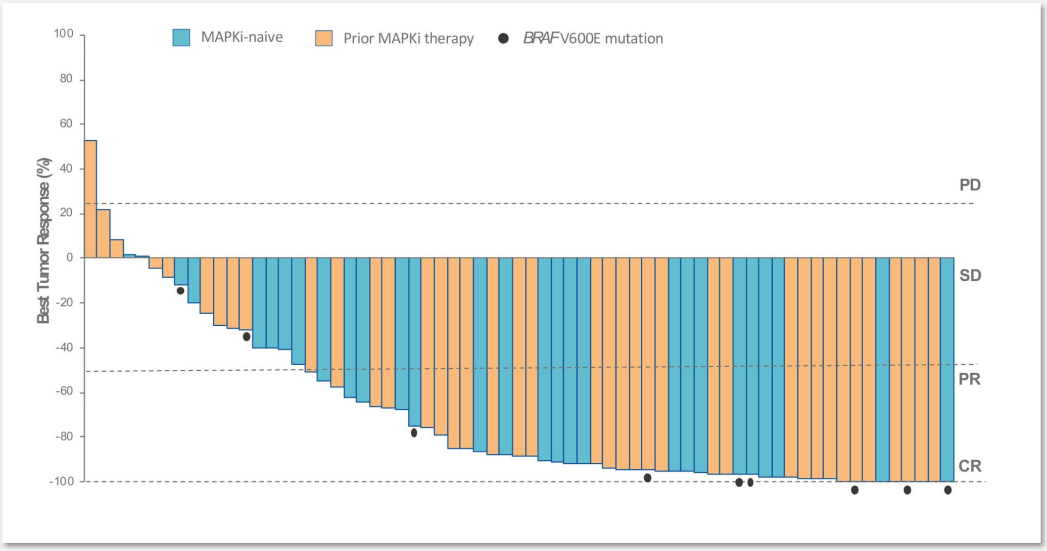
Characteristic	Arm 1 (n=77)
Median age, years (range)	8 (2-21)
Sex, n (%)	
Male	40 (52)
Female	37 (48)
Race, n (%)	
Black or African American	2 (3)
Asian	5 (6)
White	41 (53)
Multiple	3 (4)
Other	6 (8)
Not reported	20 (26)
Number of lines of prior systemic therapy	
Median (range)	2 (1-9)
1, n (%)	18 (23)
2, n (%)	21 (27)
≥3, n (%)	38 (49)
Prior MAPK pathway targeted therapy, n (%)	46 (60)





Dec 22, 2022 data cutoff. *Includes tumors that were extending into multiple regions of the brain, leptomeningeal disease, and/or spinal disease. #Includes 6 patients with BRAF duplication and 2 with BRAF rearrangement per FISH (Fluorescence in situ hybridization) or ISH (in situ hybridization). MAPK, mitogen-activated protein kinase.

Tumor Response To Tovorafenib (DAY101) For All Patients With RANO-HGG Evaluable Lesions (n=69)

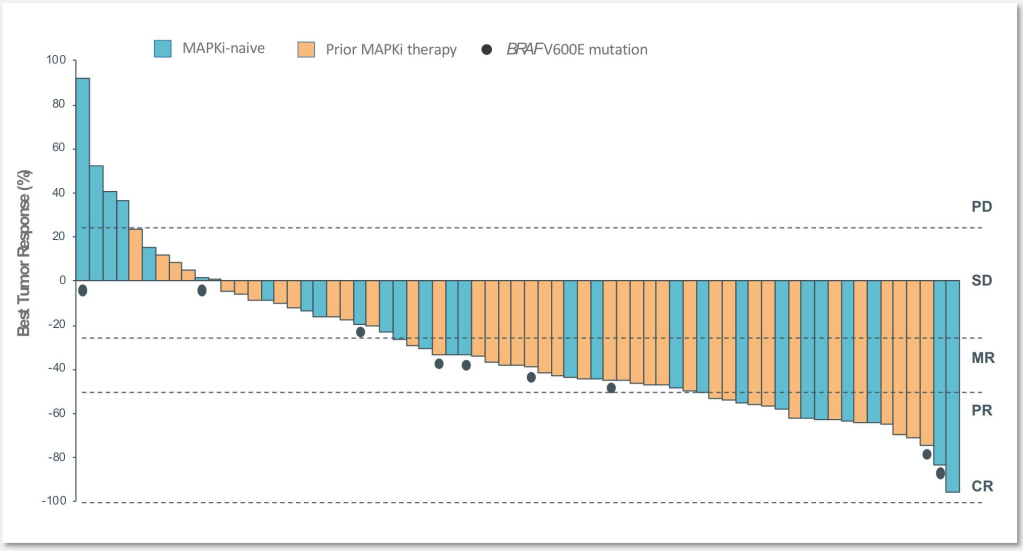


Response (IRC)	RANO-HGG[1] Evaluable n=69
ORR (cCR + cPR + uPR), n (%)	**46 (67%)***
Clinical benefit rate, n (%)	
cCR, cPR/uPR, or SD	64 (93%)
cCR, cPR/uPR, or SD for 12 mo+	49 (71%)
Best overall response, n (%)	
CR	4 (6%)
PR (includes 3 uPR)	42 (61%)
SD	18 (26%)
PD	4 (6%)
Not evaluable	1 (1%)

All 3 patients with uPR remain on treatment as of May 23, 2023

Dec 22, 2022 data cutoff. Percents may not add to 100% due to rounding. Two of 69 patients are not shown in the waterfall plot; one patient passed away due to progressive disease (not related to tovorafenib) before the first imaging assessment and one did not receive T1 Gd+ follow-up imaging. *P<0.001 from two-sided exact binomial test to test null hypothesis of ORR=21% based on Bouffet et al.[2] [1] Wen PY, et al. J Clin Oncol. 2010;28(11):1963-1972. [2] Bouffet E, et al. J Clin Oncol. 2012;30(12):1358-1363. CBR, clinical benefit rate; cCR, confirmed completed response; cPR, confirmed partial response; CR, complete response; HGG, high-grade glioma; IRC, independent radiology review committee; MAPKi, mitogen-activated protein kinase inhibitor; MR, minor response; ORR, overall response rate; PD, progressive disease; PR, partial response; RANO, Response Assessment in Neuro-Oncology; SD, stable disease; uPR, unconfirmed partial response. There are 17 patients with stable disease of less than 12 months duration and at the time of the data cutoff, 11 remain on treatment.

Tumor Response To Tovorafenib (DAY101) For All Patients With RAPNO-LGG Evaluable Lesions (n=69*)

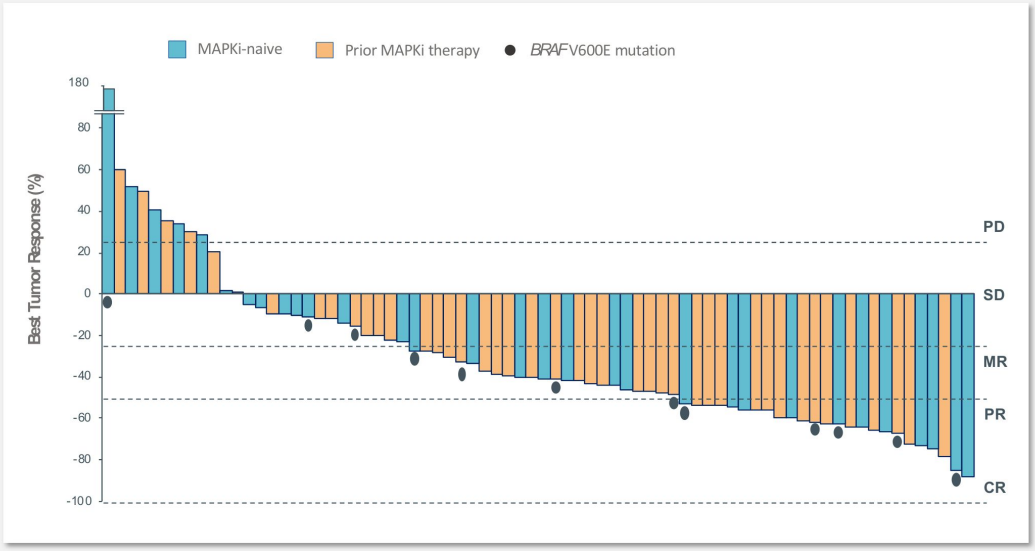


Response (IRC)	RAPNO-LGG[1] Evaluable n=69
ORR (cCR + cPR/uPR + cMR/uMR), n (%)	**35 (51%)**
Clinical benefit rate, n (%)	
cCR, cPR/uPR, cMR/uMR, or SD	60 (87%)
cCR, cPR/uPR, cMR/uMR, or SD for 12mo+	36 (52%)
Best overall response, n (%)	
CR	0 (0%)
PR (includes 4 uPR)	17 (25%)
MR (includes 4 uMR)	18 (26%)
SD	25 (36%)
PD#	8 (12%)
Not evaluable	1 (1%)

