

**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): November 17, 2023

DAY ONE BIOPHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-40431
(Commission
File Number)

83-2415215
(IRS Employer
Identification No.)

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

94005
(Zip Code)

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

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.0001 per share	DAWN	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01 Regulation FD Disclosure.

On November 17, 2023, Day One Biopharmaceuticals, Inc. (the "Company") issued a press release announcing that results from the registrational Phase 2 FIREFLY-1 trial evaluating the investigational agent tovorafenib in patients with BRAF-altered, relapsed or progressive pediatric low-grade glioma, with a data cutoff of June 5, 2023, were published in the medical journal Nature Medicine. These results will be shared in two oral plenary presentations at the 2023 Society for Neuro-Oncology Annual Meeting on Friday, November 17, 2023.

Additionally, on November 17, 2023, the Company updated its corporate presentation to reflect the registrational Phase 2 FIREFLY-1 trial results.

A copy of the press release is attached as Exhibit 99.1 to this Current Report on 8-K. A copy of the revised corporate presentation is attached as Exhibit 99.2 to this Current Report on Form 8-K.

The information furnished in this Item 7.01, including Exhibits 99.1 and 99.2, shall not be deemed "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, nor shall it be deemed incorporated by reference into any other filing under the Exchange Act or the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

<u>Exhibit Number</u>	<u>Description</u>
99.1	Press Release, dated November 17, 2023
99.2	Corporate Presentation
104	Cover Page Interactive Data File - the cover page XBRL tags are embedded within the Inline XBRL document

SIGNATURES

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

DAY ONE BIOPHARMACEUTICALS, INC.

Date: November 17, 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 Announces Tovorafenib FIREFLY-1 Data Published in *Nature Medicine*

Data subsets to be shared today in plenary oral presentations at the 2023 Society for Neuro-Oncology Annual Meeting

BRISBANE, Calif., Nov. 17, 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 the publication of the registrational Phase 2 FIREFLY-1 trial results evaluating the investigational agent tovorafenib in patients with BRAF-altered, relapsed or progressive pediatric low-grade glioma (pLGG) in *Nature Medicine*. Subsets of the data will also be presented today in two oral plenary presentations at the 2023 Society for Neuro-Oncology (SNO) Annual Meeting in Vancouver, Canada.

“The study results published in *Nature Medicine* demonstrate promising evidence with respect to the the impact of tovorafenib for children and young adults with BRAF-altered relapsed or progressive pLGG, a debilitating form of brain tumor that currently has no approved systemic therapies,” said Dr. Samuel Blackman, co-founder and head of research and development, Day One. “We look forward to continued development of tovorafenib.”

Details on today’s oral presentations and corresponding abstracts:

Title: *Clinical Activity and Safety of the RAF Inhibitor Tovorafenib in Patients with Optic Pathway Gliomas in the Registrational Pediatric Low-Grade Glioma Arm of the Phase 2 FIREFLY-1 (PNOC026) Study

Abstract Number: CTNI-24

Time: 10:15 – 10:25 AM PT

Location: Exhibit Hall C

Presenter: Karsten Nysom, MD, PhD, Copenhagen University Hospital - Rigshospitalet

*Presenter Karsten Nysom, MD, PhD received the 2023 SNO Annual Meeting Abstract Award for Excellence in Clinical Trials in connection to this oral presentation.

Title: Clinical Activity of RAF Inhibitor Tovorafenib According to Prior MAPK Inhibitor Treatment in the Registrational Pediatric Low-Grade Glioma Arm of the Phase 2 FIREFLY-1 (PNOC026) Study

Abstract Number: CTNI-37

Time: 10:25 – 10:35 AM PT

Location: Exhibit Hall C

Presenter: Daniel Landi, MD, Duke University

A New Drug Application for tovorafenib monotherapy in BRAF-altered relapsed or progressive pLGG is currently under priority review by the U.S. Food and Drug Administration (FDA) with a Prescription Drug User Fee Act target action date of April 30, 2024. In addition to FIREFLY-1, the Phase 3 FIREFLY-2/LOGGIC randomized clinical trial is evaluating tovorafenib frontline therapy for patients newly diagnosed with pLGG.

About Tovorafenib

Tovorafenib is an investigational, oral, brain-penetrant, highly-selective type II 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 350 patients to date and is currently under evaluation in two pivotal clinical trials for pLGG. Tovorafenib is also being evaluated as a combination therapy for adolescent and adult patient populations with recurrent or progressive solid tumors with MAPK pathway aberrations (FIRELIGHT-1).

Tovorafenib has been granted Breakthrough Therapy and Rare Pediatric Disease designations by the 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 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, the ability of Day One to obtain regulatory approvals for and to commercialize 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, cybersecurity events, instability in the global banking system, government shutdowns, uncertainty with respect to the federal budget, global regional conflicts and the sufficiency of Day One's cash, cash equivalents and short-term 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 MEDIA
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Day One Biopharmaceuticals

Targeted Therapies for People of All Ages

November 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, the results of any of our strategic collaborations, including the potential achievement of milestones and provision of royalty payments thereunder, 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, cybersecurity incidents, instability in the global banking system, government shutdowns, uncertainty with respect to the federal budget and global regional conflicts, 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

A Mission That Creates Value



- Develop medicines for genomically-defined cancers
- Establish first-in-class position through rapid registration pathways
- Expand to adolescent and adult populations in parallel and pursue those opportunities with the same commitment we do for children

Nasdaq: DAWN
IPO: 2021
Founded: 2018

Financial Position **Runway into 2026**

Growing Portfolio

- Lead program FIREFLY-1: FDA acceptance of NDA and priority review granted with PDUFA target action of date of April 30, 2024
- Frontline trial (FIREFLY-2) underway
- Clinical-stage MEKi asset (pimasertib), in-licensed for combination trial with tovorafenib
- Research collaboration and license agreement for preclinical program targeting VRK1



3 | NDA data set included 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).



Our Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Recent & Anticipated Milestones
Tovorafenib (DAY101) Type II RAF Inhibitor <ul style="list-style-type: none"> 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)				FDA acceptance of NDA: October 2023 PDUFA target action date: April 30, 2024 Data published in Nature Medicine: November 2023
	Frontline pLGG	FIREFLY-2 (pivotal)				First patient dosed: March 2023
Pimasertib MEK 1/2 Inhibitor	MAPK-altered solid tumors ² (Combo w/tovorafenib)	FIRELIGHT-1*				First patient dosed: May 2022
VRK1 Program³ VRK1 Inhibitor	Pediatric and adult cancers					In-licensed: August 2023

*Includes patients ≥12 years of age. ¹ FIREFLY-1 Arm 1 expected to support registration. ² Pimasertib Phase 1 dose escalation and expansion trial previously completed. ³ Research collaboration and license agreement with Sprint Bioscience for exclusive worldwide rights to a research-stage program targeting VRK1. 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 term⁶

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 mutations⁵
- Majority of patients have many years of treatment until the tumors typically senesce by their mid-20s

Disease Symptoms⁷

Cerebral gliomas:

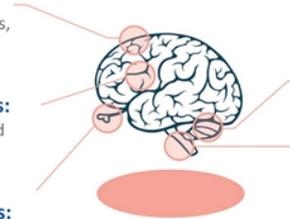
Seizures, muscle weakness, behavioral changes

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 Ostrom 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.

