UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 12, 2022

DAY ONE BIOPHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

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

395 Oyster Point Blvd., Suite 217 **South San Francisco, California** **(Address of principal executive offices)**	**94080** **(Zip Code)**

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

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

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

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

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

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

Emerging growth company ☒

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

Item 2.02 Results of Operations and Financial Condition.

On May 12, 2022, Day One Biopharmaceuticals, Inc. issued a press release announcing its financial results for the quarter ended March 31, 2022. A copy of the press release is attached as Exhibit 99.1 to this report.

Item 7.01 Regulation FD Disclosure.

On May 12, 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	Press release issued by Day One Biopharmaceuticals, Inc. regarding its financial results for the quarter ended March 31, 2022, dated May 12, 2022.
99.2	Corporate Presentation
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

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

DAY ONE BIOPHARMACEUTICALS, INC.

Date: May 12, 2022

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

Day One Reports First Quarter 2022 Financial Results and Provides Business Update

Initial data from pivotal FIREFLY-1 study with tovorafenib (DAY101) in relapsed pediatric low-grade glioma (pLGG) expected in June 2022

Company plans to initiate pivotal Phase 3 FIREFLY-2 clinical trial evaluating tovorafenib as a first-line therapy in pLGG in the second quarter of 2022

Initiated Phase 1b/2 combination study with tovorafenib and pimasertib in RAF-altered solid tumors

SOUTH SAN FRANCISCO, Calif., May 12, 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 first quarter of 2022 and highlighted recent corporate achievements.

“We continue to make excellent progress across our clinical programs and look forward to reporting initial data from our pivotal Phase 2 FIREFLY-1 trial in relapsed pLGG next month,” said Jeremy Bender, Ph.D., chief executive officer of Day One. “These initial data will provide preliminary insights into the potential of tovorafenib to transform patient care for the most common childhood brain cancer, which currently has no approved therapies. Beyond FIREFLY-1, we are preparing to initiate a pivotal Phase 3 study, FIREFLY-2, for the first-line treatment of pLGG patients and recently initiated the combination portion of our Phase 2 FIRELIGHT-1 study with tovorafenib and our investigational oral MEK inhibitor, pimasertib. As our clinical programs advance, we continue to accelerate planning for our first potential regulatory submission for tovorafenib in 2023 and execute on our business strategy to make an impact for patients of all ages with life threatening diseases.”

Program Highlights

- Initial data from FIREFLY-1, a pivotal Phase 2 clinical trial of tovorafenib in relapsed pLGG, is expected in June 2022.
- Day One anticipates releasing topline results from the fully-enrolled pivotal study in the first quarter of 2023. Pending positive results from FIREFLY-1, Day One anticipates filing a new drug application (NDA) with the U.S. Food and Drug Administration (FDA) in 2023.

- Day One has expanded the FIREFLY-1 study to include two additional study arms:
    - An expanded access arm that enables treatment for eligible patients once the primary cohort has completed enrollment; and
    - An advanced solid tumor arm to evaluate the preliminary efficacy of tovorafenib in patients aged 6 months to 25 years with a relapsed or progressive extracranial solid tumors with activating RAF fusion.

- Day One plans to initiate a pivotal Phase 3 clinical trial (FIREFLY-2) evaluating tovorafenib as a front-line therapy in pLGG in the second quarter of 2022.

- Day One is enrolling patients in the Phase 2 FIRELIGHT-1 trial evaluating tovorafenib monotherapy in adults with recurrent, progressive, or refractory solid tumors harboring MAPK pathway aberrations. Day One recently expanded FIRELIGHT-1 to include a Phase 1b/2 portion to evaluate tovorafenib in combination with pimasertib, Day One's investigational MEK inhibitor.

First Quarter 2022 Financial Highlights

- **Cash Position:** Cash and cash equivalents totaled $262.7 million on March 31, 2022. Based on Day One's current operating plan, management believes it has sufficient capital resources to fund anticipated operations into 2024.

- **R&D Expenses:** Research and development expenses were $15.0 million for the first quarter of 2022 compared to $12.6 million for the first quarter of 2021. The increase was primarily due to additional employee compensation costs, clinical trial and product development expenses which were offset by a decrease in milestone payments for licensing agreements.

- **G&A Expenses:** General and administrative expenses were $12.7 million for the first quarter of 2022 compared to $3.5 million for the first quarter of 2021. The increase was primarily due to additional employee compensation costs, initial commercial buildout, and professional expenses to support company growth.

- **Net Loss:** Net loss totaled $27.7 million for the first quarter of 2022 compared to $16.1 million for the first quarter of 2021 with non-cash stock compensation expense of $6.2 million and $0.5 million for the first quarters of 2022 and 2021, respectively.

Upcoming Events

- **2022 American Society of Clinical Oncology (ASCO) Annual Meeting**
    - A trial-in-progress poster on Day One's FIREFLY-1 pivotal study, abstract number TPS10062, will be presented at the ASCO Annual Meeting on Monday, June 6, 2022, from 8 to 11 a.m. CST.

- **The 20th International Symposium on Pediatric Neuro-Oncology (ISPNO) Annual Meeting**
    - An educational exhibit on Day One's pipeline will be displayed at Booth #F.05, at ISPNO's Annual Meeting, which is being held June 12-15, 2022.

