

**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 07, 2022**

**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 2.02 Results of Operations and Financial Condition.**

On November 7, 2022, Day One Biopharmaceuticals, Inc. issued a press release announcing its financial results for the quarter ended September 30, 2022. A copy of the press release is attached as Exhibit 99.1 to this report.

**Item 7.01 Regulation FD Disclosure.**

On November 7, 2022, Day One Biopharmaceuticals, Inc. 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	<a href="#">Press release issued by Day One Biopharmaceuticals, Inc. regarding its financial results for the quarter ended September 30, 2022, dated November 7, 2022.</a>
99.2	<a href="#">Corporate Presentation.</a>
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

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**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: November 7, 2022

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

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## Day One Reports Third Quarter 2022 Financial Results and Corporate Progress

Topline results for full pivotal FIREFLY-1 study population with tovorafenib (DAY101) in relapsed or progressive pediatric low-grade glioma (pLGG) are expected in the first quarter of 2023

Strengthened leadership team with key appointments to senior management team and board of directors

**SOUTH SAN FRANCISCO, Calif., November 7, 2022** – 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 financial results for the third quarter of 2022 and highlighted recent corporate achievements.

“Day One’s progress in 2022 has been remarkable. We announced positive interim results from our pivotal FIREFLY-1 study with tovorafenib in relapsed or progressive pLGG in patients harboring activating RAF alterations, completed a follow-on public offering, advanced our pivotal Phase 3 FIREFLY-2/LOGGIC trial for frontline pLGG as well as our Phase 2 FIRELIGHT-1 trial for MAPK-altered solid tumors, and recently entered into a CRADA agreement with the NCI to further expand therapeutic research opportunities using tovorafenib,” said Jeremy Bender, Ph.D., chief executive officer of Day One. “With this significant momentum, we believe we are well-positioned to continue to execute on our mission. We look forward to the topline results from the full FIREFLY-1 pivotal study population, expected in the first quarter of 2023, and potential subsequent NDA submission to the FDA. 2023 is poised to be another pivotal year for Day One.”

### Program Highlights

- Pivotal FIREFLY-1 trial of tovorafenib in relapsed or progressive pLGG in patients harboring activating RAF alterations continues to progress following positive initial data from the first 25 patients announced in June 2022.
    - Additional interim results from FIREFLY-1 will be presented at the Society for Neuro-Oncology (SNO) annual meeting in November 2022.
  - Day One is conducting a pivotal Phase 3 clinical trial (FIREFLY-2/LOGGIC) evaluating tovorafenib as a front-line therapy for patients newly diagnosed with pLGG.
    - The study is a randomized, monotherapy, open-label trial aiming to enroll approximately 400 patients aged 6 months to 25 years across approximately 100 sites globally, including in the United States, Europe and Asia.
    - The primary endpoint will be the ORR based upon Response Assessment for Neuro-Oncology (RANO) criteria as reported by Blinded Independent Central Review.
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- o Secondary endpoints will include safety, progression-free survival, overall survival, duration of response, functional outcomes and quality of life measures.
- Patient enrollment continues in the Phase 2 FIRELIGHT-1 trial evaluating tovorafenib as a monotherapy and as a combination with the company's investigational MEK inhibitor, pimasertib, in adults and adolescents with recurrent, progressive, or refractory solid tumors harboring MAPK pathway aberrations.
- Day One recently entered into a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute's (NCI) Division of Cancer Treatment and Diagnosis, Cancer Therapy Evaluation Program (CTEP) to expand therapeutic research opportunities using tovorafenib.
  - o NCI investigators will have the opportunity to study tovorafenib in CTEP-sponsored trials to be conducted by NCI-funded extramural clinical networks in several solid tumor and hematologic cancers.
- The company also recently announced a global collaboration with Foundation Medicine to develop FoundationOne@CDx as a companion diagnostic for tovorafenib.

### **Corporate Highlights and Upcoming Milestones**

- Garry Nicholson was appointed as chairman of Day One's board of directors. Mr. Nicholson brings more than 30 years of pharmaceutical and biotech oncology experience and previously served as president of Pfizer Oncology where he led its global oncology franchise.
- Day One strengthened its leadership team with the appointment of Adam Dubow as general counsel. Mr. Dubow joins Day One following a 22-year tenure at Bristol Myers Squibb, where he most recently served as chief compliance and ethics officer and a member of the company's management team.
- Day One anticipates releasing topline results for the full FIREFLY-1 pivotal study population in the first quarter of 2023. If the data are supportive, Day One expects to submit a new drug application (NDA) to the United States Food and Drug Administration (FDA) in the first half of 2023.
- Day One expects to dose the first patient in FIREFLY-2/LOGGIC trial in the fourth quarter of 2022.

### **Third Quarter 2022 Financial Highlights**

- **Cash Position:** Cash, cash equivalents and short-term investments totaled \$374.3 million on September 30, 2022. 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 \$22.0 million for the third quarter of 2022 compared to \$9.8 million for the third quarter of 2021. The increase was primarily due to additional employee compensation costs, clinical trial and pre-commercial manufacturing activities related to Day One's lead product candidate, tovorafenib.
- **G&A Expenses:** General and administrative expenses were \$17.7 million for the third quarter of 2022 compared to \$9.4 million for the third quarter of 2021. 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 \$37.8 million for the third quarter of 2022 compared to \$19.2 million for the third quarter of 2021 with non-cash stock compensation expense of \$8.6 million and \$5.1 million for the third quarters of 2022 and 2021, respectively.

