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): May 01, 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 May 1, 2023, Day One Biopharmaceuticals, Inc. (the "Company") issued a press release announcing its financial results for the quarter ended March 31, 2023. A copy of the press release is attached as Exhibit 99.1 to this report.

Item 5.02 Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

On May 1, 2023, the Company announced the appointment of Dr. Samuel Blackman, the Company's Co-founder and current Chief Medical Officer, to the position of Head of Research and Development of the Company, effective as of May 1, 2023.

Biographical information for Dr. Blackman may be found in the Company's definitive proxy statement relating to its 2023 Annual Meeting of Stockholders, filed with the U.S. Securities and Exchange Commission (the "SEC") on April 28, 2023.

The Company previously entered into a change-in-control and severance agreement with Dr. Blackman. The form of the change-in-control and severance agreement was previously filed with the SEC as Exhibit 10.2 to the Company's Annual Report on Form 10-K for the year ended December 31, 2021 on March 7, 2022 and is incorporated by reference herein.

There are no arrangements or understandings between Dr. Blackman and any other persons, pursuant to which he was appointed as Head of Research and Development, no family relationships among any of the Company's directors or executive officers and Dr. Blackman and he has no direct or indirect material interest in any transaction required to be disclosed pursuant to Item 404(a) of Regulation S-K.

Item 7.01 Regulation FD Disclosure.

On May 1, 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 March 31, 2023, dated May 1, 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: May 1, 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 First Quarter 2023 Financial Results and Corporate Progress

FIREFLY-1 clinical abstract selected for oral presentation at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting

Leadership team strengthened with executive appointments in clinical development and commercialization

Pre-New Drug Application (NDA) meeting held April 19, 2023 with U.S. Food and Drug Administration (FDA) for tovorafenib (DAY101) for relapsed or progressive pediatric low-grade glioma (pLGG)

Company to host conference call on June 4th at 6:00 PM CT

BRISBANE, Calif., May 1, 2023 – Day One Biopharmaceuticals (Nasdaq: DAWN), a clinical-stage biopharmaceutical company dedicated to developing and commercializing targeted therapies for people of all ages with life-threatening diseases, today announced its first quarter 2023 financial results and highlighted recent corporate achievements.

"We are excited about our upcoming milestones, including the opportunity to share new clinical data from the FIREFLY-1 trial in an oral presentation at ASCO," said Jeremy Bender, Ph.D., chief executive officer of Day One. "We are also thrilled to announce the appointment of two industry veterans to Day One's executive leadership team. Lauren Merendino will join as Chief Commercial Officer and Dr. Raphaël Rousseau will join as Chief Medical Officer. Paired with the promotion of our co-founder Dr. Samuel Blackman to Head of Research and Development, these key appointments will help shape our future and contribute to long-term value creation for the company."

Program Highlights

- On April 26, 2023, Day One announced new clinical data from the ongoing, open-label, pivotal Phase 2 FIREFLY-1 trial evaluating the investigational agent tovorafenib in relapsed or progressive pLGG will be presented on June 4, 2023, as an oral presentation at the 2023 ASCO Annual Meeting. An ASCO abstract scheduled for release on May 25, 2023 will include topline data from FIREFLY-1 as of September 28, 2022, while new detailed clinical data will be highlighted at the June 4, 2023 oral presentation.

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

- On April 19, 2023, Day One held a pre-NDA meeting with the FDA for tovorafenib for the treatment of patients with relapsed or progressive pLGG. The company remains in position to initiate the submission of the NDA as early as the second quarter of 2023.

- On April 20, 2023, Day One presented a poster titled “Clinical Activity of the Type II pan-RAF Inhibitor Tovorafenib in BRAF-fusion Melanoma” at the 19th European Association of Dermato-Oncology (EADO) Congress demonstrating initial antitumor activity in relapsed/refractory adult BRAF-fusion in the ongoing FIRELIGHT-1 study (NCT04985604).

- In March 2023, Day One dosed the first patient in its pivotal Phase 3 FIREFLY-2/LOGGIC clinical trial evaluating tovorafenib as a frontline therapy for patients newly diagnosed with pLGG.

- 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

- Samuel C. Blackman, MD, PhD, co-founder and former Chief Medical Officer (CMO), has been promoted to Head of Research and Development. In this role, he will lead the direction of Day One’s overall scientific research and development strategy. Dr. Blackman co-founded Day One and has served as CMO since November 2018. Under his leadership, the company has advanced its lead product candidate tovorafenib into a Phase 2 registrational trial in relapsed or progressive pLGG, a Phase 3 frontline trial in newly diagnosed pLGG and expanded development into evaluating tovorafenib as a monotherapy and as a combination with the investigational MEK inhibitor, pimasertib.

- Lauren Merendino, MBA, will lead Day One’s commercial organization as Chief Commercial Officer (CCO) and will focus on finalizing preparations for the commercial launch of tovorafenib and bringing commercial perspective to key company decisions. Ms. Merendino has over 25 years of commercial experience, building and leading commercial teams through multiple product launches, including both oncology and pediatric rare diseases. Most recently, she was the CCO at Myovant Sciences where she oversaw the successful launch of 2 products across 3 indications in less than 2 years. Previously, she was the VP of Neurological Rare Diseases at Genentech where she led a cross-functional team to launch a new treatment for spinal muscular atrophy, a pediatric rare disease, where the product ultimately became a new standard of care.

- Raphaël Rousseau, MD, PhD, is appointed Chief Medical Officer (CMO) and will focus on executing and expanding Day One’s clinical development programs. Dr. Rousseau was previously the CMO at Neogene Therapeutics and Gritstone Bio. Dr. Rousseau has more than 25 years of global oncology drug development experience and specifically, pediatric oncology clinical trial design. During his long tenure at Roche and Genentech, Dr. Rousseau built a team solely dedicated to developing innovative treatments for children with cancer, led or co-led the pediatric development and registration of bevacizumab, rituximab and capecitabine, and

initiated the pediatric development of cobimetinib and atezolizumab in close collaboration with European and North American academic pediatric oncology consortiums.

Fourth Quarter and Full Year 2022 Financial Highlights

- **Cash Position:** Cash, cash equivalents and short-term investments totaled $318.2 million on March 31, 2023. Based on Day One's current operating plan, management believes it has sufficient capital resources to fund anticipated operations into 2025.

- **R&D Expenses:** Research and development expenses were $27.8 million for the first quarter of 2023 compared to $15.0 million for the first quarter of 2022. The increase was primarily due to additional employee compensation costs, as well as clinical trial and pre-commercial manufacturing activities related to Day One's lead product candidate, tovorafenib.

- **G&A Expenses:** General and administrative expenses were $18.0 million for the first quarter of 2023 compared to $12.7 million for the first quarter of 2022. The increase was primarily due to additional employee compensation costs, an ongoing commercial buildout, and professional service expenses to support company growth.

- **Net Loss:** Net loss totaled $42.4 million for the first quarter of 2023 with non-cash stock compensation expense of $9.4 million, compared to $27.7 million for the first quarter of 2022 with non-cash stock compensation expense of $6.2 million.

Upcoming Events

- Day One will present two posters at the 2023 American Society of Pediatric Oncology/Hematology (ASPHO) Conference May 10-13, 2023, focused on the pLGG burden of illness and healthcare utilization data.