All 4 patients with uPR and 3 patients with uMR remain on treatment as of May 23, 2023

Dec 22, 2022 data cutoff. Percents may not add to 100% due to rounding. Two of 69 patients not shown in waterfall plot; one patient passed away due to progressive disease (not related to tovorafenib) before the first imaging assessment and one patient had visual progressive disease but no evaluable T2 measurements at the time of progression. *Pending adjudication. [1] Fangusaro J, et al. Lancet Oncol. 2020;21(6):e305-316. #PD for RAPNO-LGG was not used to determine treatment discontinuation; patients could continue treatment if there was no PD based on RANO-HGG per investigator's assessment. CBR, clinical benefit rate; cCR, confirmed completed response; cMR, confirmed minor response; cPR, confirmed partial response; CR, complete response; HGG, high-grade glioma; IRC, independent radiology review committee; LGG, low-grade glioma; MAPKi, mitogen-activated protein kinase inhibitor; MR, minor response; ORR, overall response rate; PD, progressive disease; PR, partial response; RANO, Response Assessment in Neuro-Oncology; RAPNO, Response Assessment in Pediatric Neuro-Oncology; SD, stable disease; uMR, unconfirmed minor response; uPR, unconfirmed partial response. There are 28 patients with stable disease of less than 12 months duration and at the time of the data cutoff, 11 remain on treatment.

Tumor Response To Tovorafenib (DAY101) For All Patients With RANO-LGG Evaluable Lesions (n=76)

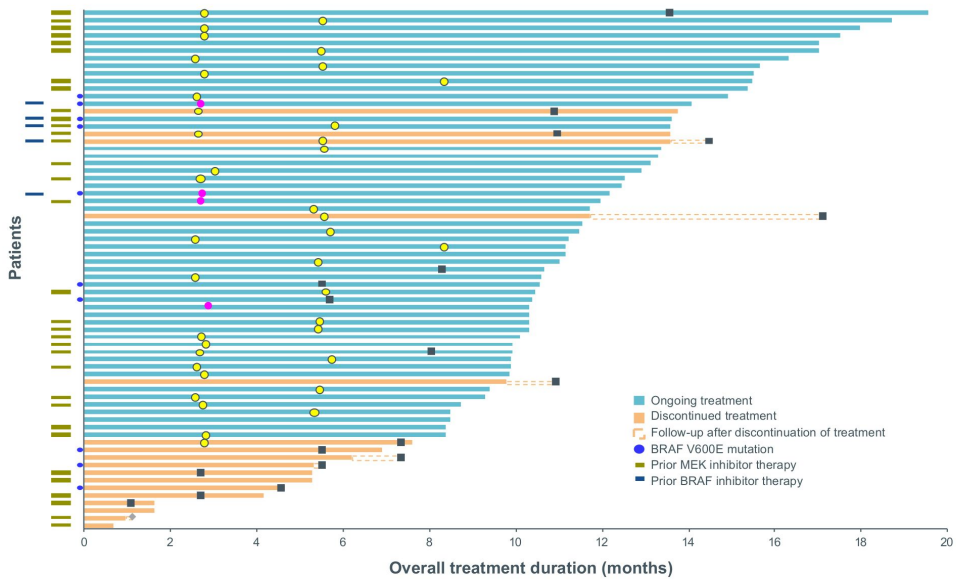


Response (IRC)	RANO-LGG[1] Evaluable n=76
ORR (cCR + cPR/uPR + cMR/uMR), n (%)	**37 (49%)**
Clinical benefit rate, n (%)	
cCR, cPR/uPR, cMR/uMR, or SD	63 (83%)
cCR, cPR/uPR, cMR/uMR, or SD for 12mo+	39 (51%)
Best overall response, n (%)	
CR	0 (0%)
PR (includes 8 uPR)	20 (26%)
MR (includes 2 uMR)	17 (22%)
SD	26 (34%)
PD[#]	11 (14%)
Not evaluable[§]	2 (3%)

All 8 patients with uPR and 2 patients with uMR remain on treatment as of May 23, 2023

Dec 22, 2022 data cutoff. Percents may not add to 100% due to rounding. [#]PD for RANO-LGG was not used to determine treatment discontinuation; patients could continue treatment if there was no PD based on RANO-HGG per investigator's assessment.[§]Two of 76 patients are not shown in the waterfall plot; one patient passed away due to progressive disease (not related to tovorafenib) before the first imaging assessment, and one patient with missing T1 Gd+ imaging at baseline was deemed NE at all timepoints but had a best SPPD decrease of 65% on T2 imaging.[1] van den Bent MJ, et al. *Lancet Oncol.* 2011;12(6):583-593. BL, baseline; CBR, clinical benefit rate; cCR, confirmed completed response; cMR, confirmed minor response; cPR, confirmed partial response; CR, complete response; HGG, high-grade glioma; IRC, independent radiology review committee; LGG, low-grade glioma; MAPKi, mitogen-activated protein kinase inhibitor; MR, minor response; ORR, overall response rate; PD, progressive disease; PR, partial response; RANO, Response Assessment in Neuro-Oncology; SD, stable disease; SPPD, sum of the products of perpendicular diameters; uMR, unconfirmed minor response; uPR, unconfirmed partial response.There are 27 patients with stable disease of ≥12 months duration and at the time of the data cutoff, 19 remain on treatment.

Duration Of Tovorafenib (DAY101) Therapy For All Patients With RANO-HGG Evaluable Lesions (n=69)

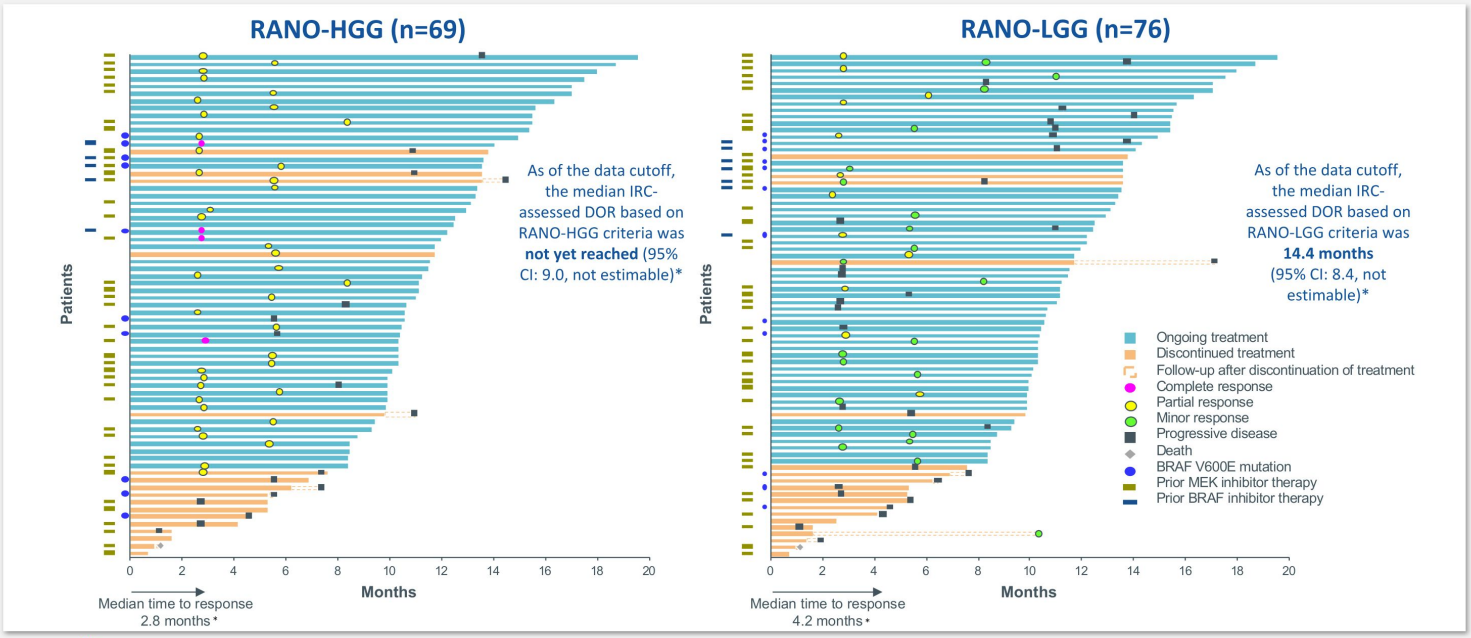


2.8 MONTHS Median time to response*

10.8 MONTHS Median duration of treatment*

* Analysis for median time to response and median duration of treatment only included confirmed responses. HGG, high-grade glioma; RANO, Response Assessment in Neuro-Oncology.