#### Upcoming Events

- Society for Neuro-Oncology (SNO) annual meeting, November 16-20, 2022
- 34<sup>th</sup> Annual Piper Sandler Healthcare Conference, November 29–December 1, 2022

#### Inducement Grants

In connection with Mr. Dubow's appointment as general counsel, the compensation committee of the company's board of directors granted Mr. Dubow 47,400 restricted stock units (RSUs) and 309,000 options to purchase shares of the company's common stock on October 31, 2022 pursuant to the terms of the Company's 2022 Equity Inducement Plan. The grants of the RSUs and options were approved by the compensation committee as inducements to Mr. Dubow commencing employment with Day One, in accordance with Nasdaq Marketplace Rule 5635(c)(4). The RSUs vest as to 25% on the first anniversary of the first Quarterly Vesting Date (as defined below), and 1/12th of the remaining RSUs will vest quarterly thereafter, on each applicable quarterly vesting date. For purposes of this announcement, "Quarterly Vesting Date" means February 15, May 15, August 15 or November 15. Each RSU is subject to the terms and conditions of the 2022 Equity Inducement Plan and restricted stock unit agreement covering the grant. The options have an exercise price per share equal to the closing selling price as reported on the Nasdaq Stock Market for the grant date. 1/4th of the options vest and become exercisable on the one-year anniversary of the grant date, and 1/48th of the options vest and become exercisable on a monthly basis thereafter, in each case, so long as the employee remains employed by Day One through the applicable vesting date. The options have a ten-year term and are subject to the terms and conditions of the 2022 Equity Inducement Plan and stock option agreement covering the grant.

**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 and solid tumors harboring activating RAF alterations. 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 pediatric low-grade glioma (pLGG), which is an area of considerable unmet need with no approved therapies for the majority of patients. Day One has also initiated a pivotal Phase 3 study (FIREFLY-2/LOGGIC) in newly-diagnosed patients with pLGG. Beyond pLGG, tovorafenib is being evaluated alone or 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 U.S. Food and Drug Administration (FDA) for the treatment of patients with pLGG harboring an activating RAF alteration. Tovorafenib has also received Orphan Drug designation from the FDA for the treatment of malignant glioma, and from the European Commission (EC) for the treatment of glioma.

**About Pimasertib**

Pimasertib is an investigational, oral, highly selective, small molecule inhibitor of mitogen-activated protein kinases 1 and 2 (MEK-1/-2) within the MAPK signaling pathway. Pimasertib has been dosed in over 850 patients to date for various tumor types. Preclinical data indicates that the combination of a MEK inhibitor, such as pimasertib, and a type II RAF inhibitor, such as tovorafenib, has synergistic anti-tumor activity.

Day One is conducting a Phase 1b/2 study (FIRELIGHT-1) to evaluate the safety, tolerability, and preliminary efficacy of combining pimasertib with tovorafenib in adolescent and adult patients ( $\geq 12$  years of age) with recurrent, progressive, or refractory solid tumors with MAPK pathway aberrations.

**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 "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 (DAY101), 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 South San Francisco. For more information, please visit [www.dayonebio.com](http://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 and Comprehensive Loss**  
**(unaudited)**  
**(In thousands)**

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Operating expenses:				
Research and development	\$ 22,035	\$ 9,849	\$ 59,598	\$ 32,395
General and administrative	17,664	9,392	44,568	18,373
Total operating expenses	39,699	19,241	104,166	50,768
Loss from operations	(39,699)	(19,241)	(104,166)	(50,768)
Interest income (expense), net	1,895	(6)	2,086	(19)
Other income (expense), net	9	7	8	(29)
Net loss	(37,795)	(19,240)	(102,072)	(50,816)
Net loss attributable to redeemable convertible noncontrolling interest	—	—	—	(2,109)
Exchange of redeemable noncontrolling interest shares – deemed dividend	—	—	—	(99,994)
Net loss attributable to common stockholders/members	\$ (37,795)	\$ (19,240)	\$ (102,072)	\$ (148,701)
Net loss per share, basic and diluted	\$ (0.53)	\$ (0.33)	\$ (1.61)	\$ (4.98)
Weighted-average number of common shares used in computing net loss per share, basic and diluted	71,008,993	57,514,218	63,522,774	29,859,883

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

	September 30, 2022	December 31, 2021
Cash, cash equivalents, and short-term investments	\$ 374,341	\$ 284,309
Total assets	381,861	289,821
Total liabilities	18,785	8,673
Accumulated deficit	(229,559)	(127,487)
Total stockholders' equity	363,076	281,148

**Contacts:**

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# Targeted Therapies for People of All Ages

November 2022

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# 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 and cash equivalents 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 profile of our product candidates, the 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 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 the COVID-19 pandemic, inflation, and rising interest rates, 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.

# Day One: Developing Targeted Therapies That Address The Urgent Needs of Children With Cancer

## 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
- Multiple key milestones
  - Top-line data from FIREFLY-1 trial in Q1 2023
  - NDA submission in 1H 2023, if data are supportive
  - First patient dosing in pivotal Phase 3 (FIREFLY-2 /LOGGIC), frontline trial expected Q4 2022

# Pediatric Markets Create Opportunity for High Impact and Capital Efficiency



## Regulatory and reimbursement tailwinds

- Lack of approved products create potential first-in-class opportunities
- Pricing flexibility for important new therapies
- Supportive and engaged advocacy and investigator community desiring better treatment options



## Rapid clinical development

- Early engagement with global regulatory authorities
- Small trials and clear endpoints that permit rapid development to clinical proof-of-concept and potential approval



## Enriched responder populations informed by underlying biology

- Many pediatric tumors are genetically simple and genomically stable
- Genetic alterations are often oncogenic

# A Senior Team with Deep Experience Developing and Commercializing Products in Pediatric and Adult Oncology Markets



**Jeremy Bender, PhD, MBA**

*Chief Executive Officer*

VP of Corporate Development at Gilead; COO Tizona Therapeutics; CBO Sutro Biopharma; founding Board member of VaxCyte



**Samuel Blackman, MD, PhD**

*Chief Medical Officer & Founder*

Pediatric Heme/Onc and Neuro-Onc; Oncology Clinical Development at Mavupharma, Silverback, Juno, Seattle Genetics, GSK



**Charles York II, MBA**

*Chief Operating and Financial Officer*

CFO and Head of Corporate Development at Aeglea; Consulting CFO at Bridgepoint Consulting; PricewaterhouseCoopers



**Mike Preigh, PhD**

*Chief Technical Officer*

Head of CMC at Array for 10+ years. Brought >20 drug candidates to IND & clinical development



**Davy Chiodin, PharmD**

*Chief Development Officer*

VP Regulatory Science, Acerta/AZ; Global Regulatory Leader, Pediatric Oncology, Roche/Genentech



**Jaa Roberson**

*Chief People Officer*

Head of Human Resources at Bellicum Pharmaceuticals; Human Resources Roles at Achaogen, Roche/Genentech