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

Surgery

- Significant recovery times
- Risks of complications
- Resection may be limited by location of tumor
- Potential for functional deficits based on location of tumor and extent of resection

Chemotherapy

- Requirement for indwelling catheter and weekly infusions
- Risk of neutropenia, hypersensitivity reactions, nausea and vomiting and peripheral neuropathy

Radiation

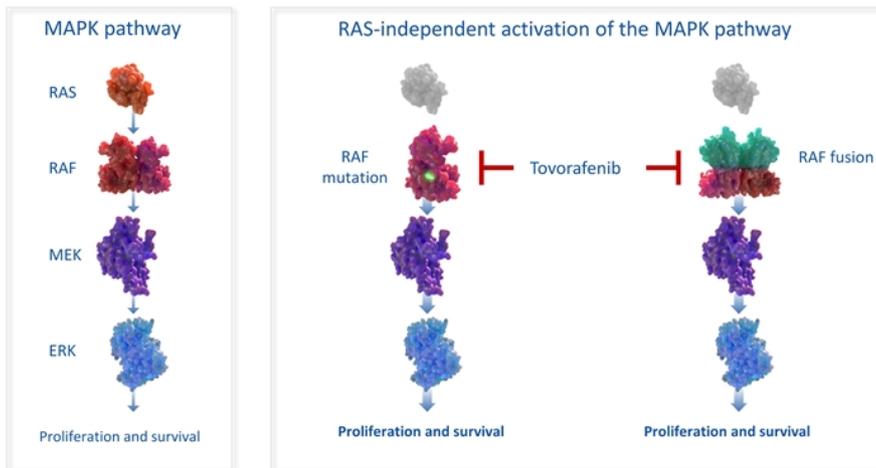
- Risk of secondary malignancy
- Risk of malignant transformation
- Risk of vascular proliferation and stroke
- Neurocognitive impact, depending on location of tumor and radiation field

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, Raghobar 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/cancers13112607. 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.



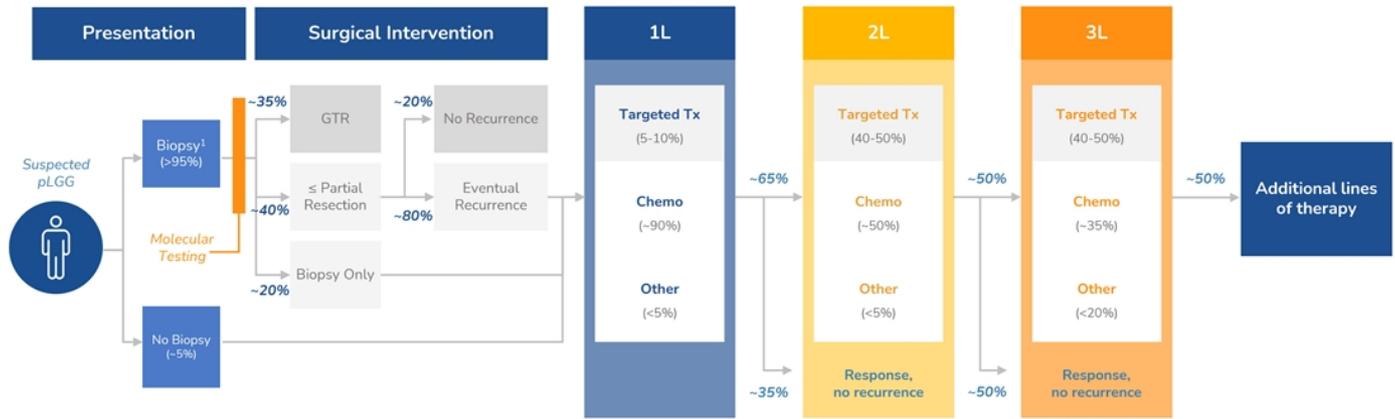
Tovorafenib (DAY101) Inhibits Both BRAF Fusions And BRAF V600 Mutations



- **Tovorafenib (DAY101) is an investigational, oral, selective, CNS-penetrant, type II 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



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.



Pivotal Phase 2 Trial Of Monotherapy Tovorafenib (DAY101) In Relapsed Or Progressive pLGG (FIREFLY-1) – Fully Enrolled & Data Submitted to FDA



Trial Design

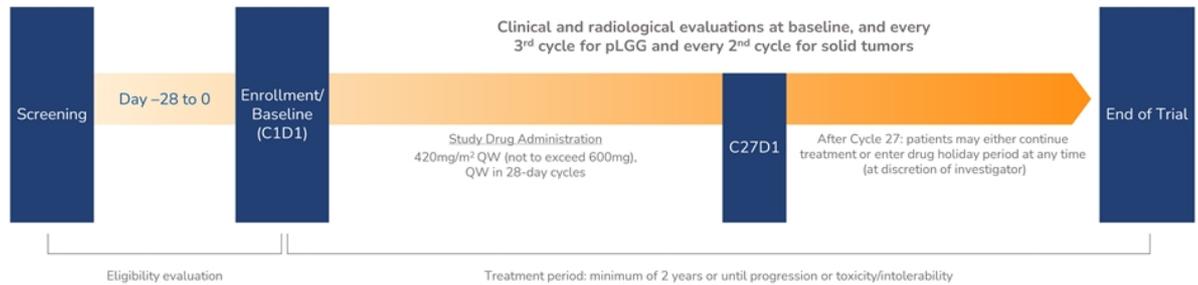
- Three arm, open-label, global registrational phase 2 trial
- **Pivotal Arm 1 (recurrent/progressive pLGG, n=77): harboring a KIAA1549-BRAF fusion or BRAF V600E mutation**
- Arm 2 (expanded access recurrent/progressive LGG, n=60): harboring an activating RAF alteration
- Arm 3 (extracranial solid tumors): harboring an activating RAF fusion

Endpoints (Pivotal Arm 1)

- **Primary endpoint: ORR based on RANO-HGG¹, assessed by blinded independent central review**
- Secondary endpoints: ORR by RAPNO-LGG² assessed by blinded independent central review; PFS, DoR; TTR, CBR; safety
- Exploratory analyses: ORR and CBR by RANO-LGG³ 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



