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): January 05, 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

(Former Name or Former Address, if Changed Since Last Report)

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

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

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

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

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

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

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

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

Emerging growth company ☒

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

Item 7.01 Regulation FD Disclosure.

On January 5, 2022, Day One Biopharmaceuticals, Inc. (the “Company”) updated its corporate presentation.

Additionally, on January 5, 2022, the Company issued a press release announcing that it will present at the 40th Annual J.P. Morgan Healthcare Conference (“J.P. Morgan Conference”) held virtually on January 11, 2022 at 10:30 a.m. Eastern Time. Dr. Jeremy Bender chief executive officer will present virtually.

A copy of the press release and the updated corporate presentation are attached as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K. The corporate presentation will also be available on the Company’s website in the Events & Presentations section at www.dayonebio.com.

The information in Item 7.01 of this report, including Exhibit 99.1 and Exhibit 99.2, shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (“Exchange Act”), or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act, nor shall it be deemed incorporated by reference into any other filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On January 5, 2022 the Company disclosed that based on its current operating plan, the Company’s management believes that the Company has sufficient capital resources to fund anticipated operations into 2024.

Forward Looking Statements

This Current Report on Form 8-K contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as: "anticipate," "intend," "plan," "goal," "seek," "believe," "project," "estimate," "expect," "strategy," "future," "likely," "may," "should," "will" and similar references to future periods. These statements are subject to numerous risks and uncertainties that could cause actual results to differ materially from what we expect. Examples of forward-looking statements include the Company’s management’s beliefs regarding the sufficiency of the Company’s capital resources. Further information on potential risk factors that could affect our business and its financial results are detailed in our most recent Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 filed with the Securities and Exchange Commission (SEC), and other reports as filed with the SEC. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press Release
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: January 5th, 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 to Present at the 40th Annual J.P. Morgan Healthcare Conference

SOUTH SAN FRANCISCO, CA, January 5, 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 that Dr. Jeremy Bender, chief executive officer, will present virtually during the 40th Annual J.P. Morgan Healthcare Conference on Tuesday, January 11 at 10:30 a.m. ET.

A live audio webcast of the presentation will be available by visiting the Events & Presentations section of the Company's website. An archived replay of the webcast will be available for 30 days following the live presentation.

About Day One Biopharmaceuticals
Day One Biopharmaceuticals is a clinical-stage biopharmaceutical company dedicated to developing and commercializing targeted therapies for people of all ages with life-threatening diseases. Day One partners with leading clinicians, families, and scientists to identify, acquire, and develop important emerging targeted treatments. The Company's lead product candidate, DAY101 (tovorafenib), is an oral, highly-selective type II pan-RAF kinase inhibitor currently being evaluated in a pivotal Phase 2 clinical trial (FIREFLY-1) in pediatric, adolescent and young adult patients with recurrent or progressive low-grade glioma (pLGG). The Company's pipeline also includes the investigational agent pimasertib, a clinical-stage, oral, small molecule found to selectively inhibit mitogen-activated protein kinases 1 and 2 (MEK) will be evaluated in a Phase 1/2 study (FIRELIGHT-1) in combination with DAY101 for adult and adolescent patients with solid tumors with MAPK pathway aberrations. Day One is based in South San Francisco. For more information, please visit www.dayonebio.com or visit us on LinkedIn or Twitter.

Contacts:

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

Investors:
LifeSci Advisors
Hans Vitzthum
hans@lifesciadvisors.com

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Day One
BIOPHARMACEUTICALS

Targeted Therapies for People of All Ages

January 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 development activities, 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.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of these securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or other jurisdiction.

Day One: Cancer Drug Development for People of All Ages

Mission That Creates Value	Specialized Team	DAY101 (tovorafenib) 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

Day One

Our Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
DAY101 (tovorafenib) 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)				**First patient dosed**: 2Q2021 **Initial data**: 1H2022
	Frontline pLGG	FIREFLY-2 (planned)				**Phase 3 initiation**: 1H2022
	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/DAY101)	FIRELIGHT-1*				**Phase 1b/2 initiation**: 1Q2022

[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

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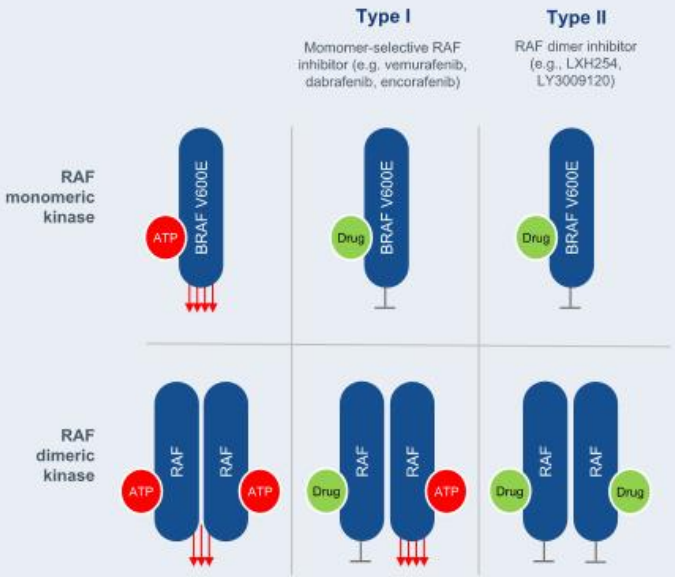
DAY101 (tovorafenib)