**Adam Dubow**

*General Counsel*

Chief Compliance & Ethics Officer at Bristol Myers Squibb (BMS); Legal leadership roles at BMS in the U.S., Asia and Europe; Partner at Sedgwick, Detert, Moran & Arnold

# Our Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Recent & Anticipated Milestones
<b>Tovorafenib (DAY101)</b> 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 gliomas ✓ EC Orphan Designation for gliomas	Relapsed pLGG	FIREFLY-1 <sup>1</sup> (pivotal) 				Pivotal cohort enrollment complete: <b>May 2022</b> Initial data presented: <b>June 2022</b> Topline data expected: <b>Q1 2023</b>
	Frontline pLGG	FIREFLY-2 (pivotal) 				Trial initiation: <b>June 2022</b> First patient dosing expected: <b>Q4 2022</b>
	RAF-altered solid tumors <sup>2</sup> (monotherapy)	FIRELIGHT-1* 				First patient dosed: <b>November 2021</b>
<b>Pimasertib</b> MEK 1/2 Inhibitor	MAPK-altered solid tumors <sup>3</sup> (Combo w/tovorafenib)	FIRELIGHT-1* 				First patient dosed: <b>May 2022</b>

<sup>1</sup>Includes patients ≥12 years of age. <sup>2</sup>FIREFLY-1 Arm 1 expected to support registration. <sup>3</sup>DAY101 adult monotherapy Phase 1 dose escalation and expansion trial previously completed. <sup>4</sup>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.  
 Day One Biopharmaceuticals

# Tovorafenib (DAY101)

Type II Pan-RAF Inhibitor

# Pediatric Low-Grade Gliomas (pLGG)

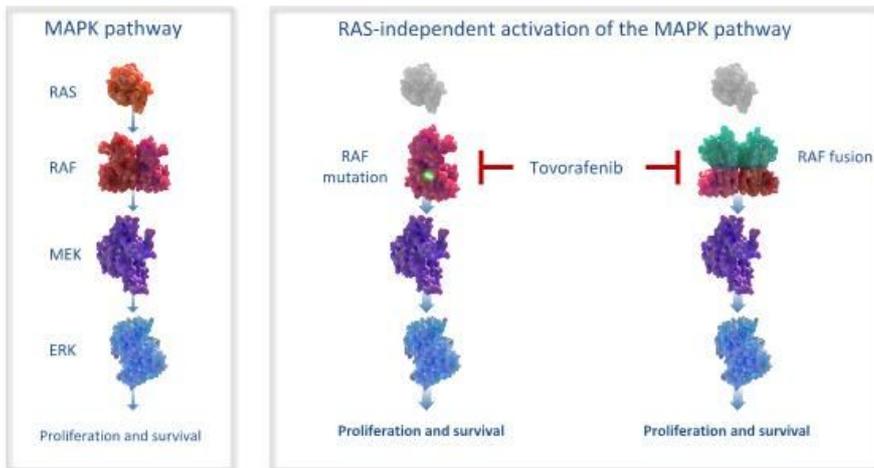


6 y/o with large relapsed BRAF fusion-positive optic pathway glioma

- 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<sup>1,2</sup>
  - 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<sup>3</sup>
  - 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<sup>1-4</sup>
  - 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. Trautwieser T et al., Neurooncol Adv. 2020; 2:vdaa094; Day One Biopharmaceuticals

# 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 wild-type fusions and BRAF V600E mutations
  - Tablet and pediatric-friendly liquid suspension; once weekly dosing
- **Currently approved type I RAFi are indicated for use only in adults and patients 6+ with relapsed tumors harboring a BRAF V600 mutation**
  - Type I RAF inhibitors cause paradoxical MAPK activation in the setting of wild-type RAF, increasing the risk of tumor growth in BRAF fusion-driven and other non-V600 mutant cancers

# 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, Bandopadhyay et al. *Pediatric Blood Cancer*, 2014; Snow and Fischer. *J Child Neurol*, 2009; ClearView Analysis; GTR: Gross Total Resection 1 Molecular testing of biopsied samples occurs in all patients; Kandets et al. *Retrospective analysis of comprehensive SIOF registry*; Hargrave et al. *Phase III*; Fangusaro et al. *Phase II*

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

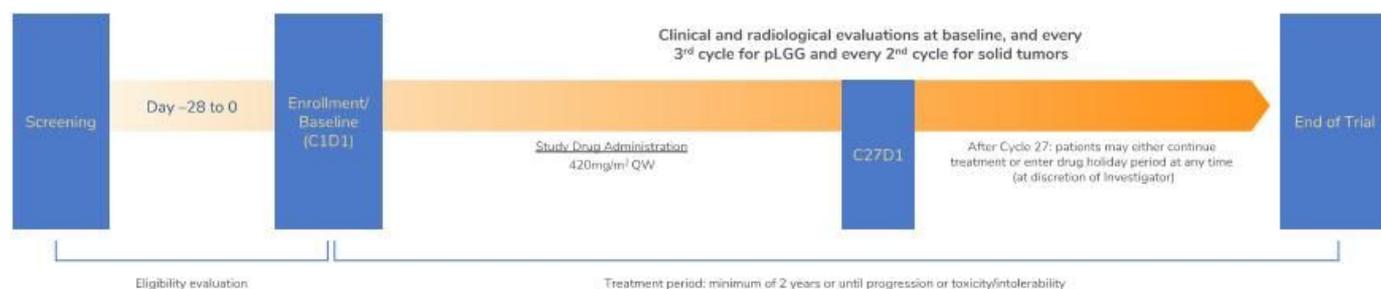


## Trial Design

- Three arm, open-label, global registrational phase 2 trial
- Pivotal Arm 1 (recurrent/progressive LGG): n = ~ 60 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 criteria, assessed by blinded independent central review
- **Secondary endpoints:** ORR by RAPNO criteria; PFS; safety