Eligibility evaluation

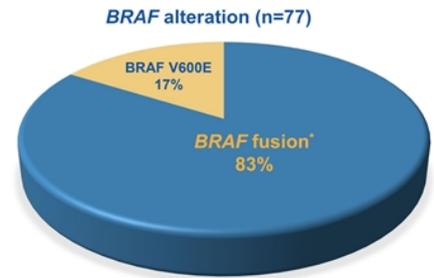
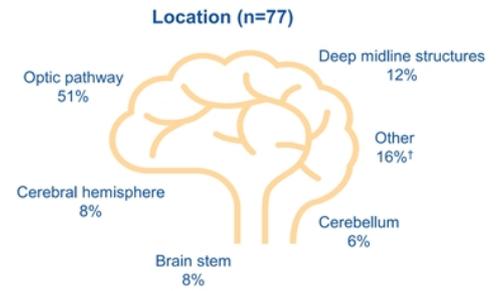
Treatment period: minimum of 2 years or until progression or toxicity/intolerability

Data from Pivotal Phase 2 FIREFLY-1 Trial

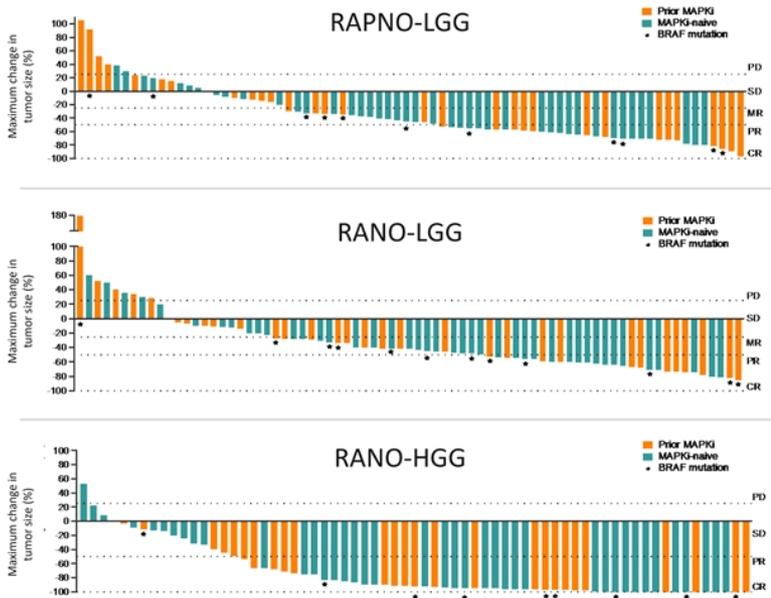
June 5, 2023 data cutoff

FIREFLY-1 Baseline Patient Characteristics

Characteristic	Arm 1 (n=77)
Median age, years (range)	8 (2-21)
Gender, n (%)	
Male	40 (52)
Female	37 (48)
Race, n (%)	
White	41 (53)
Asian	5 (6)
Black	2 (3)
Multiple	3 (4)
Other	6 (8)
Not specified	20 (26)
Number of lines of prior systemic therapy	
Median (range)	3 (1-9)
1, n (%)	17 (22)
2, n (%)	21 (27)
≥3, n (%)	39 (51)
Prior MAPK pathway targeted therapy, n (%)	
Prior MEK inhibitor	43 (56)
Prior BRAF inhibitor	8* (10)
Prior BRAF and MEK inhibitors†	5 (7)
Any MAPK inhibitor	46 (60)



Tumor Response To Tovorafenib (DAY101) Using RAPNO-LGG, RANO-LGG and RANO-HGG

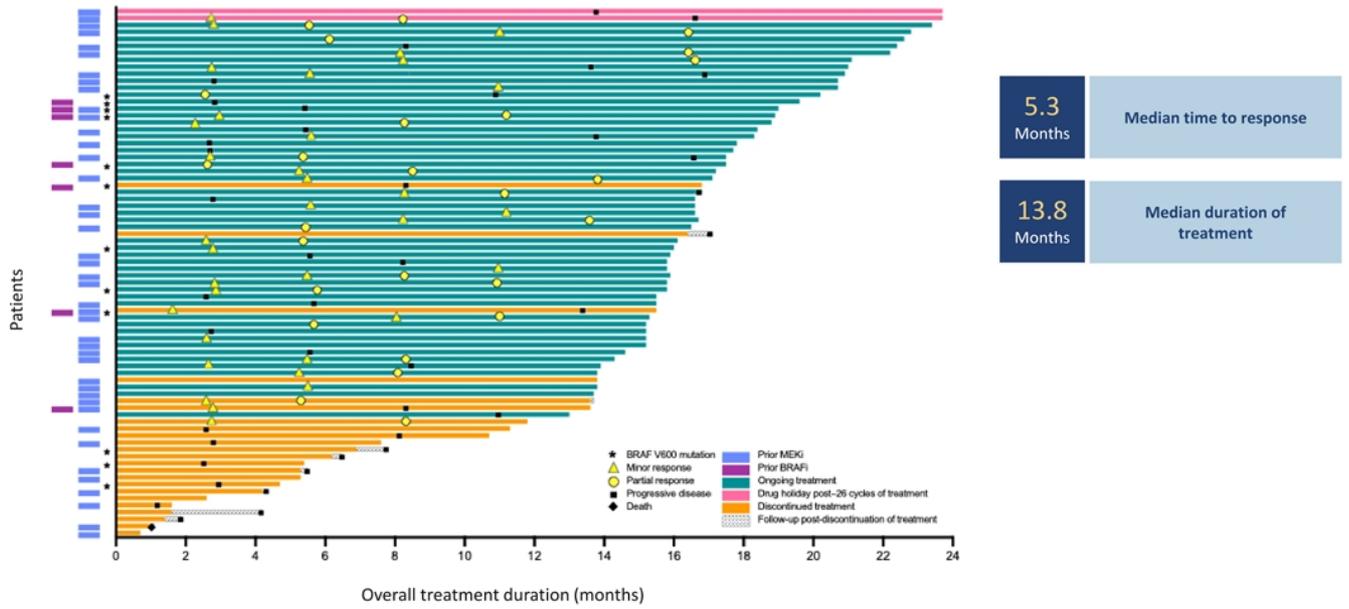


Response (IRC)	RAPNO-LGG n=76	RANO-LGG N=76	RANO-HGG N=69
ORR,* n (%)	39 (51)	40 (53)	46 (67)
95% CI	40-63	41-64	54-78
CBR,* n (%)			
SD of any length of time	62 (82)	63 (83)	64 (93)
SD ≥12 months	43 (57)	46 (61)	54 (78)
BOR,* n (%)			
CR	0	0	12 (17)
PR	28 (37)	20 (26)	34 (49)
MR	11 (14)	20 (26)	n/a
SD	23 (30)	23 (30)	18 (26)
SD <12 months	19 (25)	17 (22)	10 (14)
SD ≥12 months	4 (5)	6 (8)	8 (12)
PD	13 (17)	11 (14)	4 (6)
NE	1 (1)	2 (3)	1 (1)
Median DOR, months	13.8	14.4	16.6
95% CI	11.3-NR	11.0-NR	11.6-NR
Median TTR, months	5.3	5.5	3.0
Range	1.6-11.2	1.6-11.3	2.6-16.6

June 5, 2023 data cutoff. BOR, best overall response; CBR, clinical benefit rate; CI, confidence interval; CR, complete response; DOR, duration of response; HGG, high-grade glioma; IRC, independent radiology review committee; LGG, low-grade glioma; MR, minor response; n/a, not applicable; NE, not evaluable; NR, not reached; 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; TTR, time to response. * ORR, CBR and BOR for RAPNO-LGG and RANO-LGG included MRs.