- 2023 American Society of Clinical Oncology (ASCO) Annual Meeting, June 2-6, 2023
    - To join the Company's conference call and webcast on Sunday, June 4, 2023, at 6:00 PM CT, participants can access the conference call live via webcast from the Investors & Media page of Day One's website.

- Goldman Sachs 44th Annual Global Healthcare Conference, June 12-15, 2023

- Clinical data from the FIREFLY-1 study have been accepted as an oral presentation at the Society for Neuro-Oncology (SNO) 7th Biennial Pediatric Neuro-Oncology Research Conference from June 23-24, 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. 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 (DAY101) has also received Orphan Drug designation from the FDA for the treatment of malignant glioma, and from the European Commission (EC) 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. 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 the COVID-19 pandemic, inflation and rising interest rates 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)

	Three Months Ended March 31,	
	2023	2022
Operating expenses:		
Research and development	$ 27,828	$ 15,003
General and administrative	18,027	12,745
Total operating expenses	45,855	27,748
Loss from operations	(45,855)	(27,748)
Investment income, net	3,466	2
Other income (expense), net	(4)	(1)
Net loss attributable to common stockholders	(42,393)	(27,747)
Net loss per share, basic and diluted	$ (0.59)	$ (0.48)
Weighted-average number of common shares used in computing net loss per share, basic and diluted	71,972,888	58,382,444

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

	March 31, 2023	December 31, 2022
Cash, cash equivalents and short-term investments	$ 318,179	$ 342,269
Total assets	323,563	349,062
Total liabilities	23,148	17,023
Accumulated deficit	(312,061)	(269,668)
Total stockholders' equity	300,415	332,039

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Day One Biopharmaceuticals

Targeted Therapies for People of All Ages

May 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 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 clinical trial 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 pan-RAF inhibitor
- Being studied 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 2025
- Upcoming key FIREFLY-1 milestones
  - Pre-NDA meeting held on April 19, 2023
  - Remain in position to initiate the NDA submission in Q2 2023
  - Presentation of new clinical data in oral presentation at ASCO conference

[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).

Our Pipeline

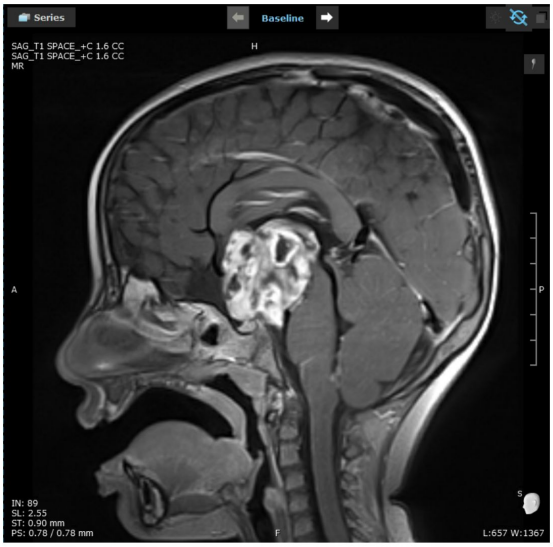
Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Recent & Anticipated Milestones
Tovorafenib (DAY101) Type II Pan-RAF Inhibitor ✓ FDA Breakthrough Therapy Designation for relapsed pLGG ✓ FDA Rare Pediatric Disease Designation (PRV Eligible) for pLGG ✓ FDA Orphan Drug Designation for malignant glioma ✓ EC Orphan Designation for glioma	Relapsed pLGG	FIREFLY-1[1] (pivotal)				**Pre-NDA meeting held:** April 19, 2023 **Remain in position to initiate NDA submission:** Q2 2023 **New clinical data presentation planned:** June 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 Pan-RAF Inhibitor

Pediatric Low-Grade Gliomas (pLGG)

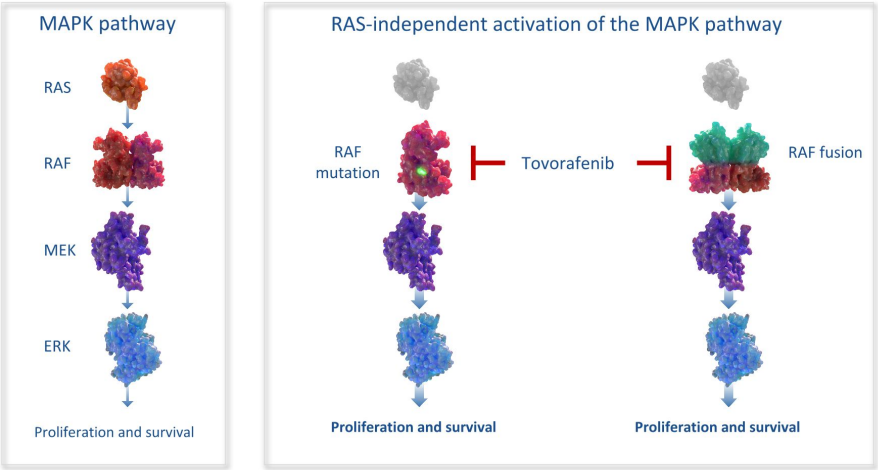


6 y/o with large relapsed BRAF fusion-positive optic pathway glioma

- **Despite being the most common brain tumor in children, there are no approved agents and no standard-of-care for the majority of patients with relapsed/progressive disease[1,2]**
  - ~70% of patients will require systemic therapy
  - Patients have a high rate of recurrence and are frequently treated with multiple lines of systemic therapy over the course of their disease
- **The majority of pLGGs are driven by BRAF alterations[3]**
  - ~85% of BRAF-altered tumors harbor a *KIAA1549-BRAF* gene fusion
  - ~15% are driven by BRAF V600E mutation
- **Despite low-grade histology and high long-term survival, pLGGs are chronic and relentless[1-4]**
  - Goal of therapy is to stabilize or shrink tumors while minimizing treatment-associated toxicities from surgery, chemotherapy, and radiation
  - Many patients today suffer profound tumor and treatment-associated morbidity and significant late effects that persist throughout life

1. Ostrum QT et al., Neuro Oncol. 2015; 16(Suppl 10):x1-x36; 2. De Blank P. et al., Curr Opin Pediatr. 2019 Feb; 31(1):21-27. 3. Jones DTW et al., Cancer Res. 2008; 68:8673–77. 4. Traunwieser T et al., Neurooncol Adv. 2020; 2:vdaa094;