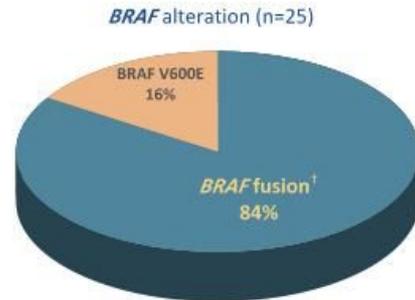
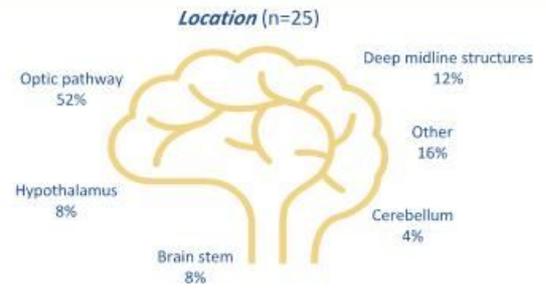


Abbreviations: C, cycle; D, day; LGG, low-grade glioma; ORR, objective response rate; PFS, progression-free survival.  
NCT04775485

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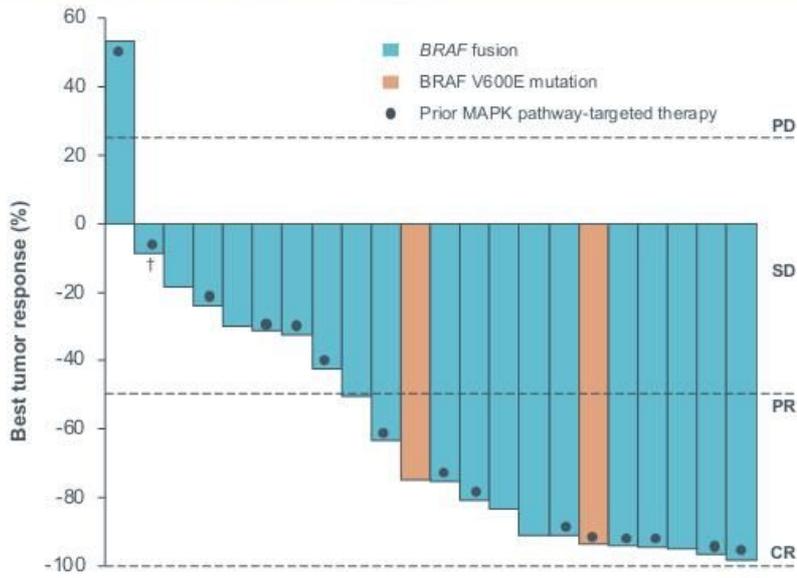
# Baseline Characteristics

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)



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.

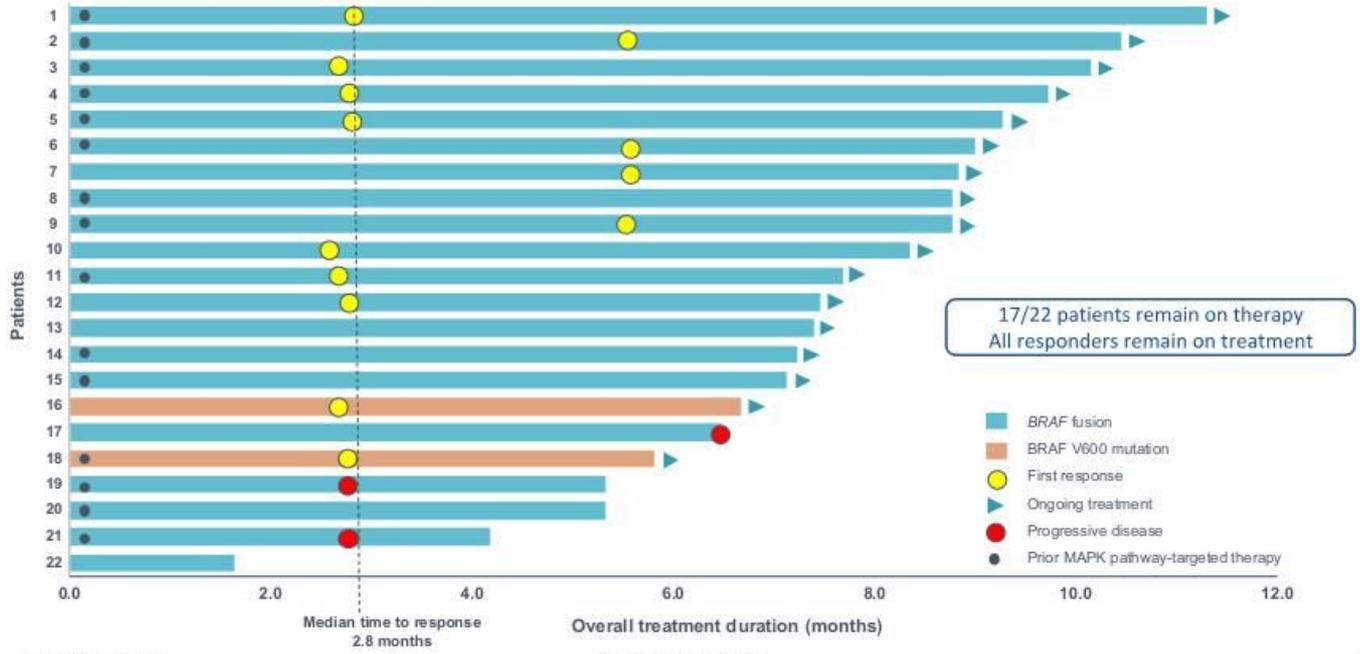
# Tumor Response To Tovorafenib (DAY101) For All Patients With RANO-Evaluable Lesions (n=22)\*



Response (IRC)	RANO 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-Evaluable Lesions (n=22)