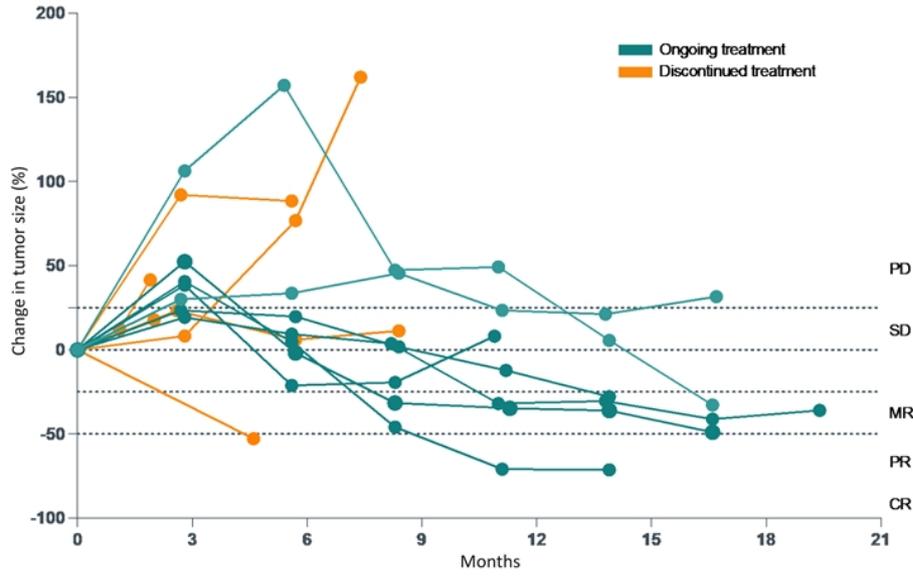


Duration Of Tovorafenib (DAY101) Therapy For All Patients With RAPNO-LGG Evaluable Lesions



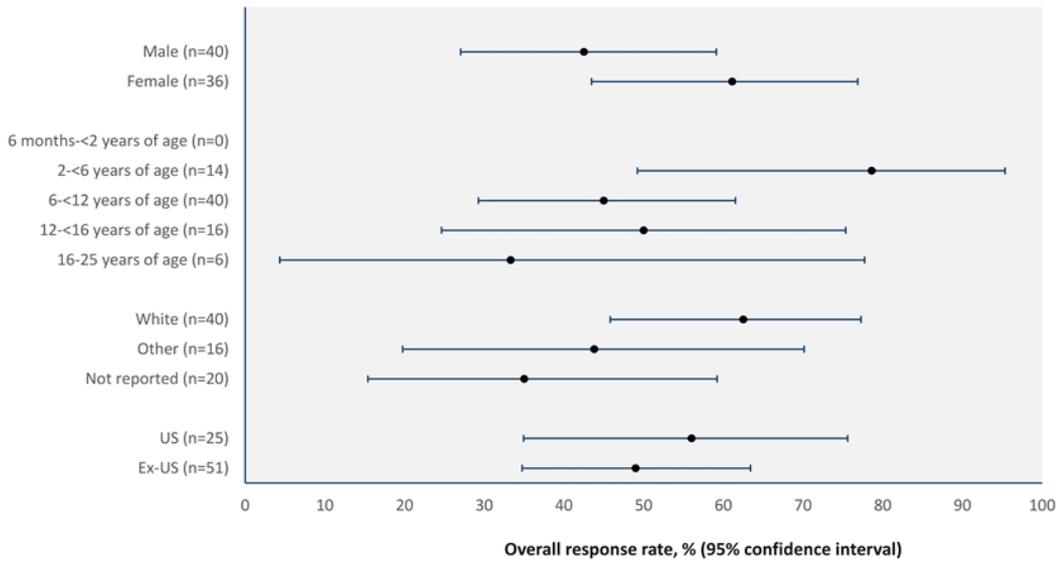
14 June 5, 2023 data cutoff.

Tumor Kinetics In Patients With Best Response Of Progressive Disease According To RAPNO-LGG



The majority of patients who had radiographic progression by RAPNO-LGG at their initial disease assessment had subsequent prolonged reductions in the size of their tumor with continued treatment.

Tumor Response To Tovorafenib (DAY101) According to RAPNO-LGG In Subgroups Defined By Baseline Characteristics



Analysis of response data across various subgroups shows no significant differences in response rate by RAPNO-LGG



Tumor Response To Tovorafenib (DAY101) Across Three Assessment Criteria Were Consistent Across BRAF Fusion And Mutation Patients, and Patients With Prior MAPK Treatment

Response (IRC)	RAPNO-LGG ²		RANO-LGG ^{3,4}		RANO-HGG ¹	
	n		n		n	
ORR,* n (%)	76	39 (51)	76	40 (53)	69	46 (67)
BRAF fusion	64	33 (52)	64	33 (52)	59	41 (69)
BRAF mutation	12	6 (50)	12	7 (58)	10	5 (50)
Prior MAPKi	45	22 (49)	45	23 (51)	41	29 (71)
MAPKi-naive	31	17 (55)	31	17 (55)	28	17 (61)
CBR,* n (%) (SD of any length of time)	76	62 (82)	76	63 (83)	69	64 (93)
BRAF fusion	64	53 (83)	64	53 (83)	59	55 (93)
BRAF mutation	12	9 (75)	12	10 (83)	10	9 (90)
Prior MAPKi	45	38 (84)	45	38 (84)	41	37 (90)
MAPKi-naive	31	24 (77)	31	25 (81)	28	27 (96)
CBR,* n (%) (SD ≥12 months)	76	43 (57)	76	46 (61)	69	54 (78)
BRAF fusion	64	37 (58)	64	39 (61)	59	49 (83)
BRAF mutation	12	6 (50)	12	7 (58)	10	5 (50)
Prior MAPKi	45	25 (56)	45	26 (58)	41	33 (80)
MAPKi-naive	31	18 (58)	31	20 (65)	28	21 (75)
Median DOR, months (95% CI)**	39	13.8 (11.3-NR)	40	14.4 (11.0-NR)	46	16.6 (11.6-NR)
BRAF fusion	33	13.8 (11.3-NR)	33	16.3 (11.0-NR)	41	16.8 (11.6-NR)
BRAF mutation	6	NR (8.4-NR)	7	12.0 (8.4-NR)	5	15.1 (8.3-NR)
Prior MAPKi	22	13.8 (11.3-NR)	23	12.0 (8.5-NR)	29	15.1 (9.0-16.8)
MAPKi-naive	17	NR (8.4-NR)	17	16.3 (8.4-NR)	17	NR (11.6-NR)

June 5, 2023 data cutoff. ¹ Fangusaro J, et al. *Lancet Oncol.* 2020;21(6):e305–316. 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. ⁴ Wen PY, et al. *J. Clin. Oncol.* 2017;35(21):2439-2449. * ORR, CBR for RAPNO-LGG and RANO-LGG included MRS. ** the 95% CI were calculated using Kaplan-Meier method.