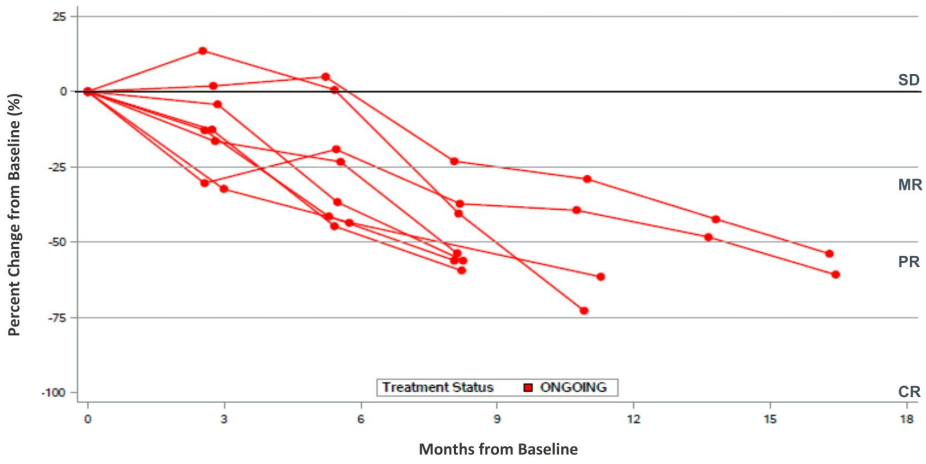
Duration Of Tovorafenib (DAY101) Therapy For All Patients With RANO-HGG & RANO-LGG Evaluable Lesions



* Analysis for median time to response and median duration of response only included confirmed responses. BOR is shown; circles indicate start of response. PD for the purpose of treatment was based on RANO-HGG, not RANO-LGG. BOR, best overall response; HGG, high-grade glioma; LGG, low-grade glioma; PD, progressive disease; RANO, Response Assessment in Neuro-Oncology; DOR, duration of response; CI, confidence interval.

All RANO-LGG Unconfirmed PR Patients Continue On Treatment With Demonstrable Deepening Of Response (n=8)

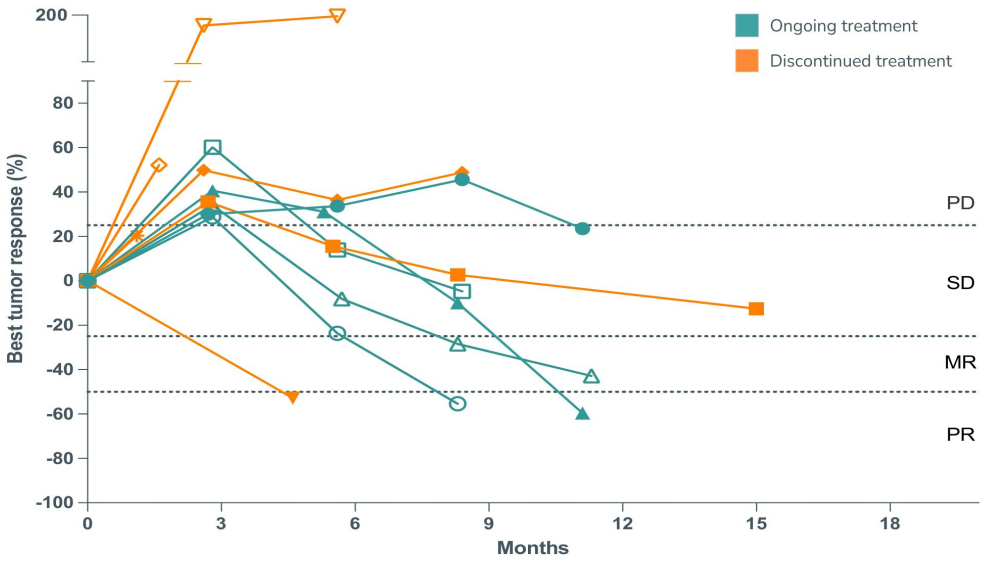
Responses for Patients with Unconfirmed Partial Response by RANO-LGG



All 8 patients with unconfirmed partial response by RANO-LGG remain on treatment as of May 23, 2023

Spider plot for SPPD – baseline and after treatment (RANO-LGG by IRC) – unconfirmed PR patients EOT status based on May 23, 2023 EDC data Individual patient response data is current as of the data cutoff of December 22, 2022; treatment status data is current as of May 23, 2023.

Nearly Half Of Patients With Best Response Of PD By RANO-LGG Have Tumor Stabilization And Response With Continued Treatment (n=11)



5/11 patients with best response of PD by RANO-LGG remain on treatment as of May 23, 2023

Individual patient response data is current as of the data cutoff of December 22, 2022; treatment status data is current as of May 23, 2023.

Tovorafenib (DAY101) Safety Data (n=136)

Preferred term, n (%)	Treatment-emergent AEs		Treatment-related AEs	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any AE	136 (100)	68 (50)	133 (98)	47 (35)
Hair color changes	96 (71)	-	96 (71)	-
Fatigue	68 (50)	4 (3)	54 (40)	4 (3)
Vomiting	59 (43)	3 (2)	24 (18)	3 (2)
Rash maculo-papular	56 (41)	10 (7)	51 (38)	10 (7)
Headache	53 (39)	1 (1)	27 (20)	-
Pyrexia	43 (32)	2 (1)	15 (11)	1 (1)
Nausea	40 (29)	-	21 (15)	-
Dry skin	39 (29)	-	34 (25)	-
Dermatitis acneiform	37 (27)	1 (1)	36 (26)	1 (1)
Constipation	36 (26)	-	28 (21)	-
Decreased appetite	35 (26)	4 (3)	25 (18)	3 (2)
Epistaxis	34 (25)	-	22 (16)	-

- The vast majority of treatment-emergent AEs were Grade 1 or 2
- 39 patients (29%) required dose modifications due to treatment-related AEs
  - Dose interruptions were brief, with the median time of dose interruption being 2 weeks
- 5 patients (4%)* discontinued due to AE, with 4 patients (3%) discontinuing due to treatment-related AEs
- The most commonly reported lab abnormalities were CPK elevation, anemia, hypophosphatemia, and AST elevation
  - Nearly all had no clinical manifestations and did not require clinical intervention or change in study treatment

Dec 22, 2022 data cutoff. Table shows treatment-emergent AEs with frequency ≥25% of any grade.Rash erythematous treatment-emergent: any grade, 14 (10%); grade ≥3 1 (1%); treatment-related: any grade, 14 (10%), grade ≥3 1 (1%). *One patient had 2 events (shunt malfunction [not related to tovorafenib] and tumor hemorrhage [related to tovorafenib]). AEs, adverse events.

Incidence And Prevalence Of BRAF-Altered pLGG In The U.S.

	2020 Estimated Incidence Under 25	2017 Estimated SEER Prevalence Under 25
US Population[1]	~105,000,000	NA
Rate of CNS Tumors (0.00521%)[2]	~5,500	~130,000[3]
Gliomas (63%)[2]	~3,500	~82,000
Low Grade (77%)[2]	~2,600	~63,000
Has Received Drug Tx (58%)[2]	~1,500	~36,000
BRAF Altered (70%)[2]	~1,100	~26,000

~1,100
Estimated Annual Incidence

~26,000
Estimated Prevalence

[1] US Census; [2] CBTRUS, Qaddoumi et al 2009, Schreck et al 2019, ClearView Analysis; [3] SEER US complete prevalence counts of patients aged under 25 with Brain and Other Nervous Systems tumors as of January 1, 2017. Estimated annual incidence and estimated prevalence are Day One calculations based on publicly available data.