About Tovorafenib
Tovorafenib is an investigational, oral, brain-penetrant, highly-selective type II pan-RAF kinase inhibitor designed to target a key enzyme in the MAPK signaling pathway, which is being investigated in primary brain tumors or brain metastases of solid tumors. Tovorafenib has been studied in over 250 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 pediatric low-grade glioma (pLGG), which is an area of considerable unmet need with no approved therapies. Tovorafenib is also 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 (≥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 developing targeted therapies for patients of all ages with life-threatening diseases. 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 is 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 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 clinical trial for DAY101 as designed, any expectations about safety, efficacy, timing and ability to complete clinical trials and to obtain regulatory approvals for DAY101 and other candidates in development, and the ability of DAY101 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 the COVID-19 pandemic 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.

Contacts:

Media:
1AB
Dan Budwick
dan@1abmedia.com

Investors:
LifeSci Advisors
Hans Vitzthum
hans@lifesciadvisors.com

Day One Biopharmaceuticals, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(unaudited)
(In thousands)

	Three Months Ended March 31,	
	2022	2021
Operating expenses:		
Research and development	$ 15,003	$ 12,632
General and administrative	12,745	3,454
Total operating expenses	27,748	16,086
Loss from operations	(27,748)	(16,086)
Interest income (expense), net	2	(7)
Other expense, net	(1)	(8)
Net loss and comprehensive loss	(27,747)	(16,101)
Net loss attributable to redeemable convertible noncontrolling interests	—	(919)
Net loss attributable to common stockholders/members	$ (27,747)	$ (15,182)
Net loss per share, basic and diluted	$ (0.48)	$ (2.58)
Weighted-average number of common shares used in computing net loss per share, basic and diluted	58,382,444	5,892,145

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

	March 31, 2022	December 31, 2021
Cash and cash equivalents	$ 262,731	$ 284,309
Total assets	267,779	289,821
Total liabilities	8,176	8,673
Accumulated deficit	(155,234)	(127,487)
Total stockholders' equity	259,603	281,148

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Day One
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Targeted Therapies for People of All Ages

May 2022

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, 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, our ability to obtain regulatory approval, the potential therapeutic benefits and economic value of our product candidates, potential growth opportunities, competitive position, industry environment and potential market opportunities, and the impact of the COVID-19 pandemic 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: Cancer Drug Development for People of All Ages

Mission That Creates Value	Specialized Team	Tovorafenib (DAY101) Lead Program	Growing Portfolio and Runway Beyond Clinical Milestones
• Develop medicines for genomically-defined cancers • Goal is to establish first-in-class position through rapid pediatric registration • Expand to adult populations in parallel	• Deep expertise in oncology, pediatric, and rare disease development, registration, and commercialization • Extensive network in the global pediatric oncology community • Proven track record of success in building biopharma companies	• Potential to be first-in-class oral, CNS-penetrant pan-RAFi • Potentially the first approval in a market with no standard of care • Monotherapy CRs and PRs in pediatric low-grade glioma (pLGG) • Breakthrough Therapy Designation, Rare Pediatric Disease Designation	• Two clinical-stage MEKi assets, in-licensed for combination trial • Projected cash runway into 2024 • Capital through pivotal data in pLGG and early adult solid tumor Phase 1b data

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

Lisa Bowers
Chief Commercial Officer
CEO of Rhia Ventures, COO of The Tara Health Foundation, VP of the North American Supply Chain and Commercial Leader at Genentech

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

Our Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Milestones
Tovorafenib (DAY101) Type II Pan-RAF Inhibitor ✓ FDA Breakthrough Therapy Designation ✓ FDA Rare Pediatric Disease Designation (PRV Eligible) ✓ FDA Orphan Drug Designation ✓ EC Orphan Designation	Relapsed pLGG	FIREFLY-1[1] (pivotal)				**Enrollment complete**: May 2022 **Initial data**: June 2022 **Topline data**: 1Q 2023
	Frontline pLGG	FIREFLY-2 (planned)				**Phase 3 initiation**: 2Q 2022
	RAF-altered solid tumors[2] (monotherapy)	FIRELIGHT-1*				**First patient dosed**: November 2021
Pimasertib MEK 1/2 Inhibitor	MAPK-altered solid tumors[3] (Combo w/Tovorafenib)	FIRELIGHT-1*				**Phase 1b/2 initiated**: March 2022

[1]Pivotal Phase 2 trial expected to support registration

[2]DAY101 adult monotherapy Phase 1 dose escalation and expansion trial previously completed