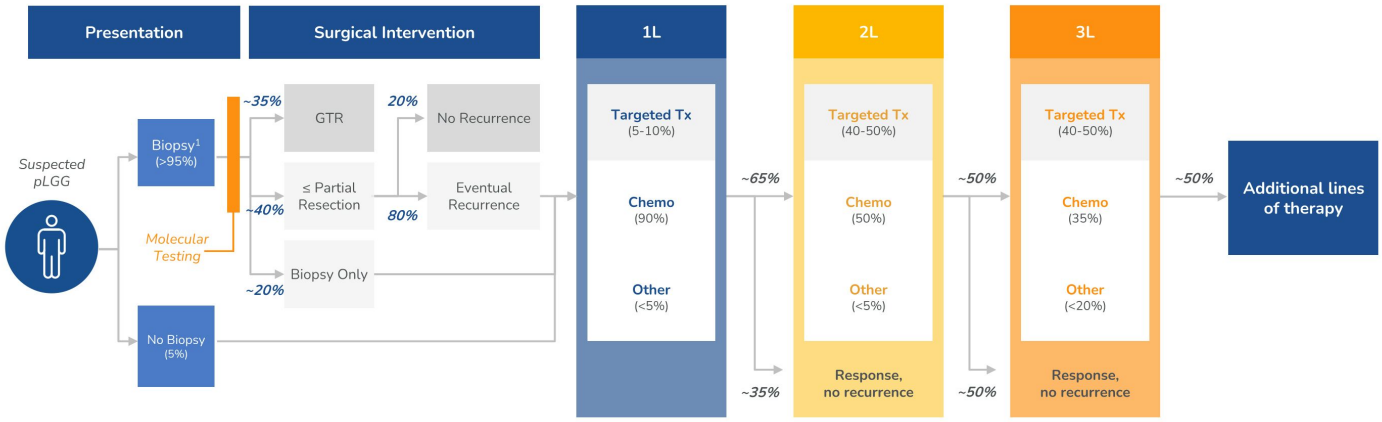
Tovorafenib (DAY101) Inhibits Both BRAF Fusions and BRAF V600 Mutations



- **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

1. Sun Y et al., Neuro Oncol. 2017; 19: 774–85; 2. Sievart 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

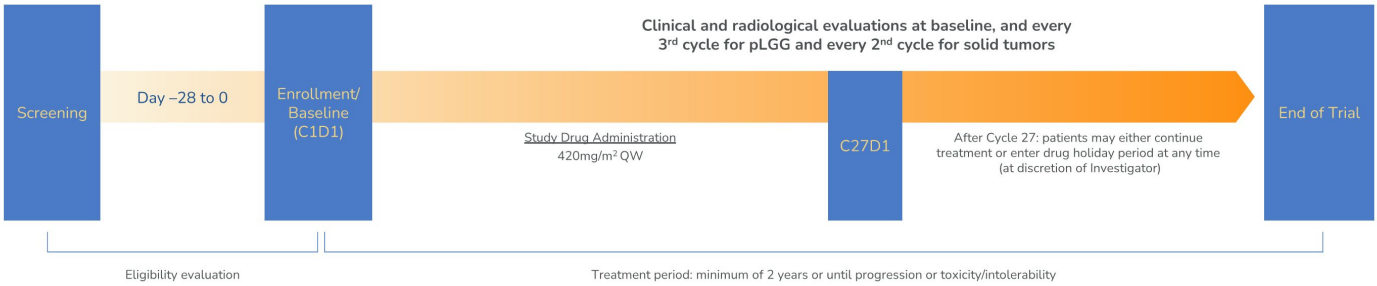
Pivotal Phase 2 Trial Of Monotherapy Tovorafenib (DAY101) in Relapsed or Progressive pLGG (FIREFLY-1)

Trial Design

- Three arm, open-label, global registrational phase 2 trial
- **Pivotal Arm 1 (recurrent/progressive pLGG): n=69 RANO-evaluable patients aged 6 months to 25 years harboring a *KIAA1549-BRAF* fusion or BRAF V600 mutation**
- Arm 2 (expanded access recurrent/progressive LGG): patients aged 6 months to 25 years harboring an activating RAF alteration
- Arm 3 (extracranial solid tumors): patients aged 6 months to 25 years harboring an activating RAF fusion

Endpoints (Pivotal Arm 1)

- **Primary endpoint: ORR based on RANO-HGG criteria, assessed by blinded independent central review**
- Secondary endpoints: ORR by RAPNO criteria; PFS; safety
- Exploratory analyses: ORR by RANO-LGG

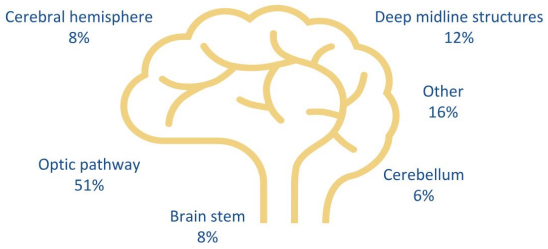


Abbreviations: C, cycle; D, day; LGG, low-grade glioma; ORR, objective response rate; PFS, progression-free survival. RANO-HGG, response assessment for neuro-oncology-high grade glioma
NCT04775485

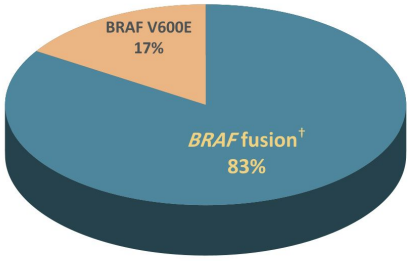
FIREFLY-1 Baseline Patient Characteristics

Characteristic	Topline Data Arm 1 (N=77)
Median age, years (range)	8 (2-21)
BRAF alteration, n (%) BRAF V600E BRAF Fusion†	 13 (17) 64 (83)
Median number of lines of prior therapy (range)	3 (1-9)
Prior MAPK pathway targeted therapy, n (%) Yes No	 46 (60) 31 (40)
Geography, n (%) U.S. Ex-U.S.	 27 (35) 50 (65)

Location (n=77)



BRAF alteration (n=77)



Sep 28, 2022 data cutoff. †Includes 8 patients with BRAF duplication or BRAF rearrangement. MAPK, mitogen-activated protein kinase; prior MAPK pathway targeted therapy indicates either prior MEKi and/or prior type I RAFi therapy.

Topline Data from Ongoing Pivotal Phase 2 FIREFLY-1 Trial

The primary endpoint of the FIREFLY-1 trial is overall response rate (ORR) by Response Assessment for Neuro-Oncology-High Grade Glioma (RANO-HGG) criteria as assessed by blinded independent central review. In the 69 RANO-evaluable patients:

- 64% ORR and 91% clinical benefit rate (complete response + partial response/unconfirmed partial response + stable disease)
  - 4% (n=3) confirmed complete responses
  - 59% (n=41) partial responses (31 confirmed and 10 unconfirmed)
  - 28% (n=19) patients with stable disease
- 86% (n=59) of patients had a BRAF fusion alteration, for which there are no approved systemic therapies, while the remaining 14% (n=10) had a BRAF mutation

Safety data, based on 77 treated patients, indicated monotherapy tovorafenib to be generally well-tolerated.

- The most common side effects reported as related to tovorafenib were change in hair color (75%), increased creatine phosphokinase (64%), anemia (46%), fatigue (42%) and maculopapular rash (42%)
- 3 patients (3.9%) discontinued treatment due to adverse events, of which 2 (2.6%) were deemed to be related to tovorafenib

Among a total of 77 treated patients:

- Participants were heavily pretreated, with a median of three prior lines of systemic therapy (range: 1-9)
- The median duration of tovorafenib treatment was 8.4 months, with 77% (n=59) of patients on treatment at the time of the data cutoff
- Nearly 60% (n=46) of patients had already received at least one prior MAPK inhibitor prior to study participation

Sep 28, 2022 data cutoff. CR, complete response. PR, partial response. SD, stable disease.

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.