Key Takeaways From FIREFLY-1 Data And Next Steps

- Clinically meaningful data from FIREFLY-1 for pediatric patients with recurrent or progressive LGG harboring *BRAF* fusions or *BRAF* V600E mutations
  - 67% ORR and 93% clinical benefit rate by RANO-HGG
  - 51% ORR and 87% clinical benefit rate by RAPNO-LGG*
  - 49% ORR and 83% clinical benefit rate by RANO-LGG
- Responses were observed in patients with either *BRAF* fusion or *BRAF* V600E mutations
- Rapid time to response regardless of response assessment criteria#
- Responses seen in a heavily-pretreated population where the majority of patients relapsed or progressed after one or more prior MAPK inhibitors
- Encouraging safety and tolerability profile indicating monotherapy tovorafenib to be generally well-tolerated

Next Steps

- Expected completion of rolling NDA by October 2023 following submission of an amended clinical study report (CSR)
- CSR will include safety and efficacy data from a planned June 2023 data cutoff

Dec 22, 2022 data cutoff. *Pending adjudication. # Analysis for median time to response only included confirmed responses.

FIREFLY-2/LOGGIC

Pivotal Phase 3 Trial of Tovorafenib (DAY101) in Frontline pLGG

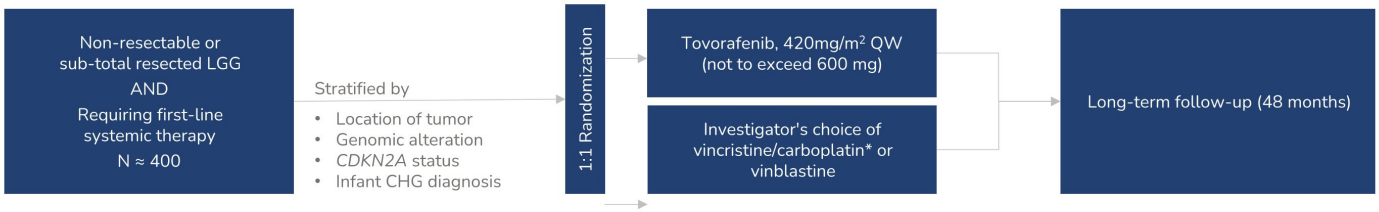
FIREFLY-2/LOGGIC Pivotal Phase 3 Trial Of Tovorafenib (DAY101) In Frontline pLGG

Trial Design

- Randomized, global, registrational Phase 3 trial of monotherapy tovorafenib (DAY101) vs SoC chemotherapy
- Eligibility: Patients aged 6 months to <25 years with LGG harboring a RAF alteration and requiring first-line systemic therapy
- Tovorafenib (DAY101) available as tablets and pediatric-friendly liquid suspension
- Patients who progress after stopping tovorafenib (DAY101) may be re-challenged
- Patients who progress in the SoC arm during or post-treatment may cross-over to receive tovorafenib

Endpoints

- **Primary endpoint: ORR based on RANO-LGG criteria, assessed by blinded independent central review[1]**
  - The ORR primary analysis is expected to occur ~12 months after the last patient randomized
- Key secondary endpoints: PFS and DoR by RANO criteria, ORR by RAPNO criteria
- Other secondary endpoints: changes in neurological and visual function, safety, and tolerability
- Key exploratory objectives: QoL and health utilization measures



* COG or SIOPe-LGG regimen. Abbreviations: CHG, chiasmatic, hypothalamic glioma; DoR, duration of response; LGG, low-grade glioma; ORR, objective response rate; QoL, quality of life; QW, once weekly; SoC, standard of care. [1] Primary endpoint of FIREFLY-2 will be ORR by RANO-LGG (2017) following full approval by FDA on March 16, 2023 of dabrafenib with trametinib in pediatric patients with low-grade glioma with a BRAF V600E mutation who require systemic therapy based on a study with the same primary endpoint.

FIRELIGHT-1

Phase 1b/2 Trials Evaluating Tovorafenib (DAY101) as a Monotherapy and as a Combination with Pimasertib

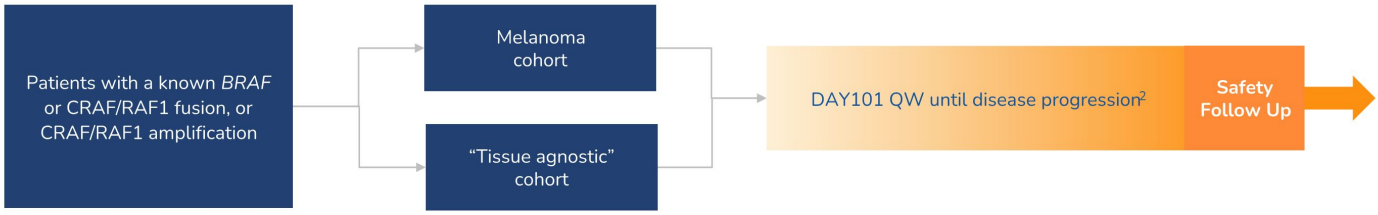
Phase 2 Study Of Monotherapy Tovorafenib (DAY101) In Solid Tumors (FIRELIGHT-1)

Trial Design[1]

- Single arm, open-label, global phase 1b/2a trial
- n = 40 patients (approximately)
- Eligibility: Patients aged 12 years and older with non-hematologic tumor with an activating BRAF fusion, CRAF/RAF1 fusion, or CRAF/RAF1 amplification

Endpoints

- Primary endpoint: ORR by RECIST version 1.1 for non-CNS solid tumors and RANO-HGG criteria for any CNS tumors
- Secondary endpoints: safety and additional efficacy parameters

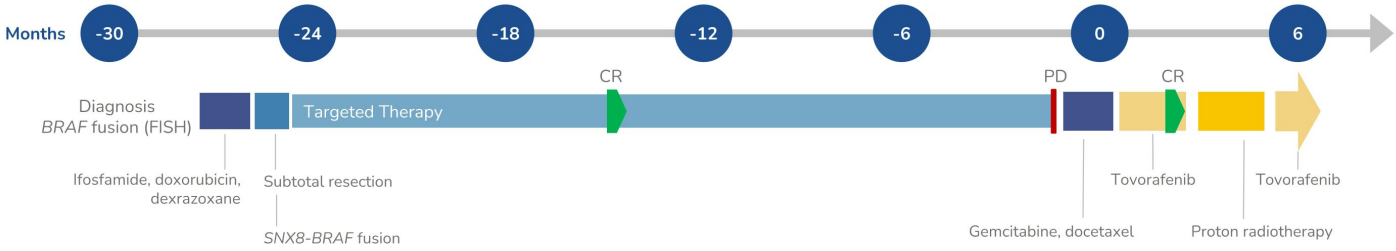


Study Drug Administration
≥ 18 years at 600 mg PO QW
12 to <18 years at 420mg/m² PO QW

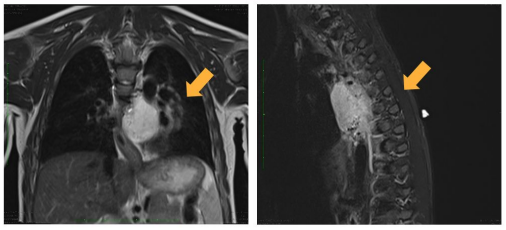
Abbreviations: ORR, objective response rate; QW, once weekly ; PO, by mouth; BRAF, B-Raf proto-oncogene. [1]Umbrella master study – DAY101-102 (main protocol) DAY101 and MAPK pathway aberration, Sub-study 1 monotherapy (DAY101-102a), Sub-study 2 MEK combo (DAY101-102b). [2]DAY101 QW until disease progression, intolerable toxicity, withdrawal of consent, or death