[3]Pimasertib Phase 1 dose escalation and expansion trial previously completed

**Includes patients ≥12 years of age*

pLGG = pediatric low-grade glioma

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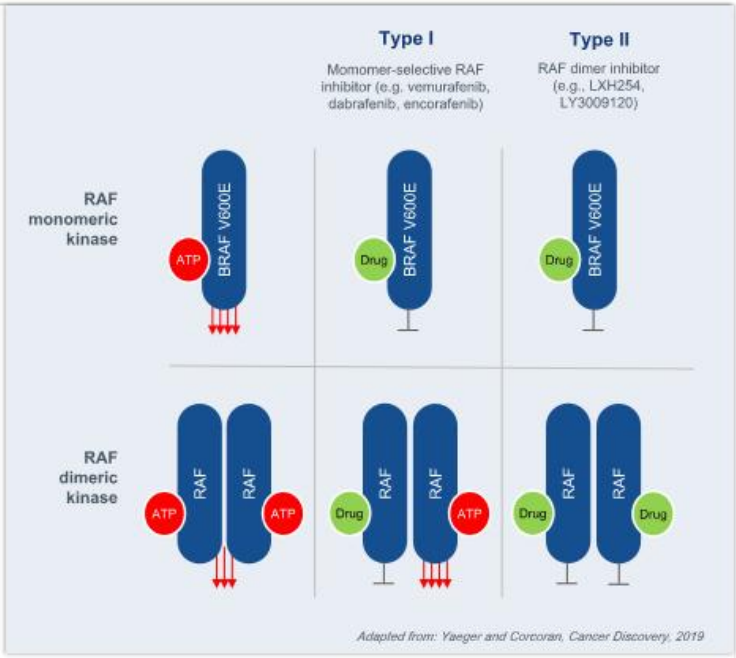
Tovorafenib (DAY101)

Type II Pan-RAF Inhibitor

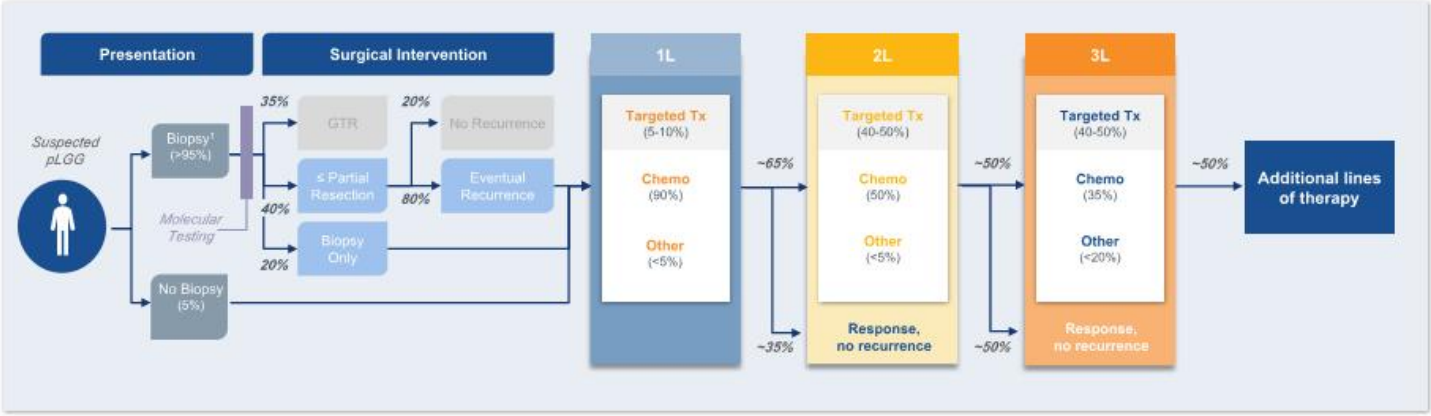
Tovorafenib (DAY101): Monotherapy Approach is Focused on RAF Fusions While Our Combination Strategy Addresses a Broad Set of MAPK Alterations

- Tovorafenib (DAY101) is a type II RAF inhibitor that selectively ***inhibits both monomeric*** and ***dimeric*** RAF kinase
- Approved BRAF products (*e.g.* vemurafenib, encorafenib) are type I RAF inhibitors that ***only inhibit*** RAF monomers and are therefore limited to use in BRAF V600-altered tumors
  - Type I inhibitors can also cause paradoxical activation of the MAPK pathway, which could potentially lead to increased tumor growth
- Tovorafenib's ***inhibition of both*** RAF monomers and dimers makes it a unique monotherapy approach for patients with tumors driven by RAF wild-type fusions, and a bespoke therapy for pediatric low-grade gliomas
  - Unlike type I RAF inhibitors, tovorafenib ***does not cause*** paradoxical activation in RAF wild-type cells
- Tovorafenib (DAY101), in combination with MEK inhibitors, may act synergistically to inhibit tumors driven by other MAPK alterations and broadens its potential clinical applications



Adapted from: Yaeger and Corcoran, Cancer Discovery, 2019

The Current pLGG Treatment Paradigm Reflects the Unrelenting Nature of this Chronic Brain Tumor