FIREFLY-2/LOGGIC

Pivotal Phase 3 Trial of Tovorafenib (DAY101) in Newly Diagnosed pLGG

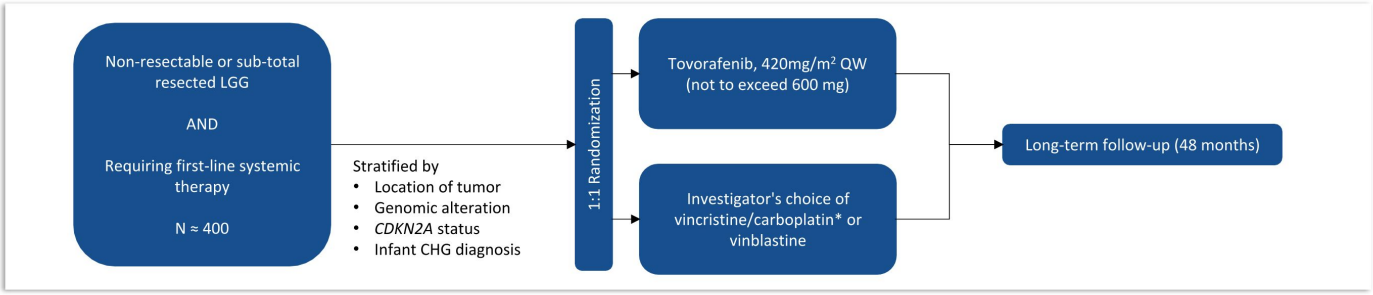
FIREFLY-2/LOGGIC Pivotal Phase 3 Trial of Tovorafenib (DAY101) in Newly Diagnosed pLGG

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.

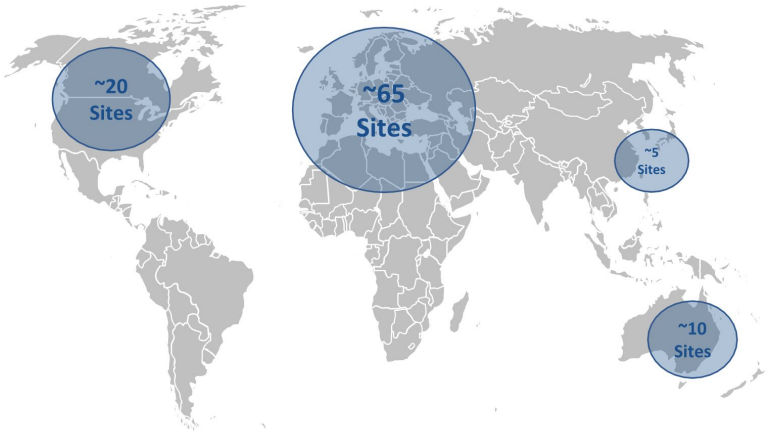
FIREFLY-2/LOGGIC: Pivotal Phase 3 Study Of Tovorafenib (DAY101) In Newly Diagnosed pLGG

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

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



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)			**Pre-NDA meeting held:** April 19, 2023 **Remain in position to initiate NDA submission:** Q2 2023 **New clinical data presentation planned:** June 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.

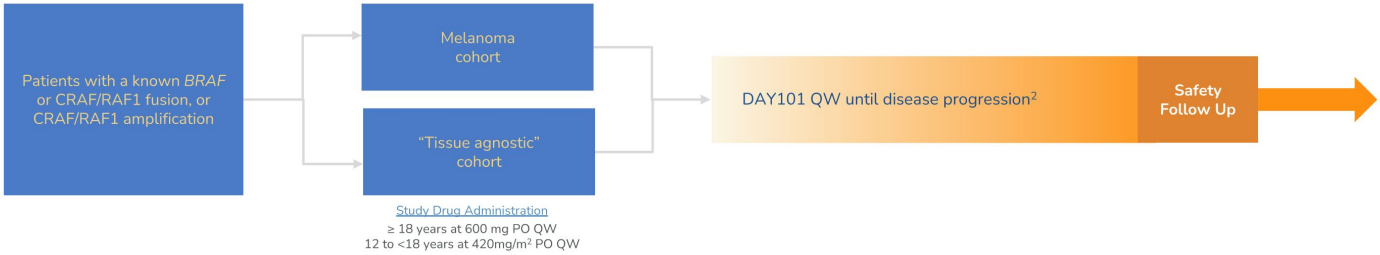
Phase 2 Study of Monotherapy Tovorafenib (DAY101) in Solid Tumors (FIRELIGHT-1)

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



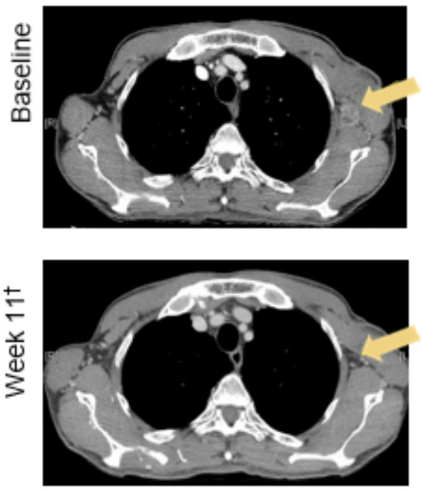
Abbreviations: ORR, objective response rate; QW, once weekly ; PO, by mouth; BRAF, B-Raf proto-oncogene.
1. Umbrella master study – DAY101-102 (main protocol) DAY101 and MAPK pathway aberration, Sub-study 1 monotherapy (DAY101-102a), Sub-study 2 MEK combo (DAY101-102b).
2. DAY101 QW until disease progression,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

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 *BRAF* Fusion Melanoma

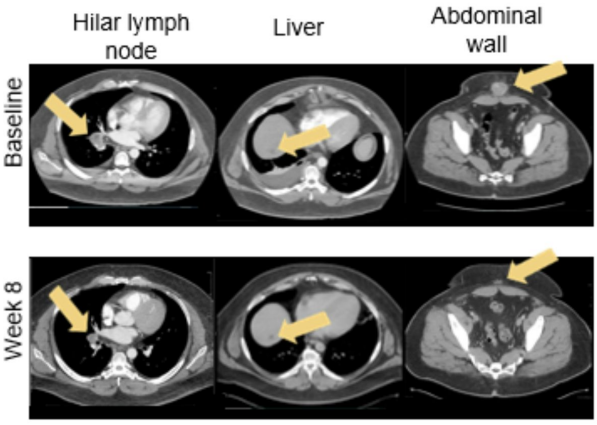
Patient 2: 35-year-old male with TRIM33-*BRAF* fusion malignant melanoma

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.

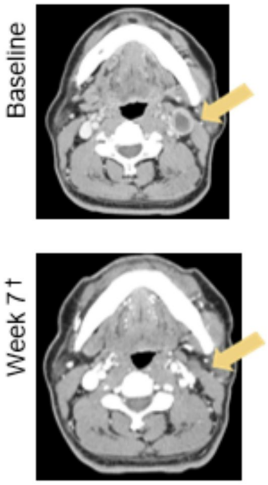
AE, adverse event; ECOG, Eastern Cooperative Oncology Group; FL-1, FIRELIGHT-1; G, grade; mo, months; PD, progressive disease; PR, partial response; QW, once weekly; RECIST, response evaluation criteria in solid tumors; TRAEs, treatment-related adverse events; y/o, years of age.