Type II Pan-RAF Inhibitor

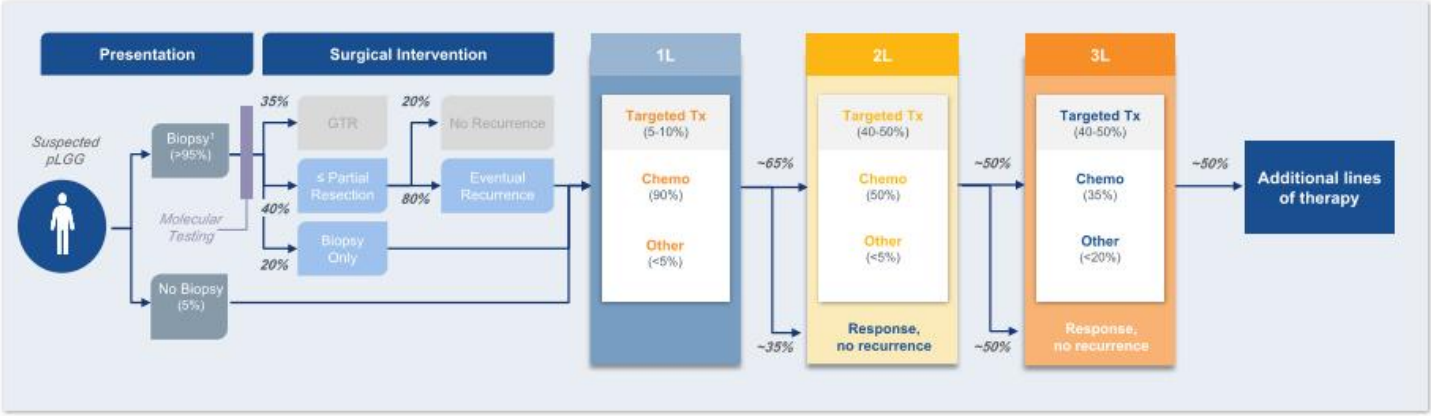
DAY101 (tovorafenib): Monotherapy Approach is Focused on RAF Fusions While Our Combination Strategy Addresses a Broad Set of MAPK Alterations

- DAY101 (tovorafenib) 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
- DAY101'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, DAY101 ***does not cause*** paradoxical activation in RAF wild-type cells
- DAY101 (tovorafenib), 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



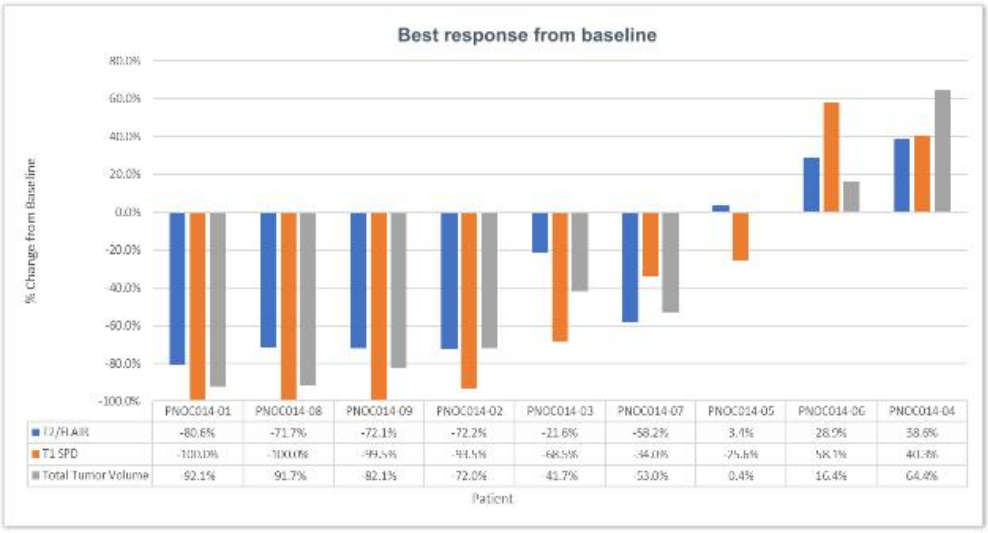
Because many pLGGs undergo senescence when patients reach their 20s, the goal of therapy is to **maximize tumor control** while **minimizing treatment-associated toxicities** from surgery, chemotherapy, and radiation. As a result, a large number of pLGG patients will undergo **multiple lines of systemic 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 DAY101 (tovorafenib)