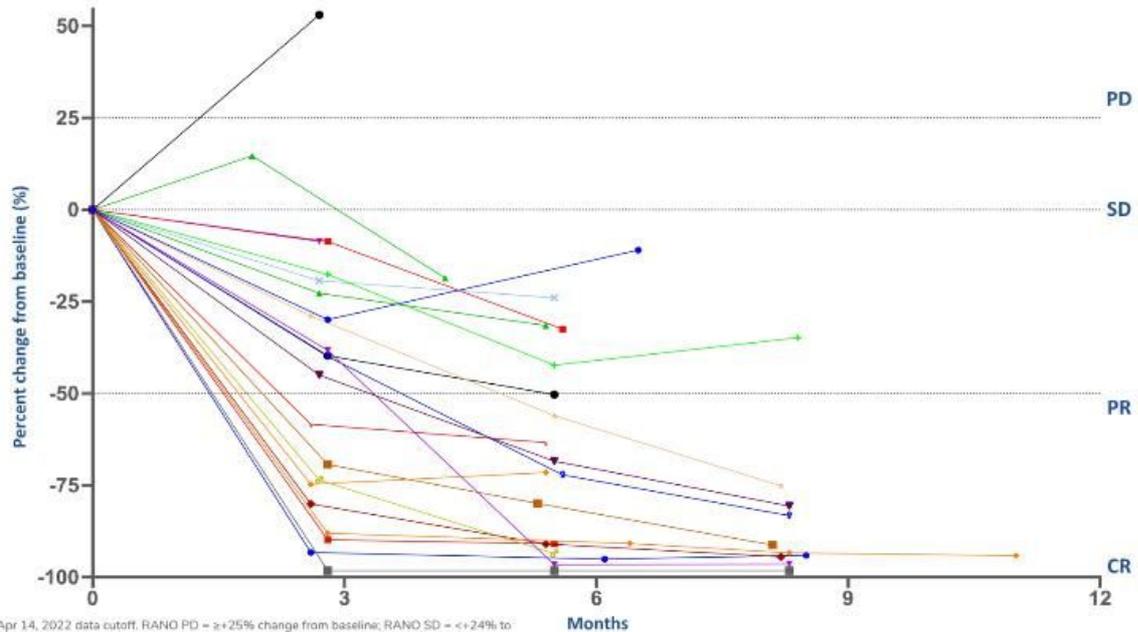
Apr 14, 2022 data cutoff.

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# Individual Patient Tumor Change From Baseline

(n=22 RANO-Evaluable By Blinded Independent Central Review)



Apr 14, 2022 data cutoff. RANO PD =  $\geq +25\%$  change from baseline; RANO SD =  $< +24\%$  to  $> -50\%$  change from baseline; RANO PR =  $\leq -50\%$  change from baseline; RANO CR =  $< -75\%$  change from baseline.

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

Preferred term, n (%)	Treatment-emergent AEs		Treatment-related AEs	
	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

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# Key Takeaways

- **Encouraging initial efficacy data from FIREFLY-1 for pediatric patients with relapsed 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-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 1H 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 criteria, assessed by blinded independent central review

# Incidence and Prevalence of BRAF-altered pLGG in the U.S.

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

	<b>~1,100</b> Estimated Annual Incidence	<b>~26,000</b> Estimated Prevalence (SEER)
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<sup>1</sup> US Census; <sup>2</sup> CBTRUS; Qaddoumi et al 2009; Schrock et al 2013; ClearView Analysis; <sup>3</sup> SEER US complete prevalence results of patients aged under 25 with Brain and Other Nervous System tumors as of January 1, 2017.

Estimated annual incidence and estimated prevalence (SEER) 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

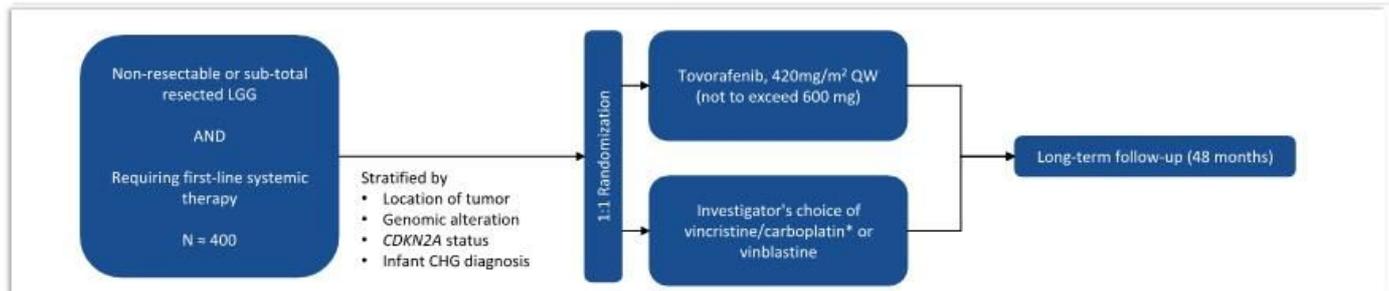


## Trial Design

- 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 criteria, assessed by blinded independent central review
- 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

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# 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**

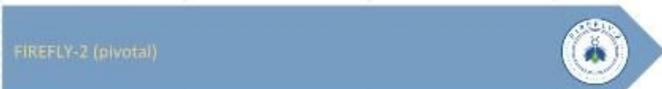
LOGGIC: Low Grade Glioma In Children



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# Our Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Recent & Anticipated Milestones
<b>Tovorafenib (DAY101)</b> 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 gliomas ✓ EC Orphan Designation for gliomas	Relapsed pLGG	FIREFLY-1 <sup>1</sup> (pivotal) 				Pivotal cohort enrollment complete: <b>May 2022</b> Initial data presented: <b>June 2022</b> Topline data expected: <b>Q1 2023</b>
	Frontline pLGG	FIREFLY-2 (pivotal) 				Trial initiation: <b>June 2022</b> First patient dosing expected: <b>Q4 2022</b>
	RAF-altered solid tumors <sup>2</sup> (monotherapy)	FIRELIGHT-1* 				First patient dosed: <b>November 2021</b>
<b>Pimasertib</b> MEK 1/2 Inhibitor	MAPK-altered solid tumors <sup>3</sup> (Combo w/tovorafenib)	FIRELIGHT-1* 				First patient dosed: <b>May 2022</b>

<sup>1</sup>Includes patients ≥12 years of age. <sup>2</sup>FIREFLY-1 Arm 1 expected to support registration. <sup>3</sup>DAY101 adult monotherapy Phase 1 dose escalation and expansion trial previously completed. <sup>4</sup>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.  
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# Tovorafenib (DAY101) is Active as a Monotherapy in Patients with RAF-altered Adult Solid Tumors and Has Shown Strong Synergy Preclinically in Combination



**Clinical activity** demonstrated in relapsed melanoma patients; preclinical activity demonstrated in RAF fusions, BRAF non-V600 mutations, and BRAF V600 mutations