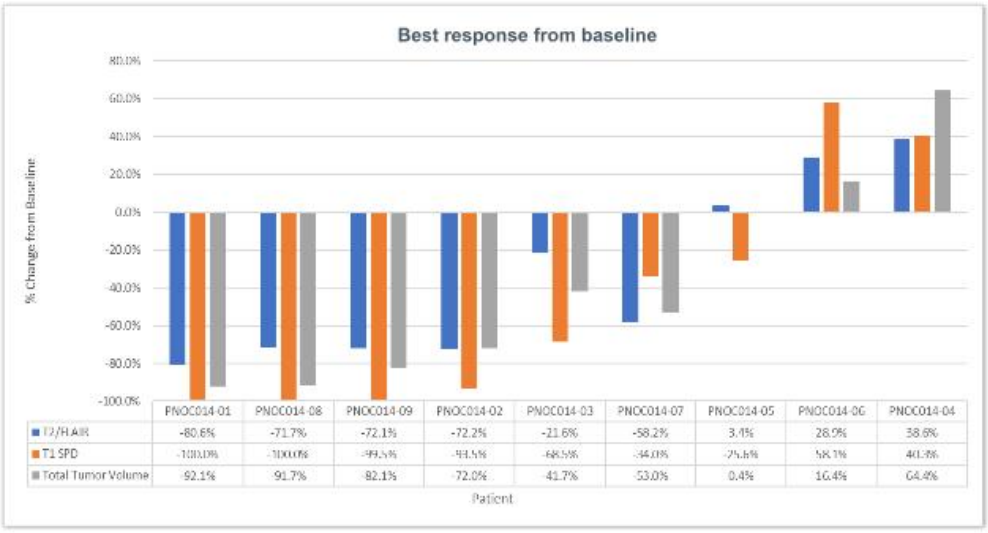
Because many pLGGs undergo senescence when patients reach their 20s, the goal of therapy is to **maximize tumor control** while **minimizing treatment-associated toxicities** from surgery, chemotherapy, and radiation. As a result, a large number of pLGG patients will undergo **multiple lines of systemic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

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

PNOC014 Study Results Demonstrated Responses or Stable Disease in Majority of pLGG Patients Treated with Tovorafenib (DAY101)

- Tovorafenib (DAY101) studied as once-weekly ***monotherapy*** in a Phase 1 dose escalation trial in relapsed pediatric glioma patients conducted by the Dana-Farber Cancer Institute and the Pacific Pediatric Neuro-Oncology Consortium (PNOC)
- Of the eight patients with RAF fusions (7 BRAF, 1 CRAF), ***two patients*** achieved a ***complete response*** by Response Assessment for Neuro-Oncology (RANO), ***three*** had a ***partial*** response, and ***two*** achieved prolonged ***stable*** disease
- Median time to achieve a response was ***10.5 weeks***, with most common side effects being skin rash and hair color changes. Most patients treated up to ***two years*** at 420 mg/m^2/week
- US FDA has ***granted DAY101 Breakthrough Therapy designation*** for the treatment of pediatric patients with advanced low-grade glioma harboring RAF alteration and ***Orphan Drug Designation*** for the treatment of malignant glioma

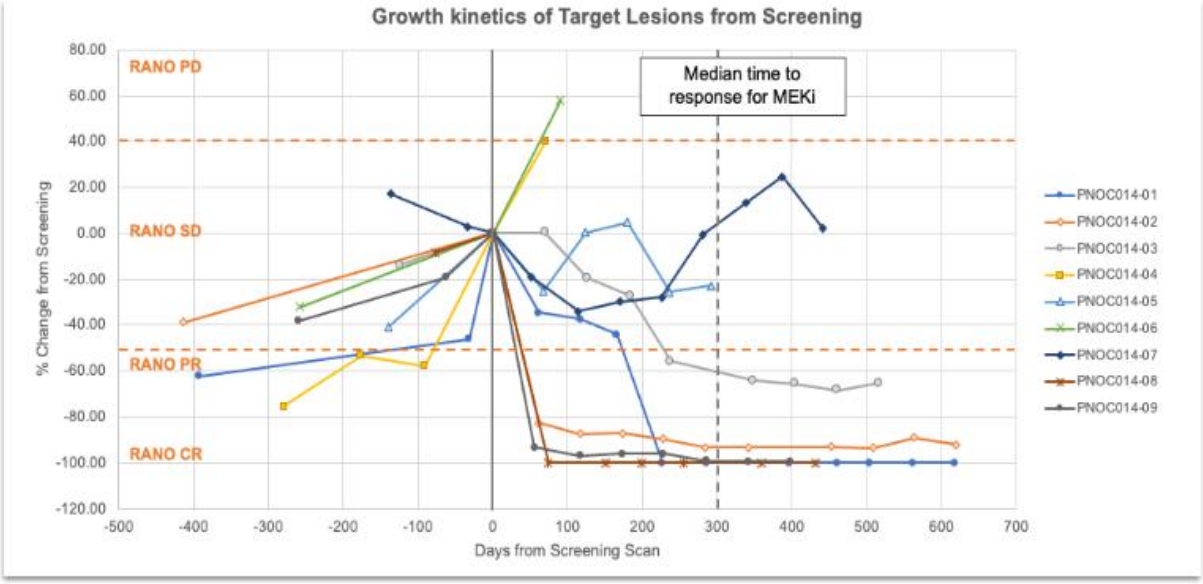
Results from Independent Radiology Review of PNOC014