Tovorafenib (DAY101) Safety Data (n=137)



Preferred Term, n (%)	TEAEs		TRAEs	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any AE	137 (100)	86 (63)	134 (98)	58 (42)
Hair color changes	104 (76)	0	104 (76)	0
Anemia	81 (59)	15 (11)	67 (49)	14 (10)
Elevated CPK	80 (58)	16 (12)	77 (56)	16 (12)
Fatigue	76 (55)	6 (4)	60 (44)	6 (4)
Vomiting	68 (50)	6 (4)	28 (20)	3 (2)
Hypophosphatemia	64 (47)	0	48 (35)	0
Headache	61 (45)	2 (1)	29 (21)	0
Maculo-papular rash	60 (44)	11 (8)	56 (41)	11 (8)
Pyrexia	53 (39)	5 (4)	17 (12)	1 (1)
Dry skin	49 (36)	0	45 (33)	0
Elevated LDH	48 (35)	0	42 (31)	0
Increased AST	47 (34)	4 (3)	41 (30)	4 (3)
Constipation	45 (33)	0	31 (23)	0
Nausea	45 (33)	0	25 (18)	0
Upper RTI	43 (31)	2 (1)	2 (1)	0
Dermatitis acneiform	42 (31)	1 (1)	41 (30)	1 (1)
Epistaxis	42 (31)	1 (1)	27 (20)	0
Decreased appetite	39 (28)	5 (4)	28 (20)	4 (3)
Paronychia	36 (26)	2 (1)	32 (23)	2 (1)
Pruritus	35 (26)	1 (1)	32 (23)	1 (1)
COVID-19	34 (25)	0	0	0

- 9 patients (7%) had TRAEs leading to discontinuation
- The most common reasons for discontinuation were tumor hemorrhage (3 patients) and decrease in growth velocity (2 patients)
- 33 patients (24%) had TRAEs leading to dose reduction; 50 patients (37%) had TRAEs leading to dose interruption
- Median duration of dose interruption was 2 weeks.



June 5, 2023 data cutoff. Treatment-emergent AEs ≥25% any grade in arms 1 & 2. AE, adverse event; ALT, Alanine transaminase; AST, aspartate aminotransferase; COVID-19, Coronavirus disease 2019; CPK, creatine phosphokinase; LDH, lactate dehydrogenase; RTI, respiratory tract infection; TEAEs, treatment-emergent adverse events; TRAEs, treatment-related adverse events.



Estimated *BRAF*-Altered pLGG Patient Population In The U.S.

Estimated *BRAF*-Altered Patients in the U.S.



- An estimated 26,000 children/young adults are living with *BRAF*-altered (*BRAF* fusions or *BRAF* V600E mutations) pLGGs in the U.S. today¹⁻⁵
- Despite significant disease burden, many pLGGs undergo senescence when patients reach their 20s driving the need to both maximize tumor control while minimizing treatment-associated toxicities
- As a result, a large number of pLGG patients will undergo multiple lines of systemic therapy over the course of their disease
- Based on progression free survival curves modeled from published literature, the estimated addressable pool of recurrent or progressive pLGG patients is ~2,000-3,000⁶ per year at steady state

¹ Selt F, van Tilburg CM, Bison B, et al. Response to trametinib treatment in progressive pediatric low-grade glioma patients. *J Neurooncol.* 2020;149(3):499-510. doi:10.1007/s11060-020-03640-3. ² Ryall S, Tabori U, Hawkins C. Pediatric low-grade glioma in the era of molecular diagnostics. *Acta Neuropathol Commun.* 2020;8(1):30. doi:10.1186/s40478-020-00902-z. ³ SEER US complete prevalence counts of patients aged under 25 with Brain and Other Nervous Systems tumors as of January 1, 2017. ⁴ CBTRUS, Qaddoumi et al 2009, Schreck et al 2019, ClearView Analysis. ⁵ US Census. Estimated annual incidence, estimated prevalence, and estimated recurrent/progressive total addressable patient population are Day One calculations based on publicly available data. ⁶ Source: Internal market research conducted by EpidStrategies, A Division of ToxStrategies, Inc. on behalf of Day One.



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 (“*BRAF*-altered”)
 - 51% ORR by RAPNO-LGG
 - 53% ORR by RANO-LGG
 - 67% ORR by RANO-HGG
- Deepening of responses observed in patients from December 2022 to June 2023 data cutoffs across all three assessment criteria
- Responses were observed in patients with either *BRAF* fusion or *BRAF* V600E mutations (“*BRAF*-altered”)
- Responses seen in a heavily-pretreated population where the majority (60%) of patients progressed on or after one or more prior MAPK inhibitors
- Safety and tolerability profile indicating monotherapy tovorafenib to be generally well-tolerated
- FDA Rare Pediatric Disease Designation for pLGG, eligible for Priority Review Voucher

Next Steps: Priority review granted with PDUFA target action date April 30, 2024



20 | June 5, 2023 data cutoff.



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

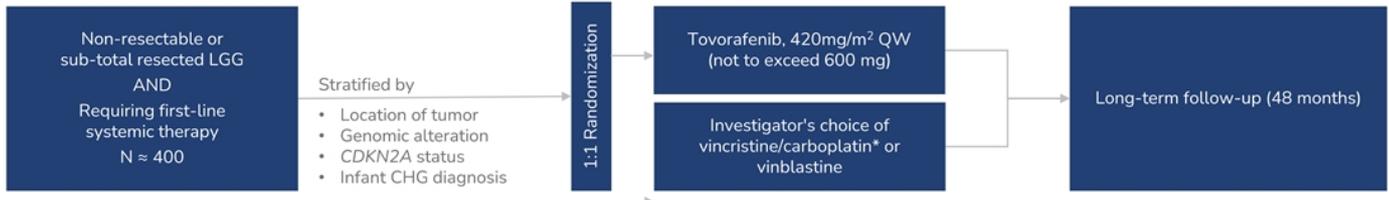


Trial Design

- 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 review¹**
 - 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