- >225 adult patient exposures
- Responses in BRAF V600E mutant tumors similar to type I BRAF inhibitors
- Responses in relapsed BRAF and NRAS-mutant melanoma, suggesting tovorafenib (DAY101) may be active in tumors currently unaddressed by approved Type I BRAF inhibitors



**Differentiated** safety profile for tovorafenib (DAY101) vs. existing BRAF and MEK inhibitors

- Less frequent and less severe acneiform rash
- No observed ophthalmologic liabilities (RVO/CSR)
- No observed CV liabilities (changes in LVEF)
- No type I BRAF SAEs: SCCs/KAs, pyrexia, arthralgia



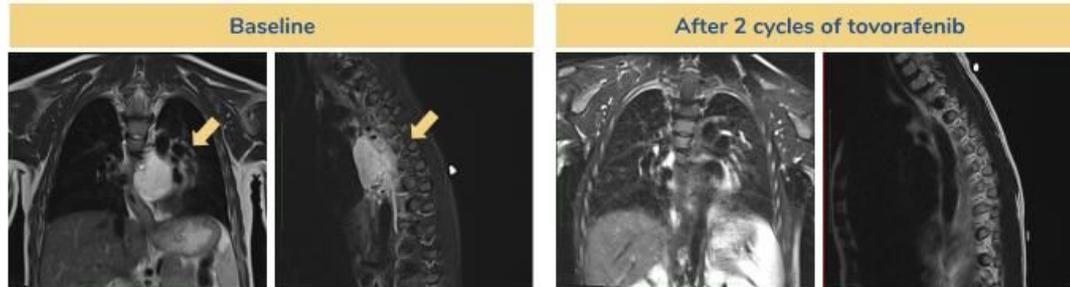
We **initiated** an adult solid tumor **study** to further evaluate monotherapy tovorafenib (DAY101) in patients with RAF altered tumors for which there are no currently approved therapies

- Same study will include combination cohorts of tovorafenib (DAY101) + pimasertib
- First patient dosed in Phase 2 monotherapy study in November 2021

Source: Oltzanaki AJ et. al. European Society for Medical Oncology Congress Poster #410P, 2017  
Unpublished clinical study results

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

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



- 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

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

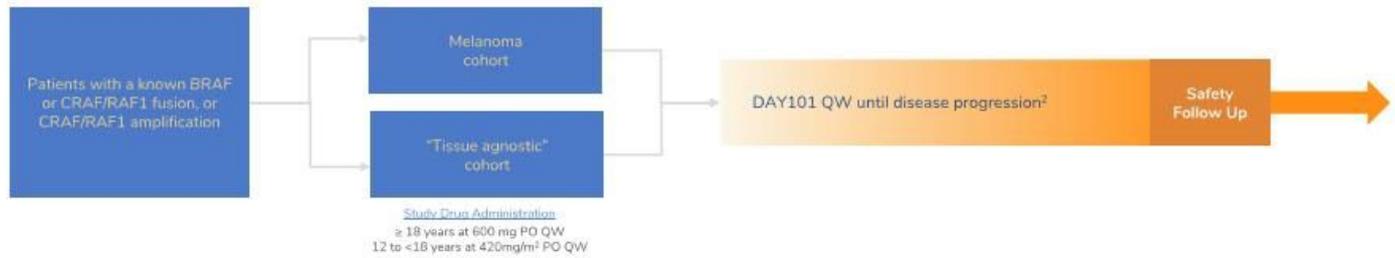


## Trial Design<sup>1</sup>

- 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 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 0

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

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

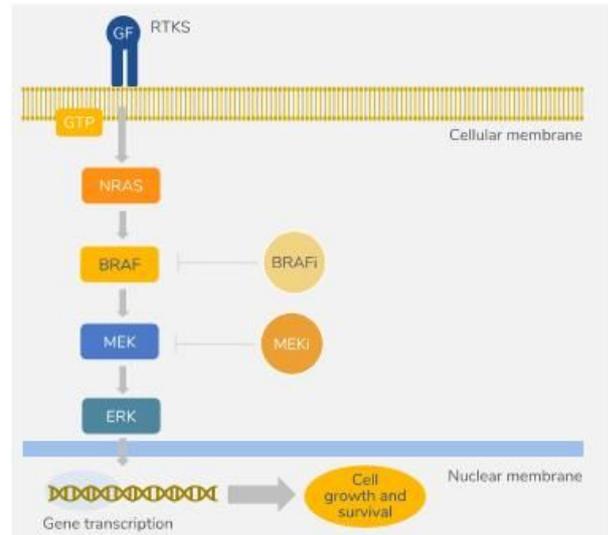
	BRAF non-V600	BRAF or CRAF WT fusion	KRAS or NRAS mutant	NF1 LOF
Signaling pathways	<p>Proliferation, survival</p>	<p>Proliferation, survival</p>	<p>Proliferation, survival</p>	<p>Proliferation, survival</p>
Potential combinations	Type II RAFi + MEKi or SHP2i	Type II RAFi + MEKi	Type II RAFi + KRAS - G12Ci or MEKi or SHP2i	Type II RAFi + SHP2i
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: Allosteric MEK1/2 Inhibitor with Demonstrated Activity in MAPK-driven Solid Tumors

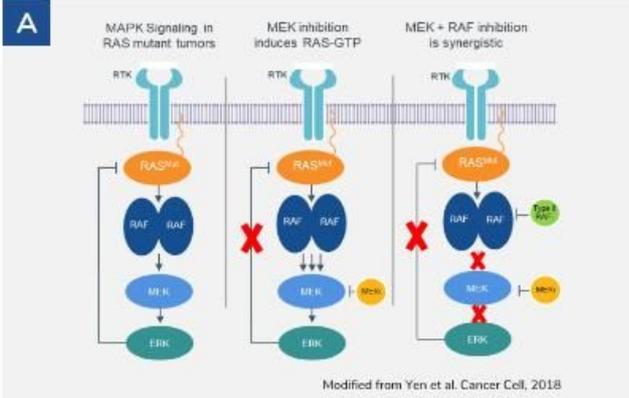
- Pimasertib is an orally-bioavailable, selective, non-competitive MEK1/2 inhibitor in-licensed from Merck KGaA in February 2021
- Extensive non-clinical and clinical development work through Phase 2, including a solid tumor trial in Japan and combinations with other MOAs
- Main AEs typical for all in-class 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