	PNOC014-01	PNOC014-08	PNOC014-09	PNOC014-02	PNOC014-03	PNOC014-07	PNOC014-05	PNOC014-06	PNOC014-04
T2/FLAIR	-80.6%	-71.7%	-72.1%	-72.2%	-21.6%	-58.2%	3.4%	28.9%	38.6%
T1 SPD	-100.0%	-100.0%	-99.5%	-93.5%	-68.5%	-44.0%	-23.6%	58.1%	40.3%
Total Tumor Volume	-92.1%	-91.7%	-82.1%	-72.0%	-41.7%	-53.0%	0.4%	16.4%	64.4%

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

Multiple Rapid, Deep and Durable Responses Observed following Initiation of Tovorafenib (DAY101) Treatment of pLGG Patients in PNOC014



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

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

DAY101 AE summary

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

Drug-related AEs for Tovorafenib (DAY101)

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

Drug-related AEs for selumetinib

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

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

Pivotal Phase 2 Study of Monotherapy Tovorafenib (DAY101) in pLGG (FIREFLY-1)

Trial Design

- Single arm, open-label, global registrational phase 2 study
- n = 60 patients (approximately)
- Eligibility: Patients aged 6 months – 25 years with LGG harboring a KIAA1549:BRAF wild-type fusion or BRAF V600 mutation

Endpoints

- Primary endpoint: ORR based on RANO criteria, assessed by independent review
- Secondary endpoints: ORR by RAPNO criteria; EFS; safety

Abbreviations: LGG, low-grade glioma; ORR, objective response rate; C, cycle; D, day

Key Product Attributes for pLGG Prescribers When Choosing a New Therapy

PFS & ORR	Safety while on therapy	Functional Improvement & Long-Term Safety	Stable Disease	Dosing and Administration	FDA Approval	MOA
"Efficacy, especially ORR and PFS, are the most important. ***You want these patients to live without progression of pLGG for as much time as possible,*** *and for the treatment to be effective for the majority of these patients."*	*"****You want to make sure the treatment is not worse than the disease,*** *and you are not making their QoL worse.* ***These are just children."***	*"As we are dealing with the brain,* ***we need to make sure these patients can function.*** *We want to make sure they can do their daily activity, and maintain motor functions and vision… this is very important for their QoL."*	*"We tell our patients that the goal is to kill the tumor, but* ***the more practical goal is to stop it from growing. Even if we achieve stable tumors, that's considered a success."***	*"Pediatric dosing is very important, but* ***efficacy and safety are a lot more important than the delivery of the drug****."*	*"****Without an indication, insurance may not pay for it…*** *it would be a higher burden for families… an FDA-approved indication also means the therapy meets general safety and efficacy regulations, so that is always a plus."*	*"****I don't really care about the mechanism of action, as long as the drug works****, and there are no big concerns with toxicity."*

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Sources: pLGG Buying Process; pLGG Demand Study

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

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

~1,100
Estimated Annual Incidence

~26,000
Estimated Prevalence (SEER)

[1]US Census; [2]CBTRUS, Qaddoumi et al 2009, Schreck et al 2019, ClearView Analysis; [3]SEER US complete prevalence counts of patients aged under 25 with Brain and Other Nervous Systems tumors as of January 1, 2017.

Estimated annual incidence and estimated prevalence (SEER) are Day One calculations based on publicly available data.

Our Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
Tovorafenib (DAY101) Type II Pan-RAF Inhibitor ✓ FDA Breakthrough Therapy Designation ✓ FDA Rare Pediatric Disease Designation (PRV Eligible) ✓ FDA Orphan Drug Designation ✓ EC Orphan Designation	Relapsed pLGG		FIREFLY-1[1] (pivotal)			**Enrollment complete**: May 2022 **Initial data**: June 2022 **Topline data**: 1Q 2023
	Frontline pLGG		FIREFLY-2 (planned)			**Phase 3 initiation**: 2Q 2022
	RAF-altered solid tumors[2] (monotherapy)		FIRELIGHT-1*			**First patient dosed**: November 2021
Pimasertib MEK 1/2 Inhibitor	MAPK-altered solid tumors[3] (Combo w/Tovorafenib)		FIRELIGHT-1*			**Phase 1b/2 initiated**: March 2022

[1] *Pivotal Phase 2 trial expected to support registration*

[2] *DAY101 adult monotherapy Phase 1 dose escalation and expansion trial previously completed*

[3] *Pimasertib Phase 1 dose escalation and expansion trial previously completed*

* *Includes patients ≥12 years of age*

pLGG = pediatric low-grade glioma

Day One

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

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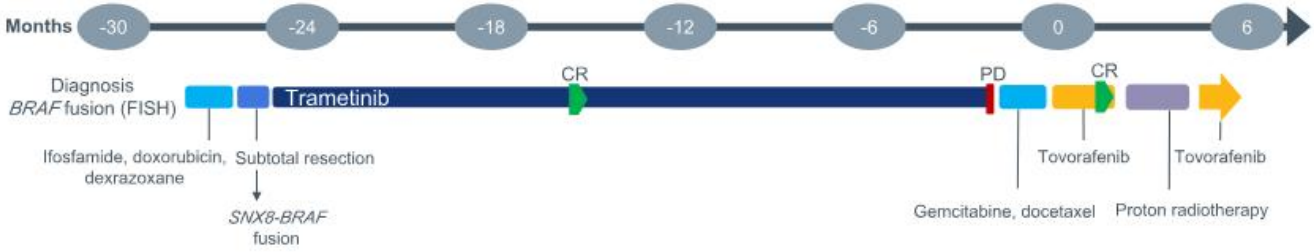
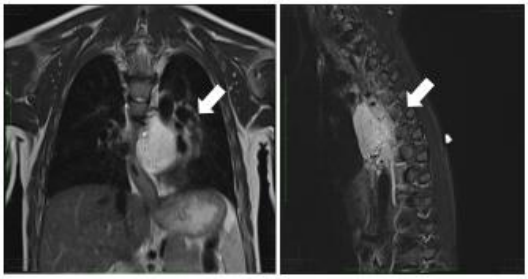
Source: Olszanski AJ et. al. European Society for Medical Oncology Congress; Poster #410P, 2017
Unpublished clinical study results