Activity of Tovorafenib (DAY101) In SNX8:BRAF Fusion Spindle Cell Sarcoma

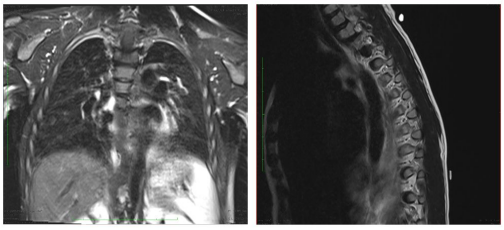
A male child spindle cell sarcoma, 5-years of age at diagnosis



Baseline



After 2 cycles of tovorafenib



- After the first dose of tovorafenib (DAY101), the patient experienced grade 2 rash, which resolved in a day following a dose of diphenhydramine
- Radiotherapy-related adverse events included hyperpigmentation overlying the spine on the upper back with no skin breaks, and mild dysphagia

Pimasertib

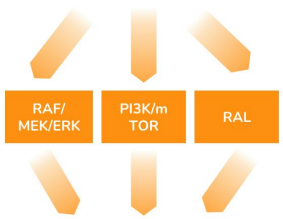
MEK1/2 Inhibitor

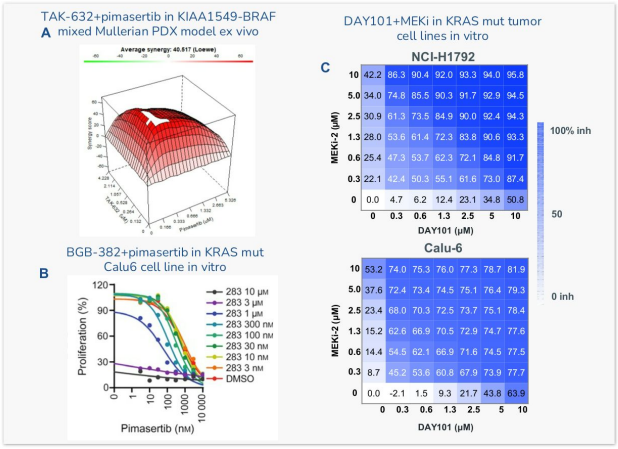
Pimasertib: Investigational Allosteric MEK1/2 Inhibitor With Demonstrated Activity In MAPK-Driven Solid Tumors

- Pimasertib is an investigational orally-bioavailable, selective, non-competitive MEK1/2 inhibitor in-licensed from Merck KGaA in February 2021
- Extensive non-clinical and clinical development work through Phase 2, including a solid tumor trial in Japan and combinations with other MOAs
- Main AEs typical for all in-class allosteric MEK inhibitors (GI, CPK elevation, skin rash, visual disturbances)
- Nearly three-fold higher CNS penetration than other MEKi inhibitors (trametinib or selumetinib)
- Pimasertib showed monotherapy clinical activity, including an improvement in median PFS versus dacarbazine in NRAS mutant melanoma
- Combination with tovorafenib (DAY101) and other targeted therapies may unlock the full value of pimasertib in advanced solid tumors

Sources: Pimasertib Investigator Brochure, v12, 2019; de Gooijer et al., Int J Cancer, 2018; Shaw et al., AACR LB-456, 2012; Lebbe et al., Cancers, 2020.

Vertical MAPK Pathway Inhibition With Tovorafenib (DAY101) And Pimasertib May Unlock Potential Synergy For Adult Solid Tumors

BRAF non-V600 mutant	KRAS or NRAS mutant
	
Proliferation, survival	Proliferation, survival
Type II RAFi + MEKI	Type II RAFi + MEKi
Non V600 BRAF dimers are effectively inhibited by type II RAFi , but not type I BRAFi	Targeting multiple nodes of MAPK pathway will drive deeper and more durable response



A Pan-RAFi + MEKi is synergistic in BRAF fusion melanoma PDX model ex vivo (internal data)

B Sensitivity of KRAS Q61 mutant cells to pimasertib is enhanced when cells are treated with the type II BRAF inhibitor BGB-283 (Yuan et al., Mol Onc 2020)

C Tovorafenib (DAY101) + MEK inhibitor is synergistic in KRAS G12C and Q61 mutant tumor cells (Venetsanakos et al, 2021 AACR poster presentation)

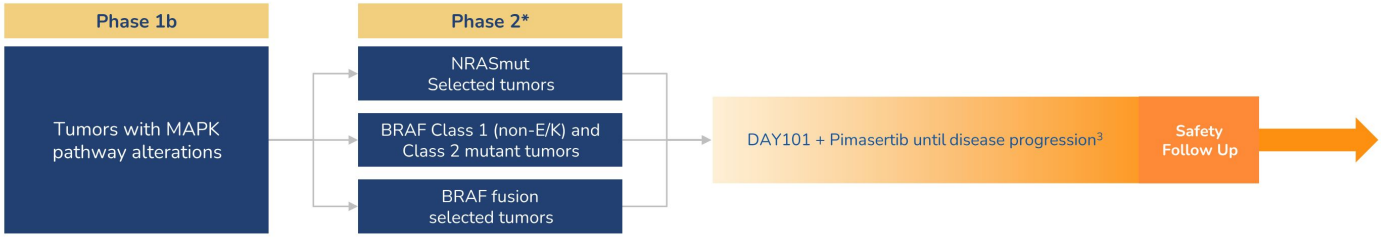
Tovorafenib (DAY101) / Pimasertib Combination To Be Evaluated In Solid Tumors (FIRELIGHT-1)

Trial Design[1]

- Combination dose escalation, global phase 1b/2 trial[2]
- Phase 1b, BOIN (adaptive), n = 10/cohort (approximately)
- Phase 2, Simon 2-stage, n = 25/cohort (approximately)
- Eligibility: Patients aged 12 years and older, dose escalation will be performed in advanced solid tumor patients with any MAPK alteration. Expansion cohorts will focus on indications with a potential path to accelerated approval

Endpoints

- Phase 1b: PK, PD and Safety, MTD/RP2D
- Phase 2: Efficacy (ORR, DOR)



Pre-identified patients with advanced solid tumors and available clinical molecular profiling information.

*Additional biomarker-selected cohorts may be pursued based on developing data

Abbreviations: BOIN, Bayesian Optimal Interval Design; BRAF, B-Raf proto-oncogene, serine/threonine kinase; MAPK, mitogen-activated protein kinase; NRAS, neuroblastoma rat sarcoma viral oncogene.
[1]Umbrella master study – DAY101-102 (main protocol) DAY101 and MAPK pathway aberration, Sub-study 1 monotherapy (DAY101-102a), Sub-study 2 MEK combo (DAY101-102b).
[2]Intend to open U.S. and ex-U.S. clinical sties. [3]DAY101 + Pimasertib until disease progression, intolerable toxicity, withdrawal of consent, or death

Summary

Financial Summary: DAWN

Cash, cash equivalents and short-term investments as of June 30, 2023: $442.9 million (no debt)	~87.0 million shares of common stock outstanding as of August 1, 2023

$ Millions	Six Months Ended 6/30/23	Six Months Ended 6/30/22
R&D Expense	$60.0	$37.6
G&A Expense	$35.1	$26.9
Net Loss	$88.3	$64.3

Projected cash runway into 2026

FIREFLY-1: Pivotal Phase 2 clinical trial of tovorafenib (DAY101)

- Initiated rolling NDA[1] in May 2023
- New clinical data presented in June 2023
- Expected completion of rolling NDA by October 2023 following submission of an amended clinical study report[2]

FIREFLY-2/LOGGIC: Pivotal Phase 3 clinical trial of tovorafenib (DAY101) in newly diagnosed pLGG

- First patient dosed in March 2023

All financial and share information is unaudited. [1]NDA data set will include analysis of primary (ORR by RANO-HGG) and secondary (ORR by RAPNO, PFS) efficacy endpoints, safety, and exploratory analyses (including ORR by RANO-LGG). [2]Amended clinical study report will include safety and efficacy data from a planned June 2023 data cutoff.