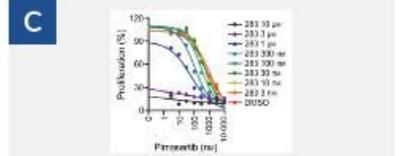
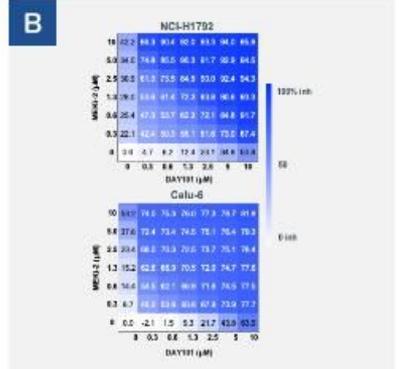
Source: Hefner, Saigues, Anjos, et al. 2017.

# Vertical MAPK Pathway Inhibition with Tovorafenib (DAY101) and Pimasertib Unlocks Potential Synergy for Adult Solid Tumors

- The MAPK pathway normally has multiple feedback loops that negatively regulate upstream (RAS/RAF) activation to ensure optimal signaling
- Monotherapy MEK inhibition disables these feedback loops and induces RAS signaling as well as RAF dimerization and activation
- Combination therapy with a MEK inhibitor and type II RAF inhibitor is synergistic in KRASmut and BRAFmut tumor models



- A** Mechanistic model for vertical MAPK pathway inhibition (modified from Yen et al. Cancer Cell, 2018).
- B** DAY101 + MEK inhibitor is synergistic in KRAS G12C and Q61 mutant tumor cell models (Day One internal data)
- C** Sensitivity of KRAS Q61 mutant cells to pimasertib is enhanced when cells are treated with the type II RAF inhibitor BGB-283 (Yuan et al., Mol Onc 2020)



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

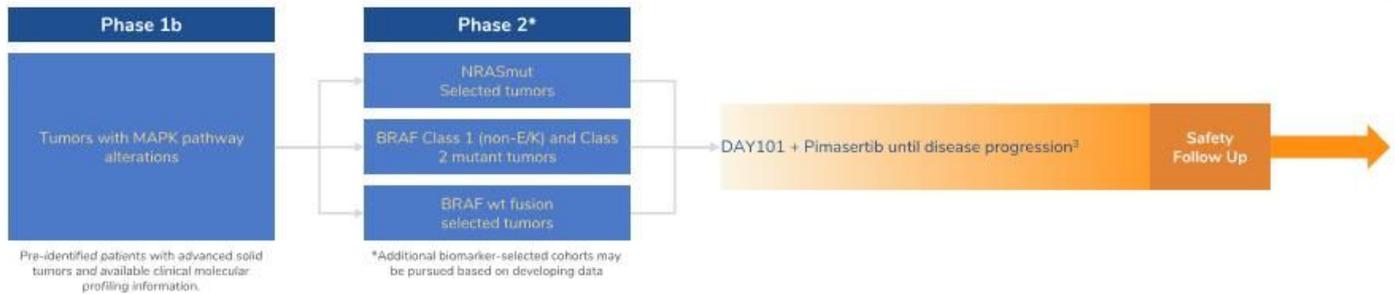


## Trial Design<sup>1</sup>

- Combination dose escalation, global phase 1b/2 trial<sup>2</sup>
- 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 sites. <sup>3</sup>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 September 30, 2022: \$374.3 million (no debt)

73.5 million shares of common stock outstanding as of November 2, 2022

\$ Millions	Nine Months Ended 9/30/22	Nine Months Ended 9/30/21
R&D Expense	\$59.6	\$32.4
G&A Expense	\$44.6	\$18.4
Net Loss	\$102.1	\$50.8

**Projected  
cash runway  
into 2025**

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

- Pivotal cohort enrollment completed in May 2022
- Initial clinical data presented in June 2022
- Full topline results expected in Q1 2023
- NDA submission planned in 1H 2023, if data from FIREFLY-1 is supportive

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

- Trial initiated in June 2022
- First patient dosing expected in Q4 2022

**FIRELIGHT-1: Tovorafenib (DAY101) and pimasertib combination**

- First patient dosed in May 2022



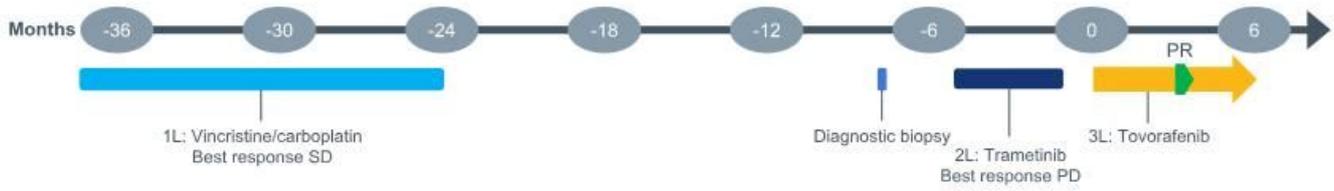
# Appendix

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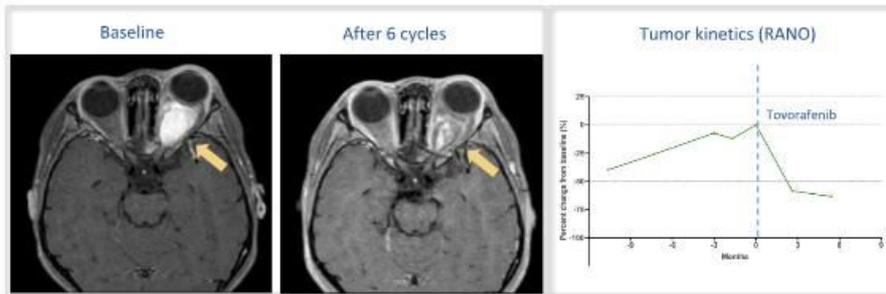


# Case Study: Activity Of Tovorafenib (DAY101) In KIAA1549-BRAF Fusion Optic Pathway Glioma

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.