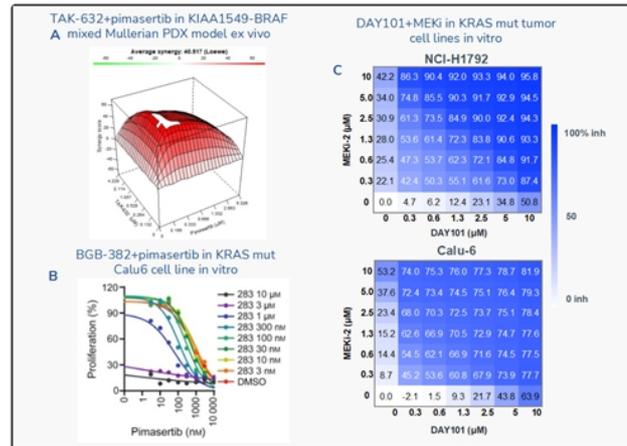
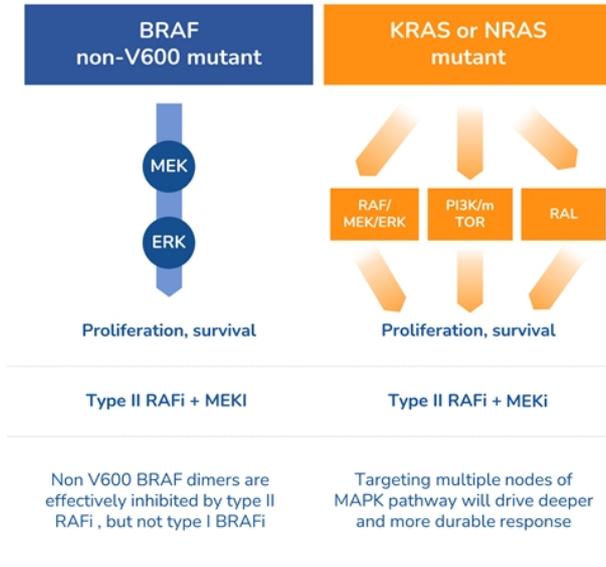
Phase 1b/2 Trials Evaluating Tovorafenib (DAY101) as a
Combination with Pimasertib

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



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



- A** Type II 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 BGG-283 (Yuan et al., Mol Onc 2020)
- C** Tovorafenib (DAY101) + MEK inhibitor is synergistic in KRAS G12C and Q61 mutant tumor cells (Venetsanos et al., 2021 AACR poster presentation)

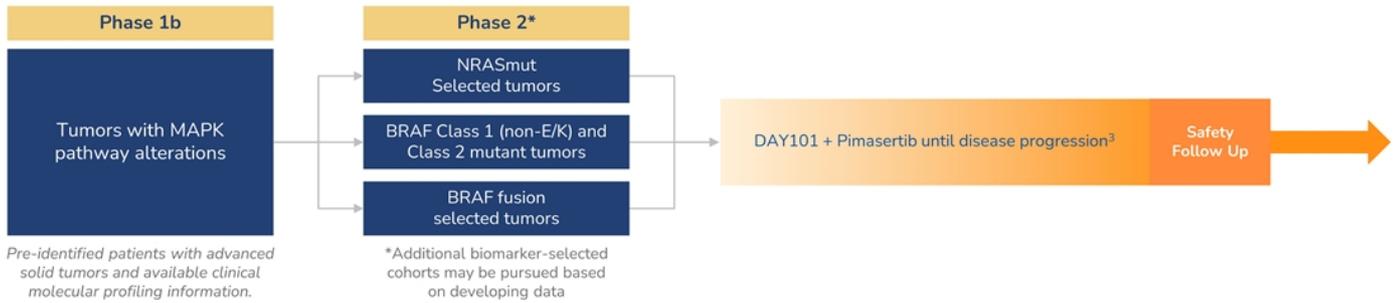


Trial Design¹

- Combination dose escalation, global phase 1b/2 trial²
- 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)



Summary

Financial Summary: DAWN

Cash, cash equivalents and short-term investments as of September 30, 2023: \$405.5 million (no debt)

~87.0 million shares of common stock outstanding as of November 1, 2023

\$ Millions	Nine Months Ended 9/30/23	Nine Months Ended 9/30/22
R&D Expense	\$93.2	\$59.6
G&A Expense	\$53.4	\$44.6
Net Loss	\$134.4	\$102.1

Projected cash runway into 2026

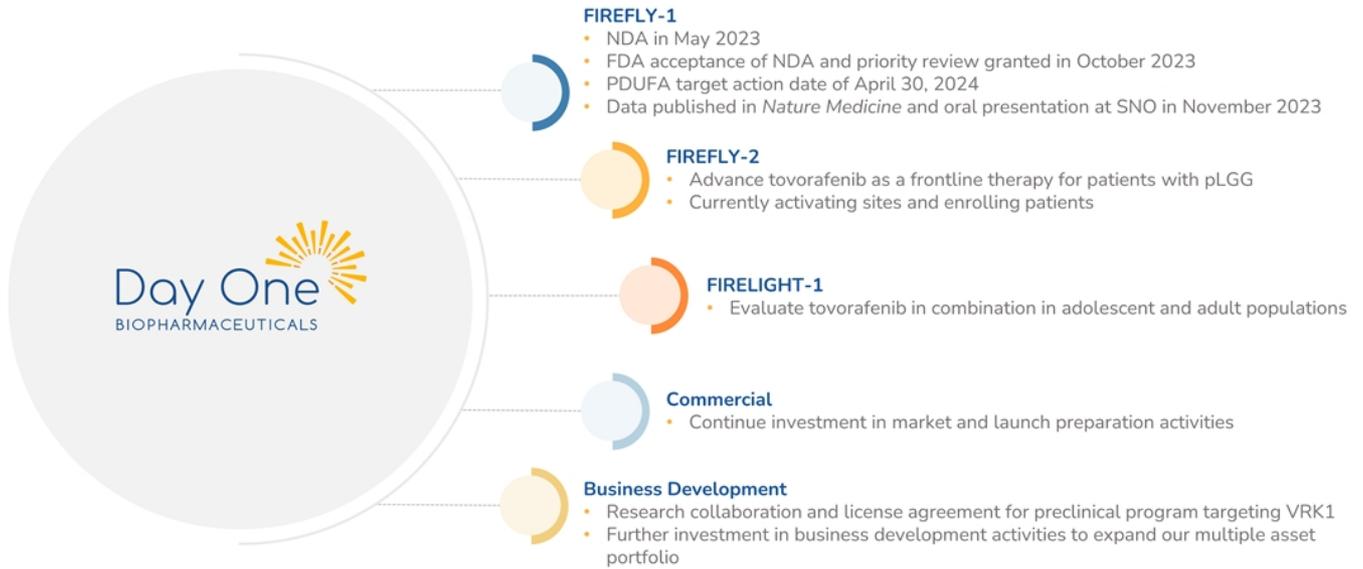
FIREFLY-1: Pivotal Phase 2 clinical trial of tovorafenib (DAY101)

- NDA¹ in May 2023
- FDA acceptance of NDA and priority review granted in October 2023
- PDUFA target action date of April 30, 2024 (PRV eligible)
- Data published in *Nature Medicine* and oral presentation at SNO in November 2023