Next Steps

FIREFLY-1
- Initiated rolling NDA in May 2023
- New clinical data presented in June 2023
- Expected completion of rolling NDA byOctober 2023 following submission of an amended clinical study report[1]

FIREFLY-2
- Advance tovorafenib as a frontline therapy for patients with pLGG

FIRELIGHT-1
- Evaluate tovorafenib in combination and as monotherapy in adolescent and adult populations
- Monotherapy abstract presented at EADO in April 2023

Commercial
- Continue investment in market and launch preparation activities

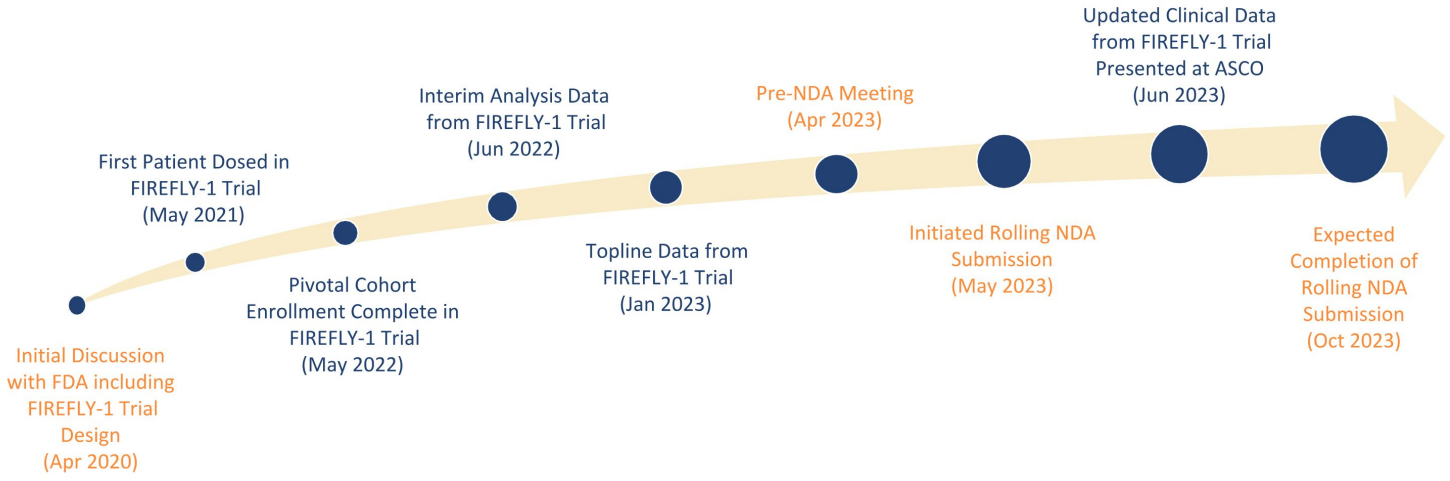
Business Development
- Further investment in business development activities to expand our multiple asset portfolio

[1]Amended clinical study report will include safety and efficacy data from a planned June 2023 data cutoff.

Appendix

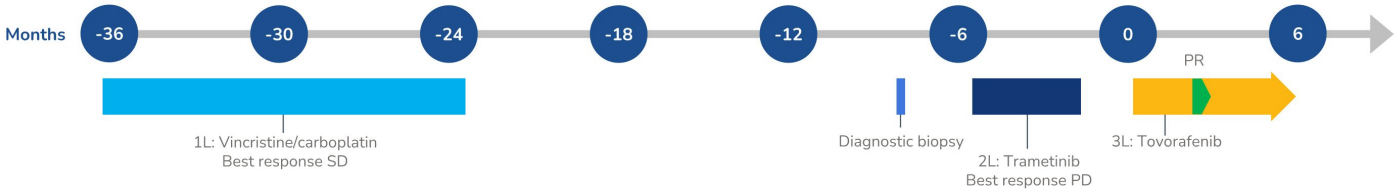
Day One
BIOPHARMACEUTICALS

Progress Of FIREFLY-1 Program: Monotherapy Tovorafenib In Relapsed pLGG

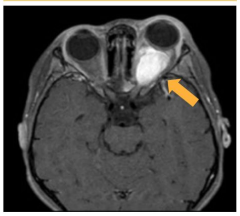
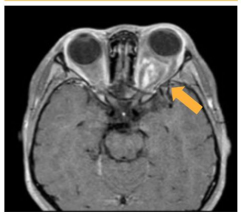
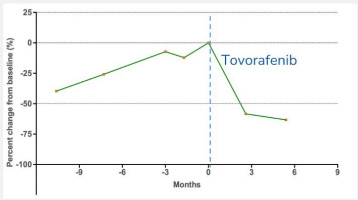


Case Study: Activity Of Tovorafenib (DAY101) In KIAA1549-BRAF Fusion Optic Pathway Glioma

A 7-years-old female child with an optic pathway glioma, with very poor vision, entropion, folliculitis, eczema, mouth ulceration and xerosis



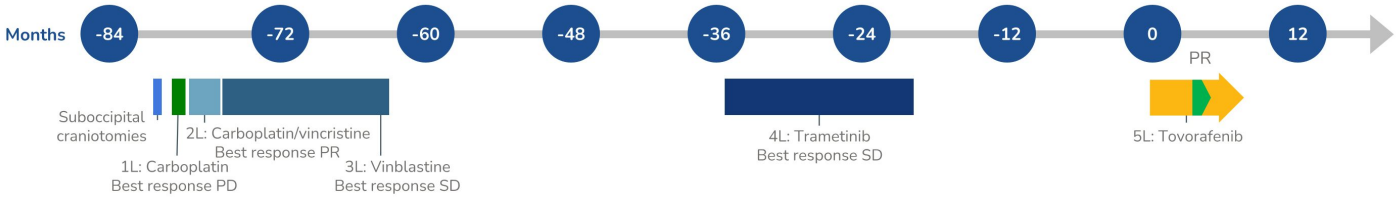
- PR (-58%) and improvement in vision reported at cycle 3
- AEs included grade 3 erythematous rash requiring dose interruption and dose reduction (400 mg QW to 300 mg QW in cycle 1), and grade 2 eczema and maculopapular rash
- Patient continues to receive weekly tovorafenib

Baseline	After 6 cycles	Tumor kinetics (RANO)
		

Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

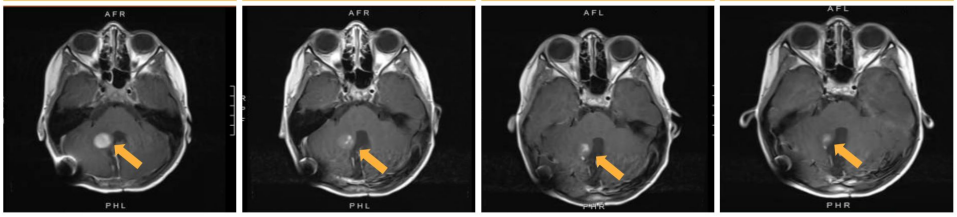
Case Study: Activity Of Tovorafenib (DAY101) In KIAA1549-BRA Fusion Posterior Fossa Pilocytic Astrocytoma

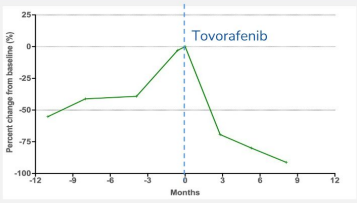
An 8-years-old female child with a posterior fossa pilocytic astrocytoma, eczema, nausea and constipation



- PR (-69%) at cycle 3 with 500 mg QW tovorafenib, with a deepening of response (80% and 91% in cycles 6 and 9, respectively) over time
- AEs included grade 2 decrease in neutrophil count, pustular rash, and upper respiratory infection
- Patient continues to receive weekly tovorafenib

Baseline	After 3 cycles	After 6 cycles	After 9 cycles	Tumor kinetics



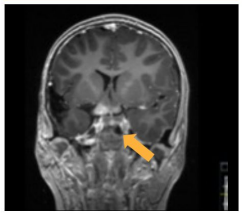
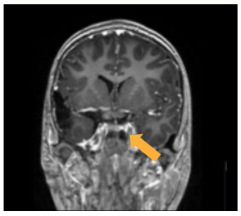
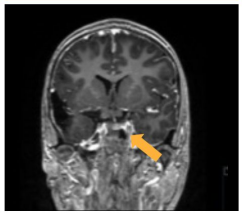
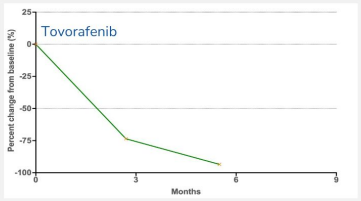


Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

Case Study: Activity Of Tovorafenib (DAY101) In BRAF V600E Mutation Deep Midline Astrocytoma

A 9-year-old female child with deep midline BRAF V600E-mutant astrocytoma with precocious puberty

- PR (-74%) at cycle 3, with a deepening of response (-94%) at cycle 6
- AEs included grade 3 maculopapular rash and increased CPK, requiring drug interruption and dose reduction (500 mg QW to 400 mg QW in cycle 1)
- Tovorafenib dose was re-escalated back to 500 mg QW in cycle 4; patient continues on treatment

Baseline	After 3 cycles	After 6 cycles	Tumor kinetics
			

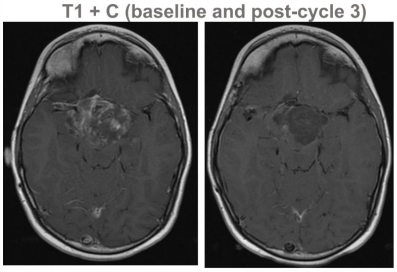
Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

Case Study: Activity Of Tovorafenib (DAY101) In KIAA1549-BRAF Fusion Optic Pathway Glioma

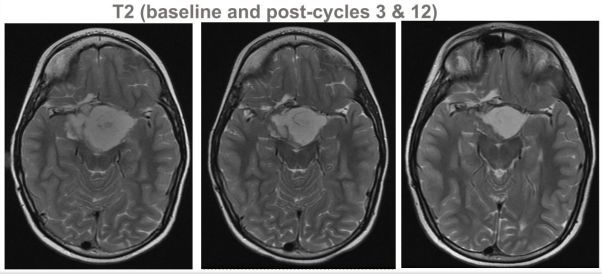
8-year-old boy with relapsed pilomyxoid astrocytoma of the optic pathway, with visual loss in right eye, visual field loss in left eye, fatigue, intermittent nausea/vomiting, intermittent headaches, anorexia, and temperature regulation disorder

- Initiated treatment with tovorafenib 400 mg/QW following 3 prior therapies, including binimetinib and trametinib, which were discontinued due to PD
- At cycle 3, PR (-88%) per RANO-HGG, and MR (-32% and -40%) per RAPNO-LGG and RANO-LGG, respectively
  - Sustained improvements in visual acuity reported; logMAR change 0.2 → 0
  - PD criteria met (-94% to -91%) with RANO-HGG at cycle 15; continued treatment as investigator deemed no radiographic progression with subsequent reduction in target lesion (-97%)
- AEs were G2 (drug eruption, elevated CPK) and G1 (hair color change, paronychia, growth retardation)

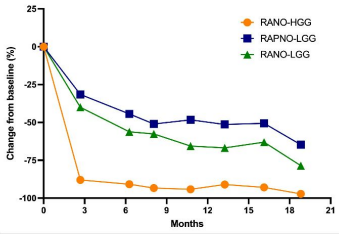
T1 + C (baseline and post-cycle 3)



T2 (baseline and post-cycles 3 & 12)



Tumor kinetics



Dec 22, 2022, data cut-off. AEs, adverse events; C, contrast; CPK, creatine phosphokinase; G, grade; HGG, high-grade glioma; LGG, low-grade glioma; logMAR, Logarithm of the Minimum Angle of Resolution;MR, minor response; PD, progressive disease; PR, partial response; QW, once weekly; RANO, Response Assessment in Neuro-Oncology; RAPNO, Response Assessment in Pediatric Neuro-Oncology; VC, vincristine-carboplatin..

FIREFLY-2/LOGGIC: Pivotal Phase 3 Study Of Tovorafenib (DAY101) In Newly Diagnosed pLGG

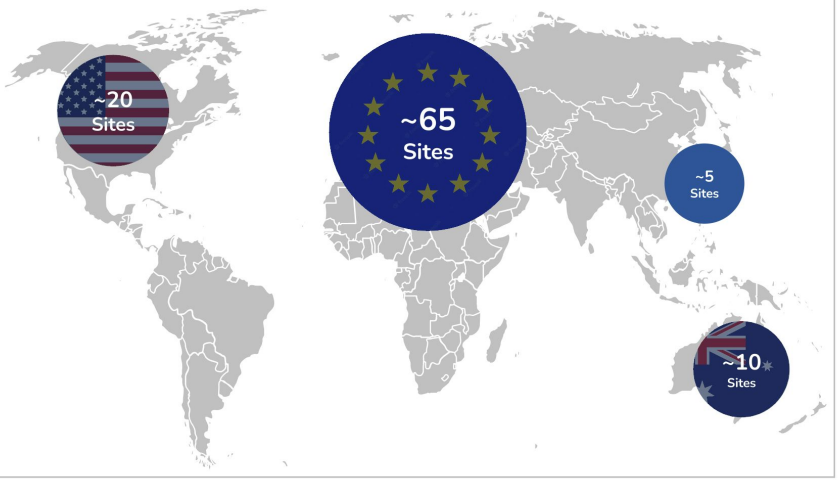
- **Collaboration between Day One and the LOGGIC consortium, internationally recognized experts in pLGG research**
  - Coupled with the LOGGIC-CORE molecular diagnostic program
  - Worked jointly on the study design and discussions with the U.S. and EU regulatory authorities

LOGGIC EUROPE

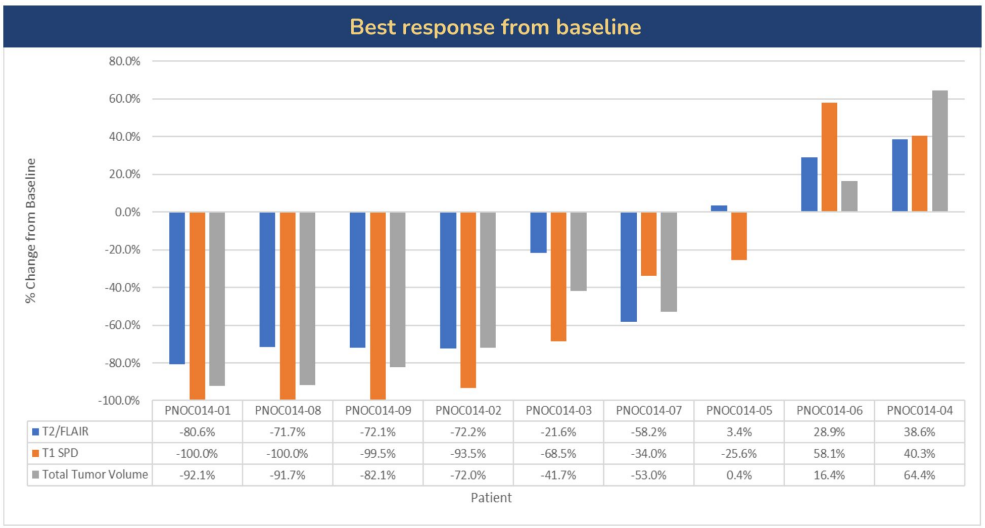
LOGGIC: LOw Grade Glioma In Children

KiTZ Hopp Children's Cancer Center Heidelberg | German Cancer Research Center (DKFZ) Heidelberg University Hospital Heidelberg University

Approximately 100 potential sites (~65 from the LOGGIC consortium)



Results From Independent Radiology Review Of PNOC014



	PNOC014-01	PNOC014-08	PNOC014-09	PNOC014-02	PNOC014-03	PNOC014-07	PNOC014-05	PNOC014-06	PNOC014-04
T2/FLAIR	-80.6%	-71.7%	-72.1%	-72.2%	-21.6%	-58.2%	3.4%	28.9%	38.6%
T1 SPD	-100.0%	-100.0%	-99.5%	-93.5%	-68.5%	-34.0%	-25.6%	58.1%	40.3%
Total Tumor Volume	-92.1%	-91.7%	-82.1%	-72.0%	-41.7%	-53.0%	0.4%	16.4%	64.4%