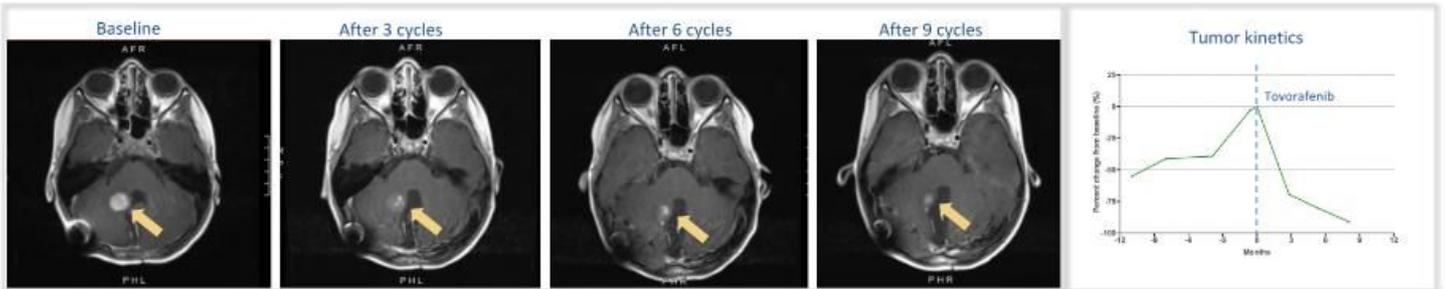
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# Case Study: Activity Of Tovorafenib (DAY101) In KIAA1549-BRAF Fusion Posterior Fossa Pilocytic Astrocytoma

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



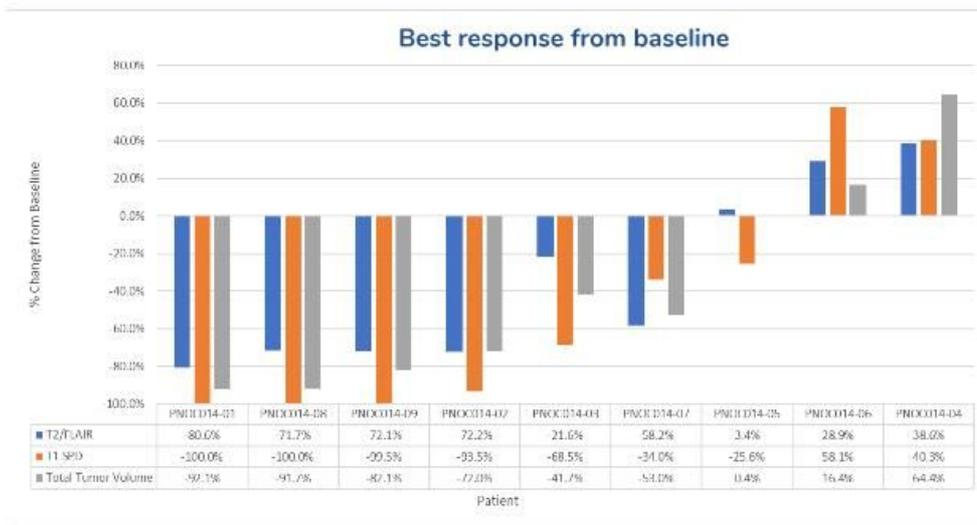
Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

# FIREFLY-1 Study Status

- First patient dosed in May 2021. Registrational pLGG arm completed enrollment in May 2022
- ~35 sites opened across 11 countries
- Expanded access to patients with pLGG (arm 2) and *RAF* fusion-positive solid tumors (arm 3)
- Interim efficacy and safety analysis in the first 25 consecutively enrolled patients who had:
  - Received at least 1 dose of study treatment
  - At least 6 months of follow-up as of April 14, 2022
- Tumor assessments according to RANO criteria, as determined by a blinded independent radiological review committee
- 22 patients with RANO-evaluable tumors

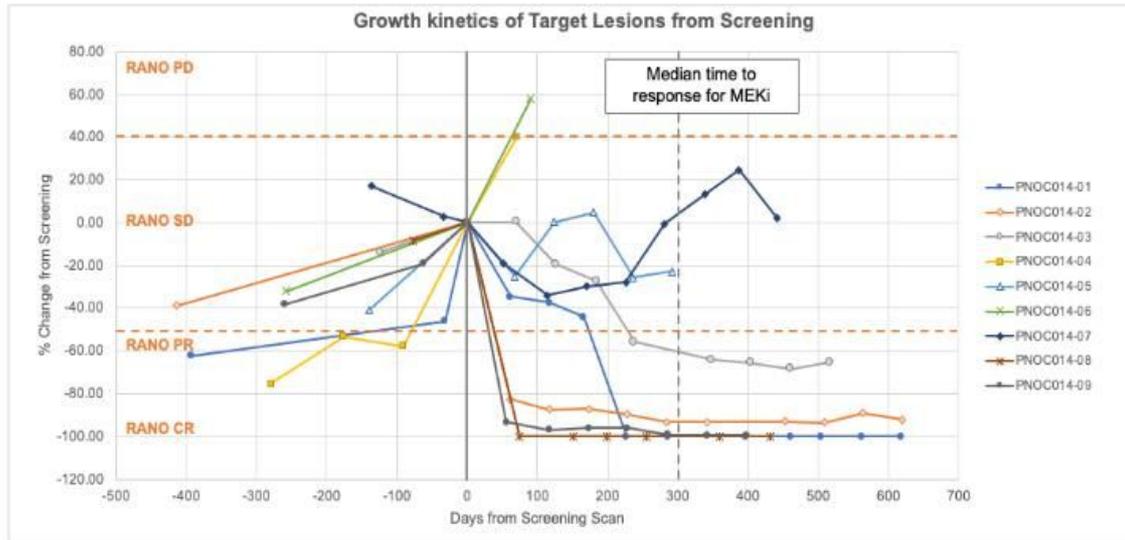


# Results from Independent Radiology Review of PNOC014



- RANO: Response assessment for neuro-oncology (FDA standard)
- Volumetric image analysis (exploratory)
- RAPNO: Response assessment for pediatric neuro-oncology (exploratory)

# 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 CTN1-19.2020  
Fangusaro J et al. Lancet Oncol 2019

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# 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 monotherapy 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%)		