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

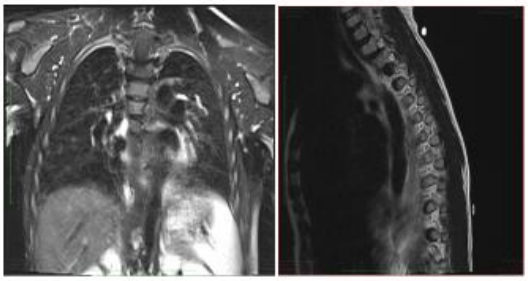
A male child with spindle cell sarcoma, 5-years of age at diagnosis



Baseline



After 2 cycles of tovorafenib



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

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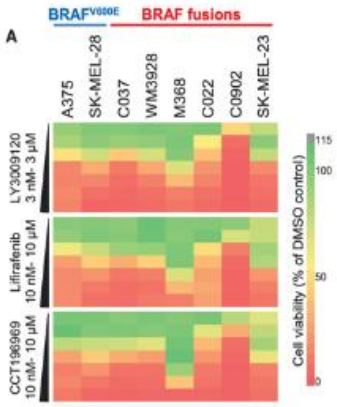
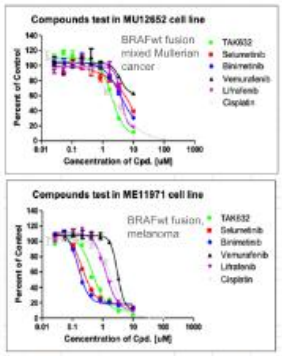
Data cut off: September 30, 2021

Next-generation RAF Inhibitors are Unique in Their Ability to Address Adult Cancers Associated with RAF Wild-type Fusions

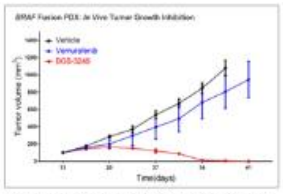


Botton T et al, Cell Reports, 2019

LY3009120: Lilly pan-RAFi
Lifirafenib: Beigene pan-RAF/EGFRi
CCT196969: CRUK RAF "paradox breaker"



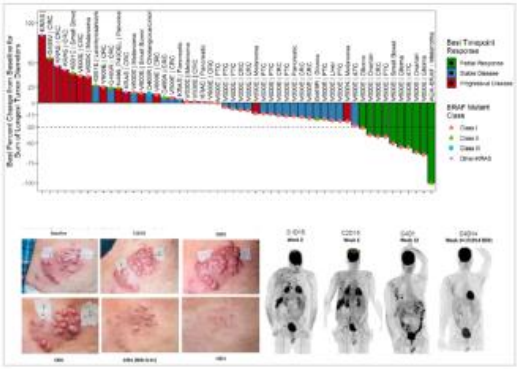
Day One/CrownBio internal data
E5251-U2001 (Sep 2020)



Springworks 2020 Corp Presentation

Only tovorafenib (DAY101) has demonstrated ***monotherapy clinical activity*** in KIAA1549:BRAF and SRGAP3:CRAF wild-type fusions in pLGG

Activity of BRAF dimer-breaker PLX-8394 in BRAF wild-type fusion melanoma



Gouda M et al,
ESMO 2020

CR observed at 1800 mg BID = 3x higher total AUC over 900 mg BID

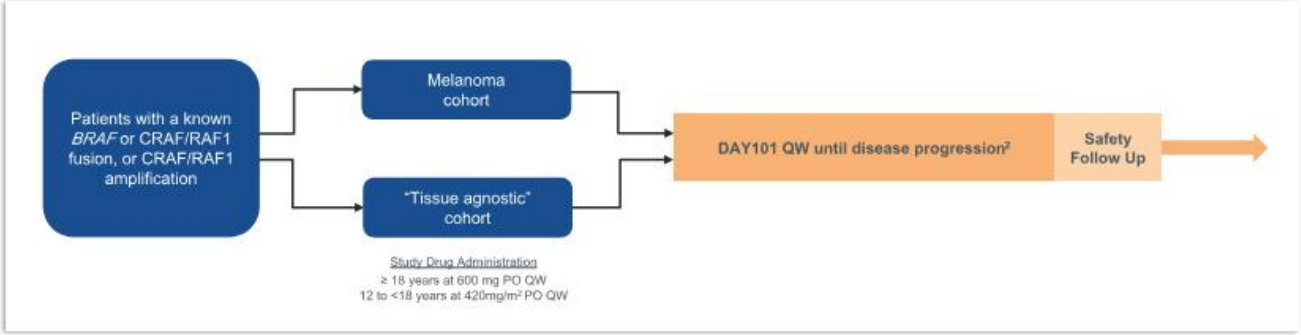
Phase 2 Study of Monotherapy Tovorafenib (DAY101) in Solid Tumors (FIRELIGHT-1)