RANO-HGG: Response assessment for neuro-oncology-high grade glioma

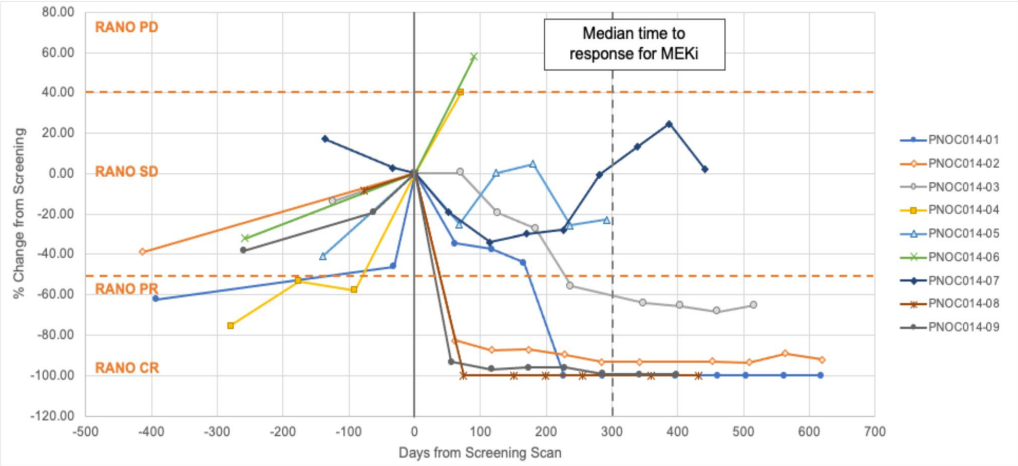
Volumetric image analysis (exploratory)

RAPNO: Response assessment for pediatric neuro-oncology (exploratory)

Date of data cutoff: 02 JAN 2020
Wright K et. al. Neuro Oncology Abstract CTNI-19. 2020

Multiple Rapid, Deep And Durable Responses Observed Following Initiation Of Tovorafenib (DAY101) Treatment Of pLGG Patients In PNOC014

Growth kinetics of Target Lesions from Screening



Date of data cutoff: 02 JAN 2020
Adapted from Wright K et. al. Neuro Oncology Abstract CTNI-19. 2020
Fangusaro J et al. Lancet Oncol 2019

Drug-related Adverse Events Observed for Tovorafenib (DAY101) in PNOC014 Showed Favorable Safety and Tolerability Profile in pLGG

DAY101 AE summary

- Most common toxicity: skin
- AEs reversible and all manageable
- Single, reversible Grade 3 event
- No Grade 4 AEs
- No dose reductions (vs. 40% of patients on selumetinib montherapy required dose reductions)

Drug-related AEs for Tovorafenib (DAY101)

Toxicities	Grade 1-2	Grade 3	Grade 4
Anemia	6 (67%)		
Hypophosphatemia	4 (44%)		
Fatigue	5 (55%)		
Rash	8 (89%)		
Achromotrichia	7 (78%)		
Pruritis	6 (67%)		
Photosensitivity	1 (11%)		
Nevus	7 (78%)		
Alopecia	3 (34%)		
Epistaxis	2 (22%)		
Dry skin	3 (34%)		
Myalgias/arthralgias	3 (34%)		
Anorexia	2 (22%)		
Cheilitis	3 (34%)		
Hypermagnesemia	1 (11%)		
Bleeding gums	1 (11%)		
Increased AST	4 (44%)		
Nausea/vomiting	3 (33%)		
CPK elevation		1 (11%)	
Weight loss	2 (22%)		

Drug-related AEs for selumetinib

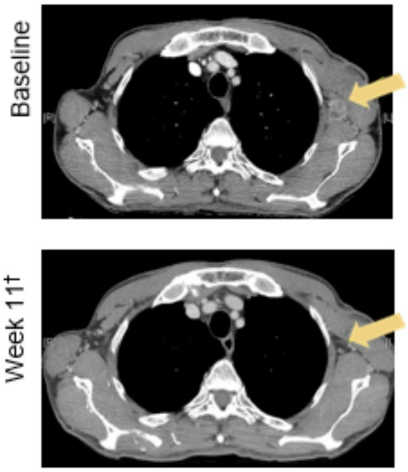
Toxicities	Grade 1-2	Grade 3	Grade 4
Increased ALT	20 (40%)	1 (2%)	
CPK elevation	34 (68%)	5 (10%)	
Diarrhea	27 (54%)	2 (4%)	
Decreased ejection fraction	19 (38%)	1 (2%)	
Gastric haemorrhage		1 (2%)	
Headache	14 (28%)	1 (2%)	
Decreased lymphocyte count	19 (38%)		1 (2%)
Neutropenia	14 (28%)	3 (6%)	
Paronychia	19 (38%)	3 (6%)	
Rash (acneiform)	29 (58%)	2 (4%)	
Rash (maculopapular)	26 (52%)	5 (10%)	
Skin infection	7 (14%)	1 (2%)	
Tooth infection		1 (2%)	
Weight gain	5 (10%)	1 (2%)	
Vomiting	22 (44%)		
Nausea	21 (42%)		
Increased AST	25 (50%)		
Anemia	28 (56%)		
Pruritis	10 (20%)		
Dyspnea	30 (60%)		

Date of DAY101 data cutoff: 02 JAN 2020; Wright K et. al. Neuro Oncology Abstract CTNI-19. 2020; Fangusaro J et al. Lancet Oncol 2019

Preliminary Clinical Activity Of Tovorafenib (DAY101) Monotherapy In *BRAF* Fusion Melanoma

Patient 1: 53-year-old male with AGK-*BRAF* fusion non-spitzoid cutaneous melanoma

Parameter	Description/outcome
Stage at diagnosis	III
EGOC status	0
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)

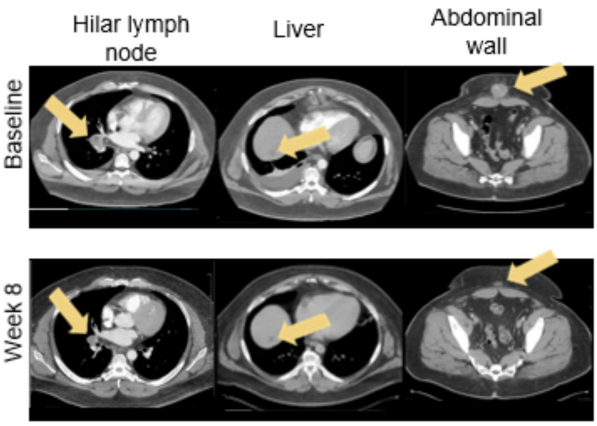


*Data cutoff Feb 8, 2023. †Out of window per protocol. ‡per RECIST v1.1. AE, adverse event; CR, complete response; ECOG, Eastern Cooperative Oncology Group; FL-1, FIRELIGHT-1; G, grade; QW, once weekly; RECIST, response evaluation criteria in solid tumors; SD, stable disease; TEAE, treatment-emergent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

Preliminary Clinical Activity Of Tovorafenib (DAY101) Monotherapy In *BRAF* Fusion Melanoma

Patient 2: 35-year-old male with TRIM33-BRAF fusion malignant melanoma

Parameter	Description/outcome
Stage at diagnosis	Unknown
EGOC status	1
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)

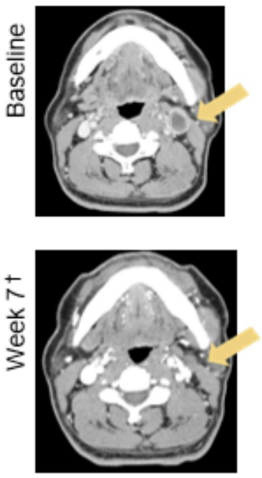


*Data cutoff Feb 8, 2023. †per RECIST v1.1. AE, adverse event; ECOG, Eastern Cooperative Oncology Group; FL-1, FIRELIGHT-1; G, grade; mo, months; PD, progressive disease; PR, partial response; QW, once weekly; RECIST, response evaluation criteria in solid tumors; TRAEs, treatment-related adverse events; y/o, years of age.

Preliminary Clinical Activity Of Tovorafenib (DAY101) Monotherapy In *BRAF* Fusion Melanoma

Patient 3: 71-year-old male with MKRN1-BRAF fusion non-spitzoid cutaneous melanoma

Parameter	Description/outcome
Stage at diagnosis	II
EGOC status	0
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; ECOG, Eastern Cooperative Oncology Group; FL-1, FIRELIGHT-1; G, grade; mo, months; PR, partial response; QW, once weekly; RECIST, response evaluation criteria in solid tumors; SD, stable disease; TRAEs, treatment-related adverse events; y/o, years of age.