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

- First patient dosed in March 2023

Next Steps

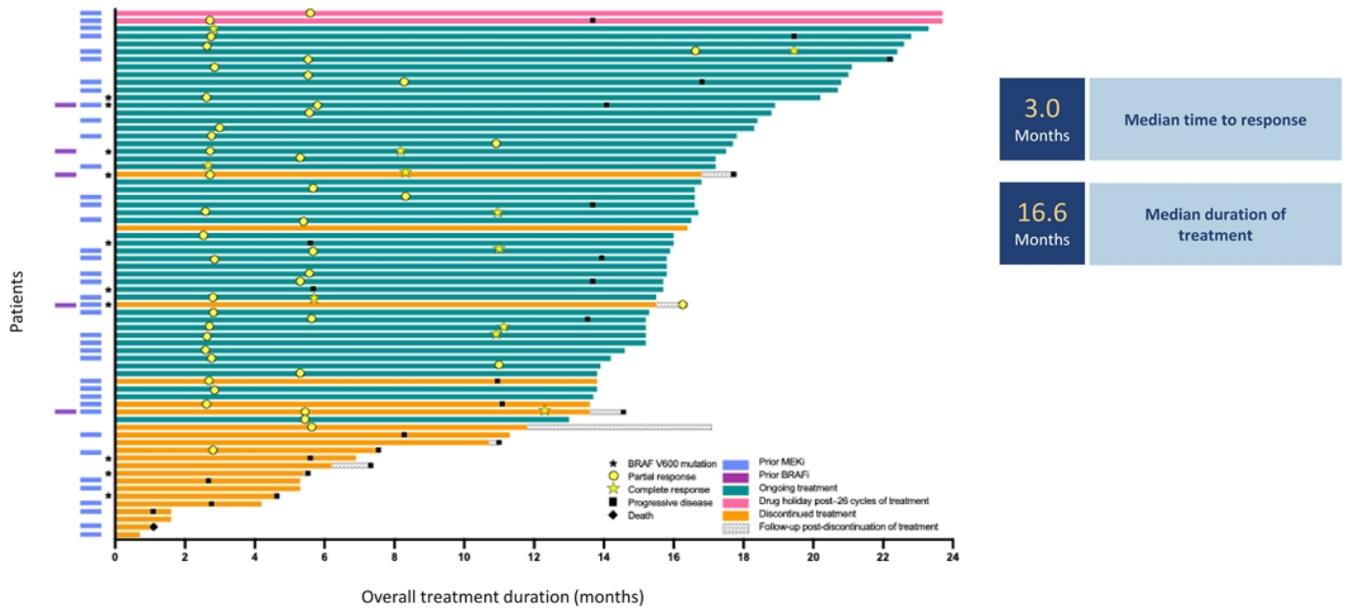




Appendix

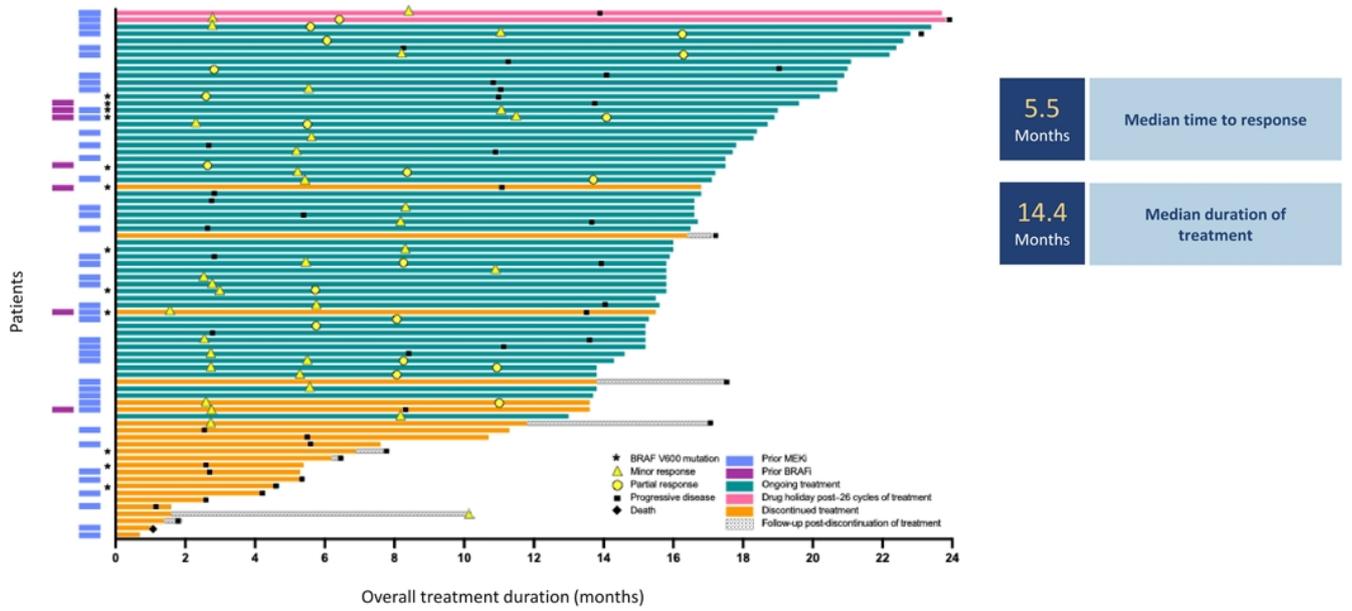
Day One
BIOPHARMACEUTICALS

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



31 June 5, 2023 data cutoff.

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

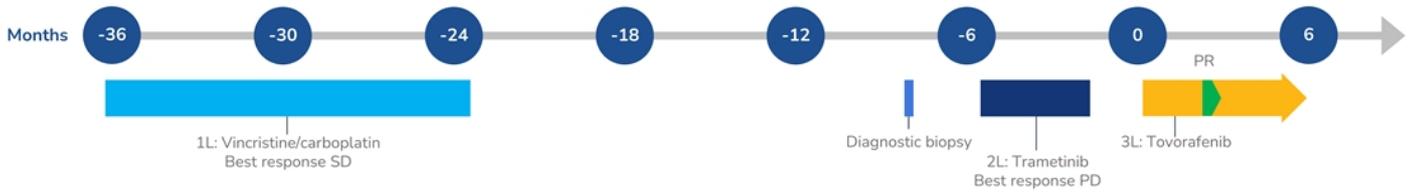


32 June 5, 2023 data cutoff.

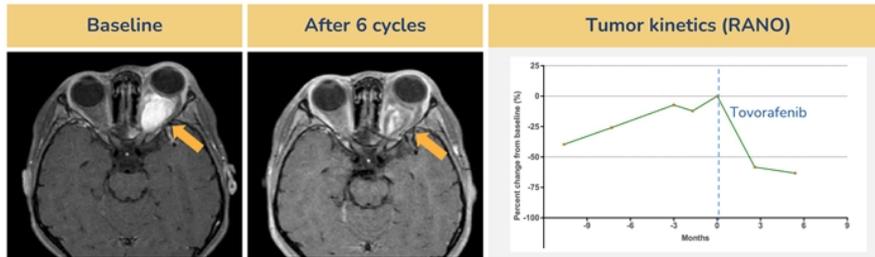


Case Study: Activity Of Tovorafenib (DAY101) In KIAA1549-BRAF Fusion Optic Pathway Glioma