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)

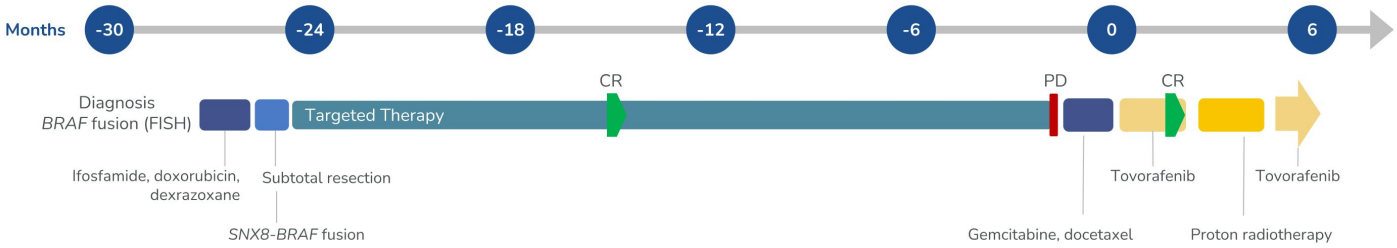


*Data cutoff Feb 8, 2023. †In window per protocol. ‡per RECIST v1.1.

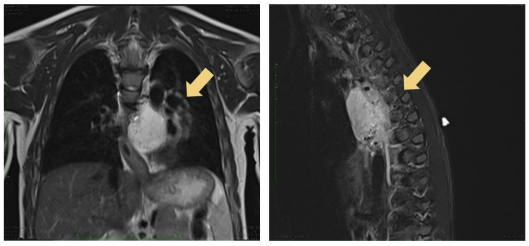
AE, adverse event; ECOG, Eastern Cooperative Oncology Group; FL-1, FIRELIGHT-1; G, grade; mo, months; PR, partial response; QW, once weekly; RECIST, response evaluation criteria in solid tumors; SD, stable disease; TRAEs, treatment-related adverse events; y/o, years of age.

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

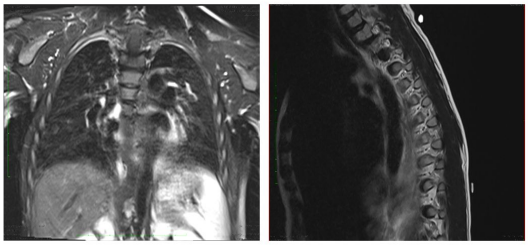
A male child spindle cell sarcoma, 5-years of age at diagnosis



Baseline



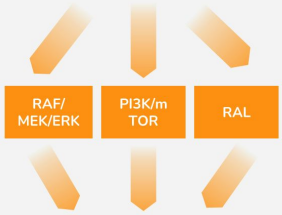
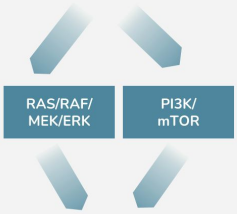
After 2 cycles of tovorafenib



- 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

Data cut off: September 30, 2021

Strong Scientific Rationale for Combining Tovorafenib (DAY101) with Additional MAPK Pathway Inhibitors

	BRAF non-V600	BRAF or CRAF fusion	KRAS or NRAS mutant	NF1 LOF
Signaling pathways	 Proliferation, survival	 Proliferation, survival	 Proliferation, survival	 Proliferation, survival
Potential combinations	Type II RAFi + MEKi or SHP2i	Type II RAFi + MEKi	Type II RAFi + KRAS - G12Ci or MEKi or SHP2i	Type II RAFi + MEKi
Rationale	Non V600 BRAF dimers are effectively inhibited by type II, but not type I, RAFi	BRAF fusion dimers are effectively inhibited by type II, but not type I RAFi	Targeting multiple nodes of MAPK pathway will drive deeper and more durable response	Targeting multiple pathways will drive deeper response

Pimasertib

MEK1/2 Inhibitor

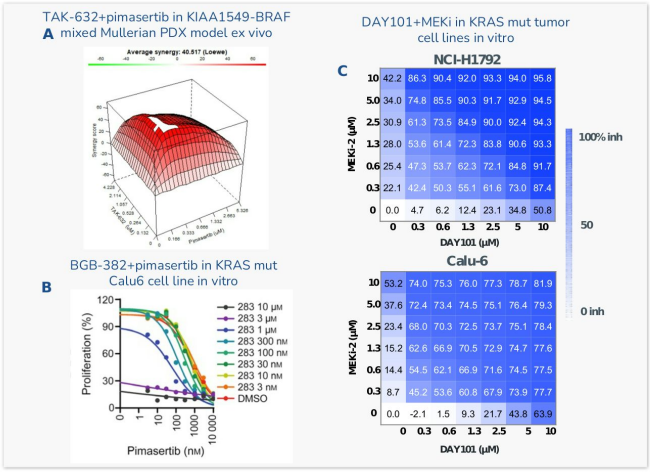
Pimasertib: Investigational Allosteric MEK1/2 Inhibitor with Demonstrated Activity in MAPK-driven Solid Tumors

- 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
MEK ERK Proliferation, survival	RAF/ MEK/ERK PI3K/m TOR RAL 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)

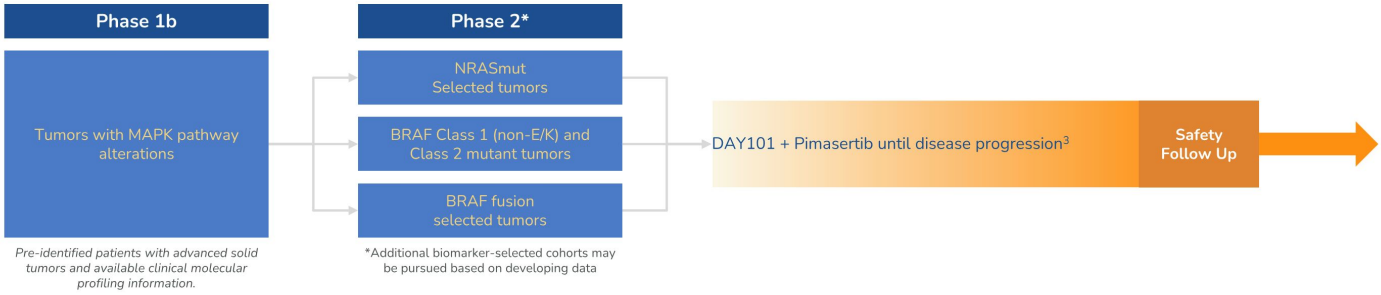
Tovorafenib (DAY101) / Pimasertib Combination to be Evaluate in Solid Tumors (FIRELIGHT-1)

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)



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 March 31, 2023: $318.2 million (no debt)	73.6 million shares of common stock outstanding as of April 25, 2023

$ Millions	Three Months Ended 3/31/23	Three Months Ended 3/31/22
R&D Expense	$27.8	$15.0
G&A Expense	$18.0	$12.7
Net Loss	$42.4	$27.7

Projected cash runway into 2025

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

- Pre-NDA meeting held on April 19, 2023
- Remain in position to initiate the NDA submission in Q2 2023
- Presentation of new clinical data[1] in oral presentation at ASCO in June 2023

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).