Trial Design[1]

- Single arm, open-label, global phase 1b/2a study
- 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

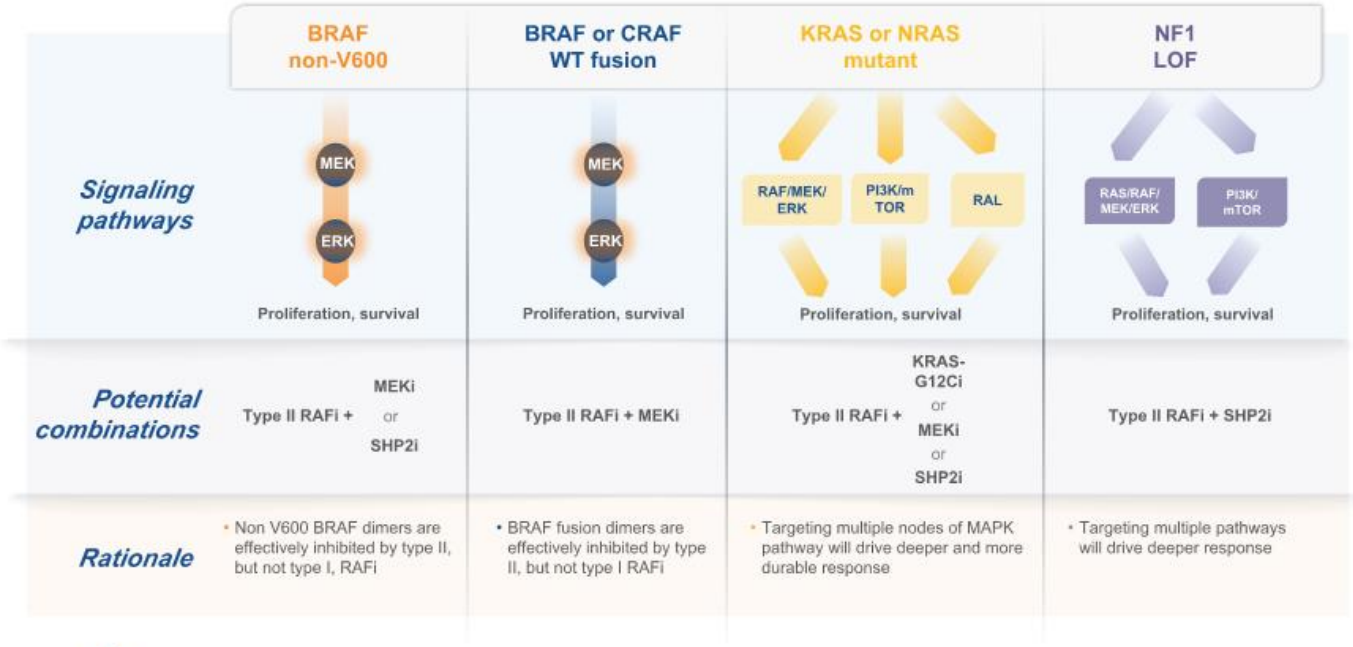
Endpoints

- 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.
[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



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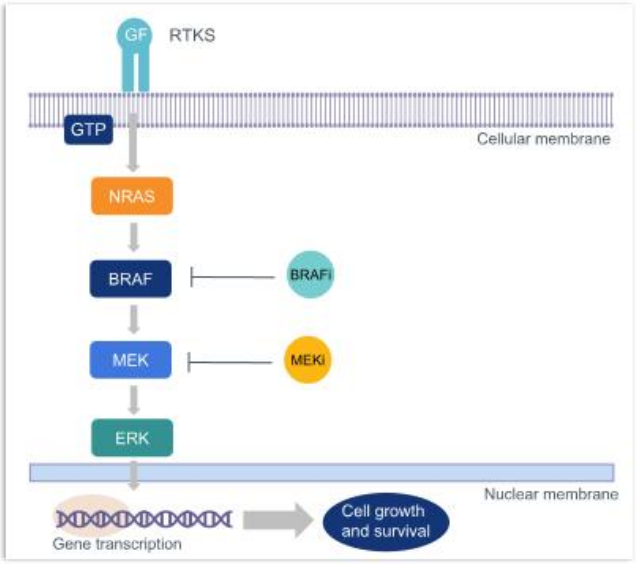
Pimasertib

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



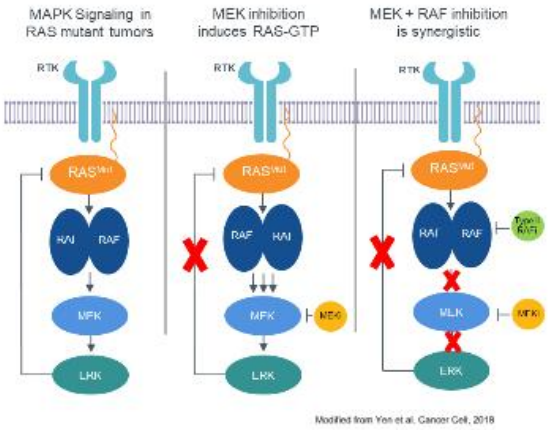
Source: Hepner, Salgues, Anjos, et al. 2017.