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

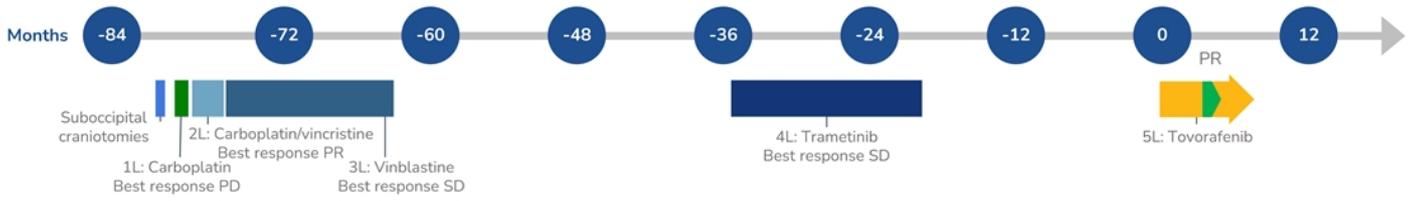


- PR (-58%) and improvement in vision reported at cycle 3
- AEs included grade 3 erythematous rash requiring dose interruption and dose reduction (400 mg QW to 300 mg QW in cycle 1), and grade 2 eczema and maculopapular rash
- Patient continues to receive weekly tovorafenib

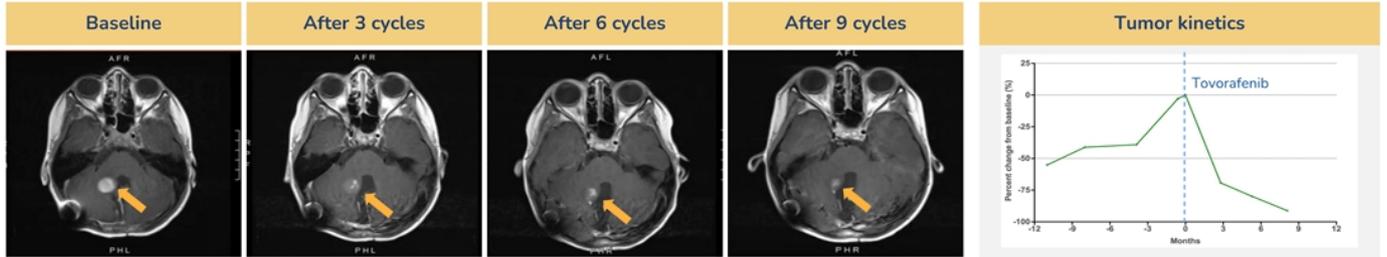


Case Study: Activity Of Tovorafenib (DAY101) In KIAA1549-BRAF Fusion Posterior Fossa Pilocytic Astrocytoma

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

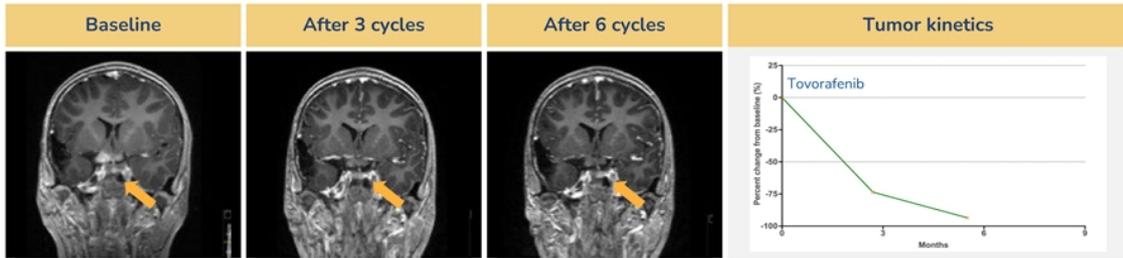


Case Study: Activity Of Tovorafenib (DAY101) In BRAF V600E Mutation Deep Midline Astrocytoma

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

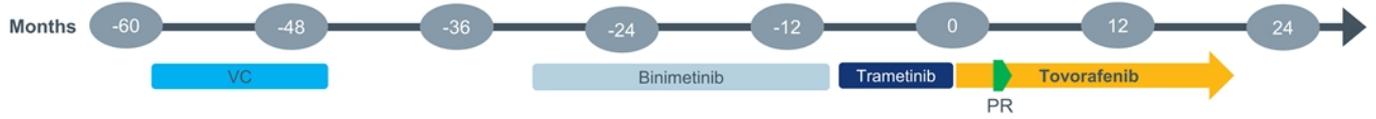


- PR (-74%) at cycle 3, with a deepening of response (-94%) at cycle 6
- AEs included grade 3 maculopapular rash and increased CPK, requiring drug interruption and dose reduction (500 mg QW to 400 mg QW in cycle 1)
- Tovorafenib dose was re-escalated back to 500 mg QW in cycle 4; patient continues on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

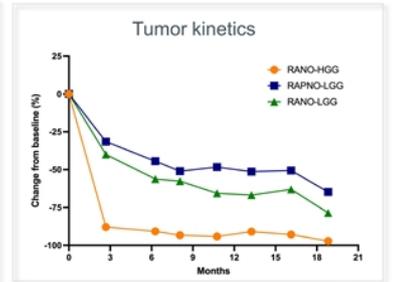
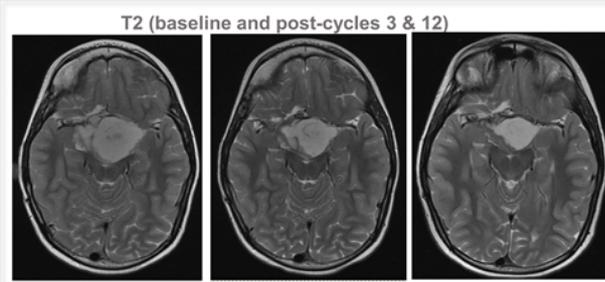
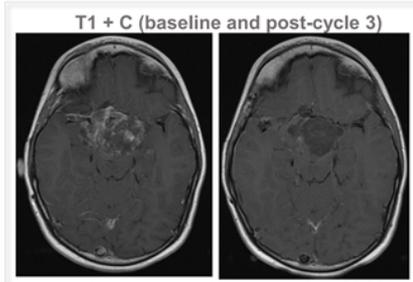


Case Study: Activity Of Tovorafenib (DAY101) In *KIAA1549-BRAF* Fusion Optic Pathway Glioma

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)



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
German Cancer Research Center (DKFZ)
Heidelberg University Hospital
Heidelberg University

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