Next Steps

Day One BIOPHARMACEUTICALS

Topline data from pivotal Phase 2 FIREFLY-1 trial demonstrating meaningful responses with tovorafenib in recurrent or progressive pLGG

Overall response rate of 64% and clinical benefit rate of 91% in 69 heavily-pretreated, RANO-HGG evaluable patients

Median duration of 8.4 months on therapy as of data cut, with 77% of patients remaining on treatment

Safety data, based on the 77 treated patients, indicated monotherapy tovorafenib to be generally well-tolerated

FIREFLY-1

- Pre-NDA meeting held on April 19, 2023
- Remain in position to initiate the NDA submission in Q2 2023
- Presentation of new clinical data in oral presentation at ASCO conference

FIREFLY-2

- Advance tovorafenib as a front-line therapy for patients newly diagnosed 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

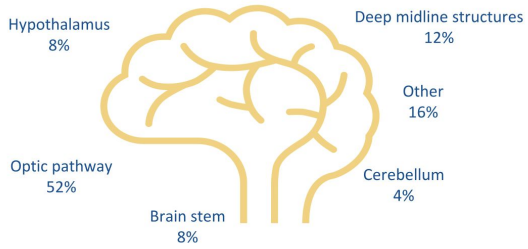
Data cut off as of September 28, 2022. Overall response rate of 64% in 69 heavily-pretreated, RANO-evaluable patients includes confirmed and unconfirmed CR and PR. Clinical benefit rate (complete response + partial response/unconfirmed partial response + stable disease). ORR by RANO-HGG


Appendix
Day One Biopharmaceuticals
Day One
BIOPHARMACEUTICALS

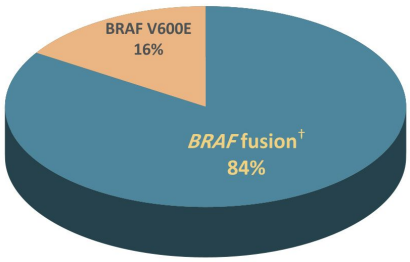
FIREFLY-1 Baseline Characteristics

Characteristic	Arm 1 (N=25)
Median age, years (range)	8 (3-18)
Sex, n (%)	
Male	13 (52)
Female	12 (48)
Race, n (%)	
Black or African American	1 (4)
Asian	2 (8)
White	15 (60)
Other*	7 (28)
Karnofsky/Lansky performance status, n (%)	
50-70	1 (4)
80-100	24 (96)
Number of lines of prior therapy	
Median (range)	3 (1-9)
1, n (%)	5 (20)
2, n (%)	6 (24)
≥3, n (%)	14 (56)
Prior MAPK pathway targeted therapy, n (%)	
Yes	18 (72)
No	7 (28)

Location (n=25)

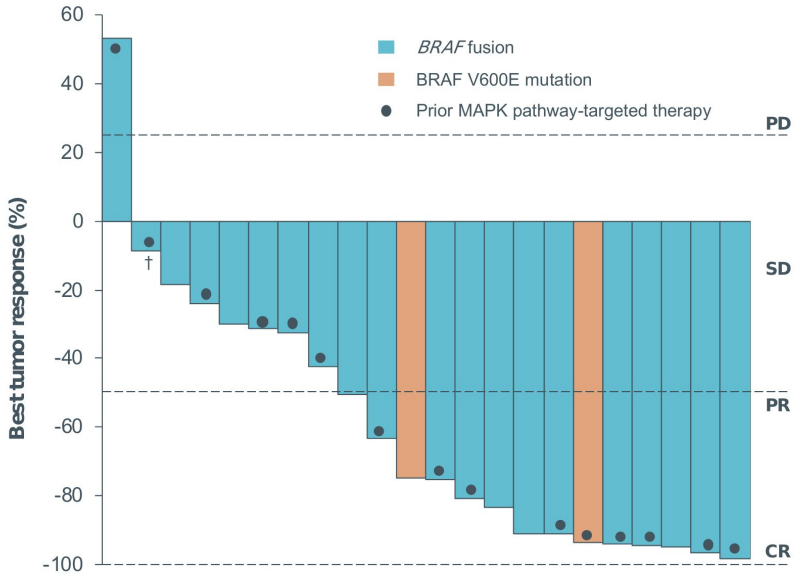


BRAF alteration (n=25)



Apr 14, 2022 data cutoff; *Includes 4 patients with race not specified. †Includes 2 patients with BRAF duplication and 1 with BRAF rearrangement per fluorescence in situ hybridization. MAPK, mitogen-activated protein kinase; prior MAPK pathway targeted therapy indicates either prior MEKi and/or prior type I RAFi therapy.

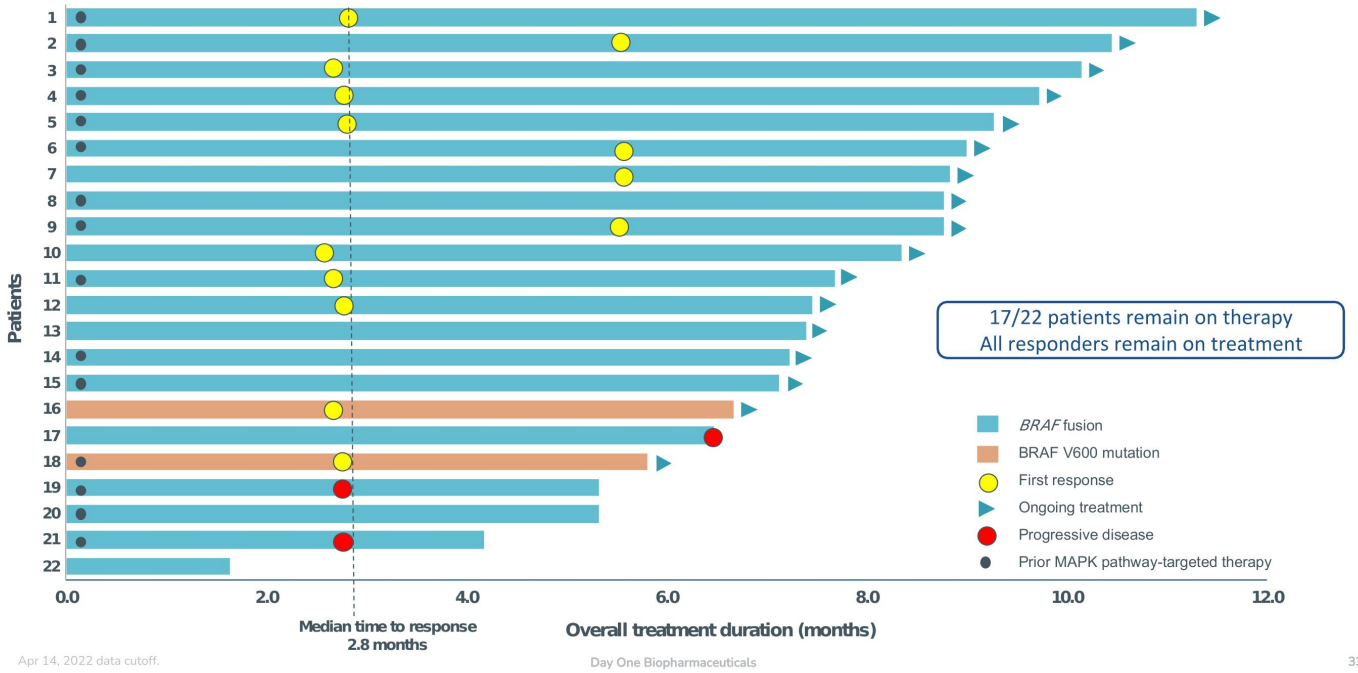
Tumor Response To Tovorafenib (DAY101) For All Patients With RANO-HGG Evaluable Lesions (n=22)*