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

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

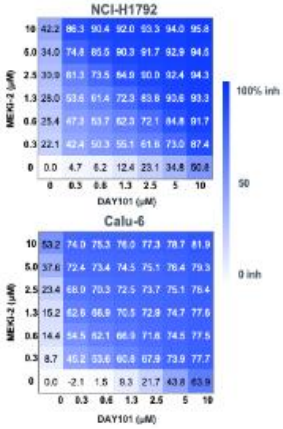
- The MAPK pathway normally has multiple feedback loops that negatively regulate upstream (RAS/RAF) activation to ensure optimal signaling
- Monotherapy MEK inhibition disables these feedback loops and induces RAS signaling as well as RAF dimerization and activation
- Combination therapy with a MEK inhibitor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

A

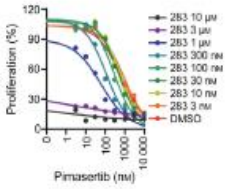


Modified from Yen et al. Cancer Cell, 2018

B



C



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)

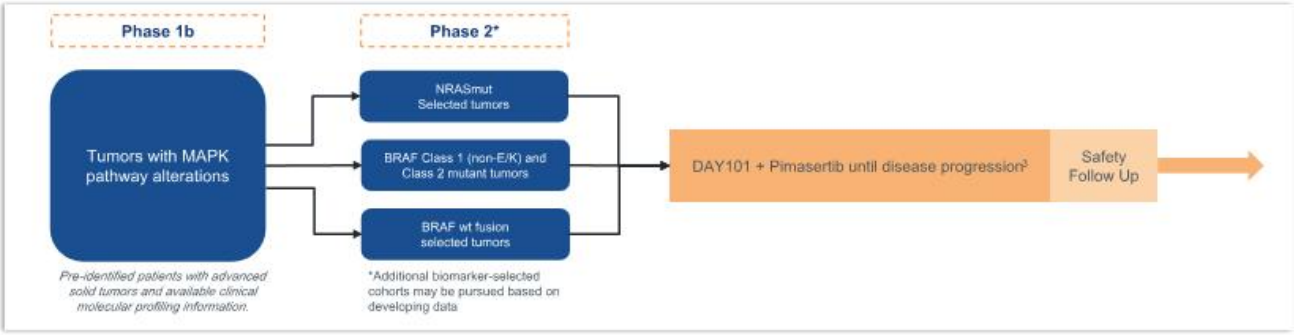
Tovorafenib (DAY101) / Pimasertib Combination to be Evaluated in Solid Tumors (FIRELIGHT-1)

Trial Design[1]

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

Endpoints

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



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

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Summary

Financial Summary: DAWN

- Cash and cash equivalents as of March 31, 2022: $262.7 million (no debt)
- 61.9 million shares of common stock outstanding

$ Millions	Three Months Ended 3/31/22	Three Months Ended 3/31/21
R&D Expense	$15.0	$12.6
G&A Expense	$12.7	$3.5
Net Loss	$27.7	$16.1

Projected cash runway into 2024

FIREFLY-1: Pivotal Phase 2 clinical trial of tovorafenib (DAY101)
- Enrollment complete in May 2022
- Initial clinical data expected in June 2022
- Full topline results expected in 1Q 2023
- Anticipated NDA filing in 2023, if data from FIREFLY-1 are supportive

FIRELIGHT-1: Tovorafenib (DAY101) and pimasertib combination
- Trial initiated in March 2022

Momentum for a More Inclusive Era of Drug Development, Starting at Day One Pursuing Fast-to-Market Pediatric and Adult Targeted Therapies

Key Highlights

Tovorafenib (DAY101)[1]

FIREFLY-1 (Relapsed pLGG)

- First patient dosed in Pivotal FIREFLY-1 trial: May 2021
- Enrollment complete in May 2022
- Breakthrough Therapy Designation & Rare Pediatric Disease Designation

FIRELIGHT-1 (RAF-altered solid tumors - monotherapy)

- First patient dosed in phase 2 monotherapy trial: November 2021

Intellectual Property

- Composition of matter to mid-2030s with PTE, potential exclusivity to late 2030s / early 2040s via broad patent portfolio

Pimasertib[1]

FIRELIGHT-1 (MAPK-altered solid tumors – Combo w/Tovorafenib)

- Initiated combination dose escalation, global phase 1b/2 trial: March 2022

2022 Outlook

Tovorafenib (DAY101)

FIREFLY-1 (Relapsed pLGG)

- Initial data expected: June 2022
- Topline data expected: 1Q 2023

FIREFLY-2 (Frontline pLGG)

- Phase 3 trail initiation: 2Q 2022

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[1] *Worldwide rights for all indications*

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Thank you