Response (IRC)	RANO-HGG Evaluable N=22*
ORR (95% CI)	64% (41-83)
BRAF fusion (n=20)	60%
BRAF V600E (n=2)	100%
CBR#	91%
Best overall response	
PR (13/22)	59%
uPR (1/22)	5%
SD (6/22)	27%

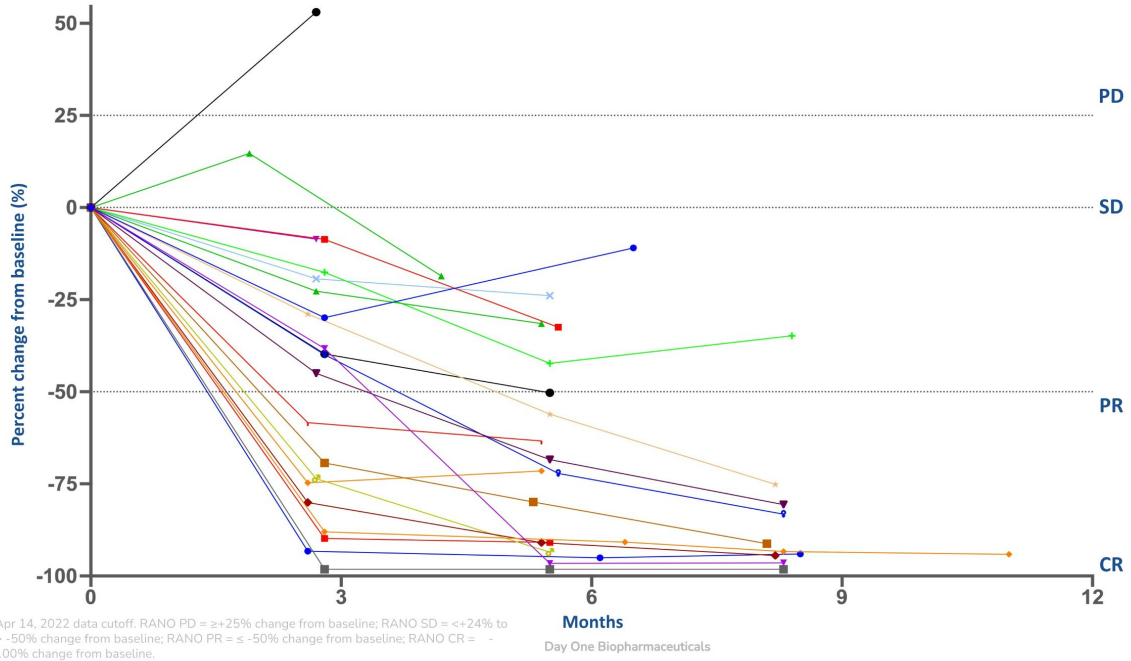
Apr 14, 2022 data cutoff. Total % of response maybe may be different than the sum of the individual overall response due to rounding. *3/25 patients lacked evaluable lesions per RANO criteria based on IRC evaluation. †Progressive disease due to presence of new lesions. #patients with best overall response of CR, PR/uPR and SD. CBR, clinical benefit rate; IRC, independent radiological review committee; ORR, overall response rate; MAPK, mitogen-activated protein kinase; PR, partial response; SD, stable disease; uPR, unconfirmed partial response.

Duration of Tovorafenib (DAY101) Therapy For All Patients with RANO-HGG Evaluable Lesions (n=22)



Apr 14, 2022 data cutoff.

Individual Patient Tumor Change From Baseline
(n=22 RANO-HGG Evaluable By Blinded Independent Central Review)



Apr 14, 2022 data cutoff. RANO PD = ≥+25% change from baseline; RANO SD = <+24% to > -50% change from baseline; RANO PR = ≤ -50% change from baseline; RANO CR = -100% change from baseline.

Tovorafenib (DAY101) Safety Data For the First 25 Enrolled Patients (TEAEs ≥25% Any Grade)

	Treatment-emergent AEs		Treatment-related AEs	
Preferred term, n (%)	Any grade	Grade ≥3	Any grade	Grade ≥3
Blood creatine phosphokinase increased	20 (80)	2 (8)	18 (72)	2 (8)
Hair color changes	17 (68)	-	17 (68)	-
Anemia	14 (56)	3 (12)	10 (40)	2 (8)
Aspartate aminotransferase increased	14 (56)	-	12 (48)	-
Vomiting	14 (56)	2 (8)	6 (24)	1 (4)
Rash*	13 (52)	3 (12)	13 (52)	3 (12)
Blood lactate dehydrogenase increased	12 (48)	-	9 (36)	-
Headache	10 40)	-	3 (12)	-
Dry skin	9 (36)	-	7 (28)	-
Epistaxis	9 (36)	-	4 (16)	-
Constipation	8 (32)	-	5 (20)	-
Hypocalcemia	8 (32)	-	6 (24)	-
Nausea	8 (32)	-	3 (12)	-
Alanine aminotransferase increased	7 (28)	1 (4)	4 (16)	1 (4)
Fatigue	7 (28)	-	7 (28)	-

- Most treatment-emergent AEs were grade 1 or 2 (96%)
- Other important treatment-emergent AEs included:
  - Decreased weight (24%)
  - Decreased appetite (16%)
  - Hyponatremia (16%)
- 7 patients (28%) required dose modifications due to treatment-related AEs
- No patient discontinued treatment due to AEs

Apr 14, 2022 data cutoff. AE, adverse event. TEAE, treatment-emergent adverse event. *Includes maculopapular and erythematous rash

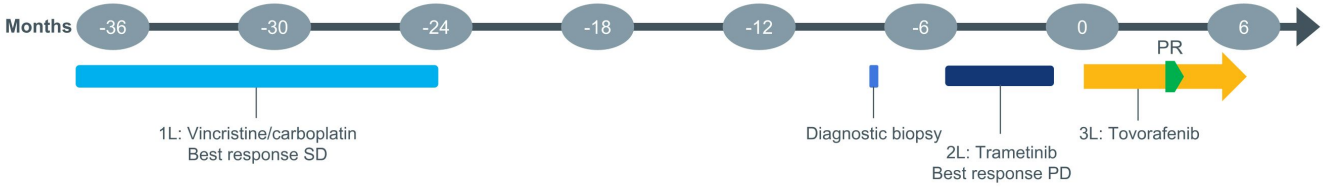
Key Takeaways

- **Encouraging initial efficacy data from FIREFLY-1 for pediatric patients with recurrent or progressive LGG harboring *BRAF* fusion or BRAF V600 mutation, for whom there is no standard-of-care and no approved agents for the majority of patients**
  - 64% ORR and 91% clinical benefit rate (partial response/unconfirmed partial response + stable disease) in the 22 RANO-HGG evaluable patients:
    - 14 partial responses (13 confirmed responses and 1 unconfirmed response)
    - 6 patients with stable disease
  - All patients with stable disease (n=6) were noted to have tumor shrinkage, ranging between 19% and 43%
  - Responses were observed in patients with both BRAF fusions and BRAF V600E mutations who received prior MAPK-targeted therapy
  - The median-time-to-response was 2.8 months
  - A heavily-pretreated population, with a median of 3 prior lines of therapy (range: 1-9)
  - All patients who responded remain on therapy (n=14) and no patients have discontinued treatment due to treatment-related adverse events
- **Initial safety data, based on the first 25 patients, indicated monotherapy tovorafenib (DAY101) to be generally well-tolerated**
  - Majority of AEs were grade 1 or 2; most common treatment-related AEs were CPK elevation, rash, and hair color changes
  - Treatment-related AEs of grade 3 or greater occurred in nine patients (36%)
- **Plan to present additional initial study results from FIREFLY-1 at the Society for Neuro-Oncology (SNO) annual meeting**
- **Topline results from the full registrational cohort (n=~60) of FIREFLY-1 expected to be available 1Q 2023, with NDA submission planned for Q2 2023**
- **Early results from FIREFLY-1 support plan to evaluate tovorafenib (DAY101) in parallel with a pivotal Phase 3 frontline pLGG study (FIREFLY-2)**
  - Primary endpoint of ORR based on RANO-LGG (2017)[1] criteria, assessed by blinded independent central review

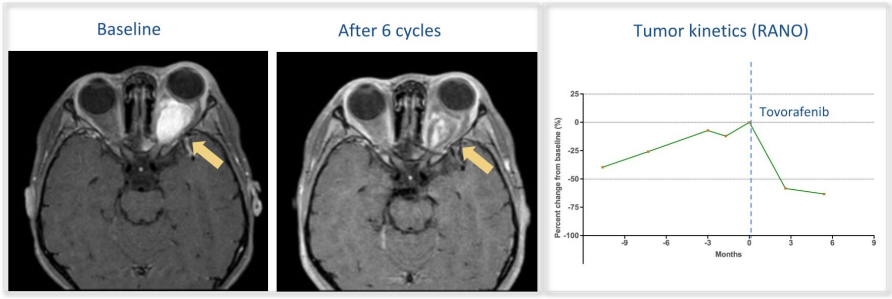
[1]1Primary endpoint of FIREFLY-2 will be ORR by RANO-LGG (2017) following full approval by FDA on March 16, 2023 of dabrafenib with trametinib in pediatric patients with low-grade glioma with a BRAF V600E mutation who require systemic therapy based on a study with the same primary endpoint.

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

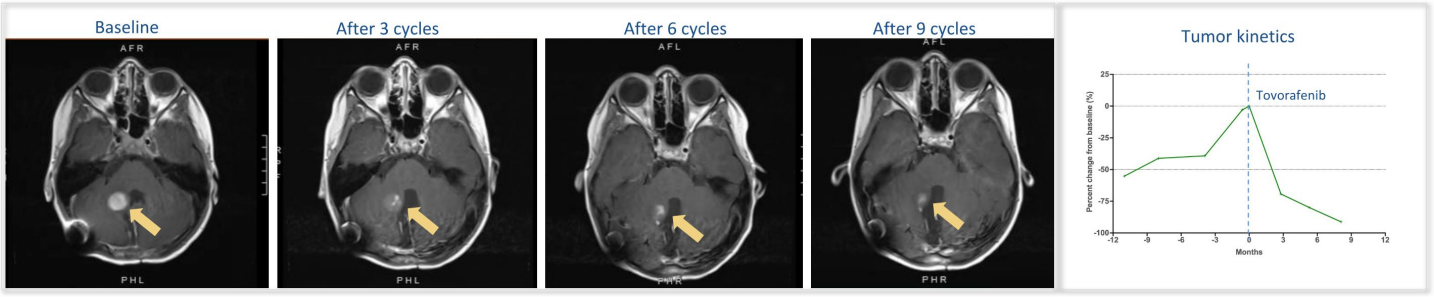


Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

Case Study: Activity Of Tovorafenib (DAY101) In *KIAA1549-BRAF* Fusion 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

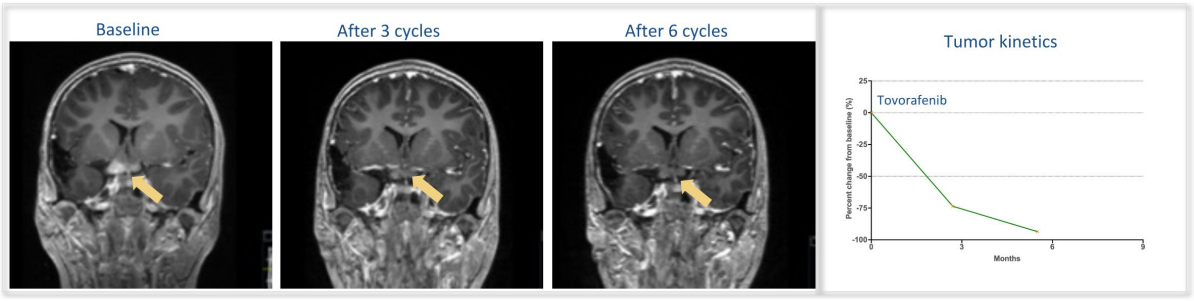


Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

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

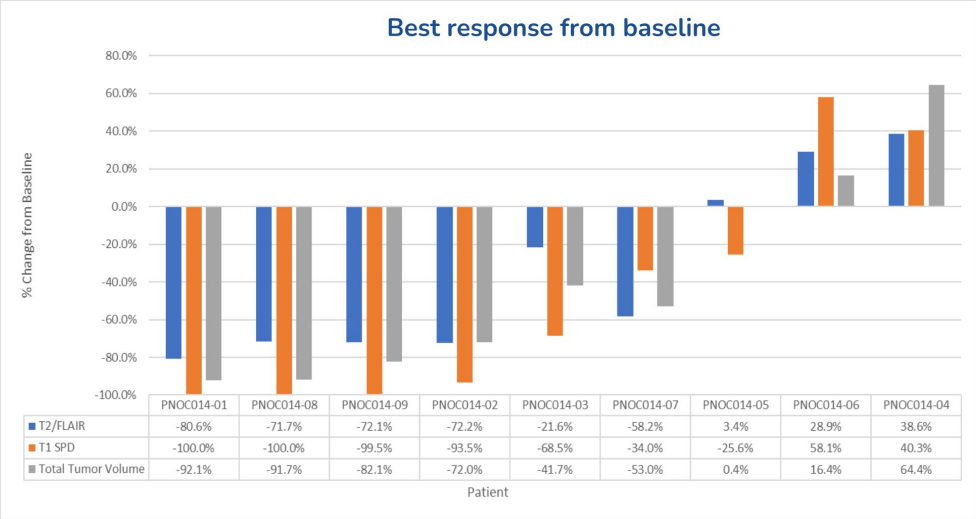
A 9-year-old female child with deep midline BRAF V600E-mutant astrocytoma with precocious puberty

- 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



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

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

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