- DAY101 (tovorafenib) 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



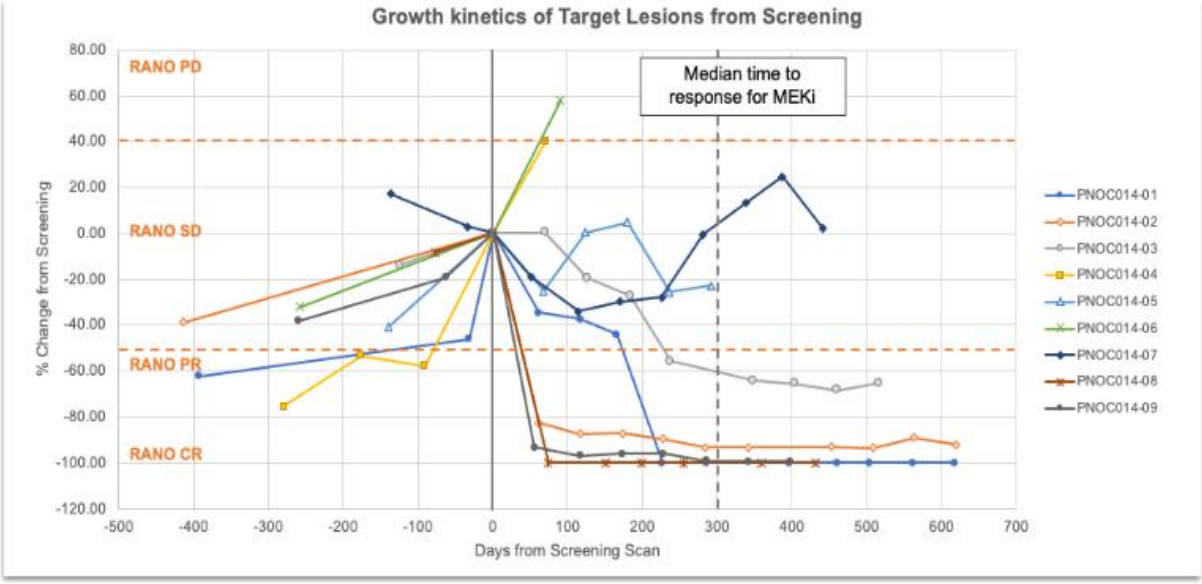
RANO: Response assessment for neuro-oncology (FDA standard)

Volumetric image analysis (exploratory)

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

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

Multiple Rapid, Deep and Durable Responses Observed following Initiation of DAY101 (tovorafenib) 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 DAY101 (tovorafenib) 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 DAY101 (tovorafenib)

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%)		

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Data 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 DAY101 (tovorafenib) 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

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
DAY101 (tovorafenib) 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)				**First patient dosed**: 2Q2021 **Initial data**: 1H2022
	Frontline pLGG	FIREFLY-2 (planned)				**Phase 3 initiation**: 1H2022
	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/DAY101)	FIRELIGHT-1*				**Phase 1b/2 initiation**: 1Q2022

[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

DAY101 (tovorafenib) 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 DAY101 (tovorafenib) may be active in tumors currently unaddressed by approved Type I BRAF inhibitors

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

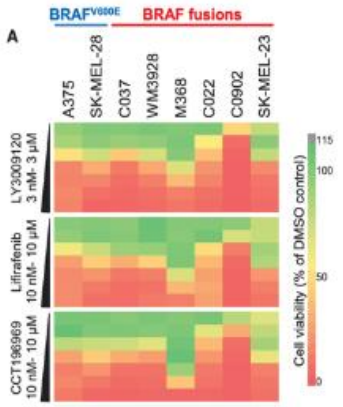
- Less frequent and less severe acneiform rash
- No observed ophthalmologic liabilities (RVO/CSR)
- No observed CV liabilities (changes in LVEF)
- No type I BRAF SAEs: SCCs/KAs, pyrexia, arthralgia

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

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

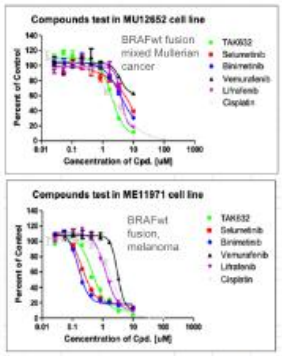
Source: Olszanski AJ et. al. European Society for Medical Oncology Congress; Poster #410P, 2017
Unpublished clinical study results

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

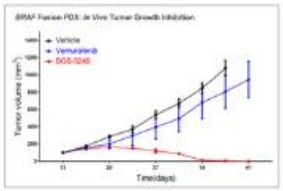


Botton T et al, Cell Reports, 2019

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



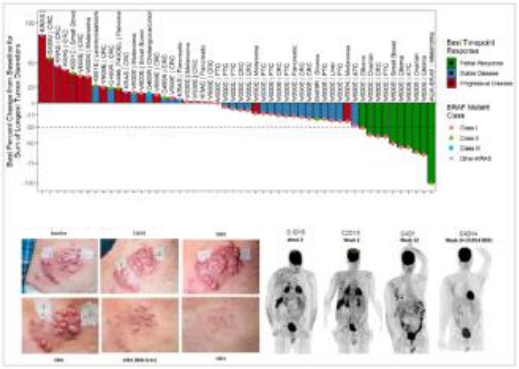
Day One/CrownBio internal data
E5251-U2001 (Sep 2020)



Springworks 2020 Corp Presentation

Only 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

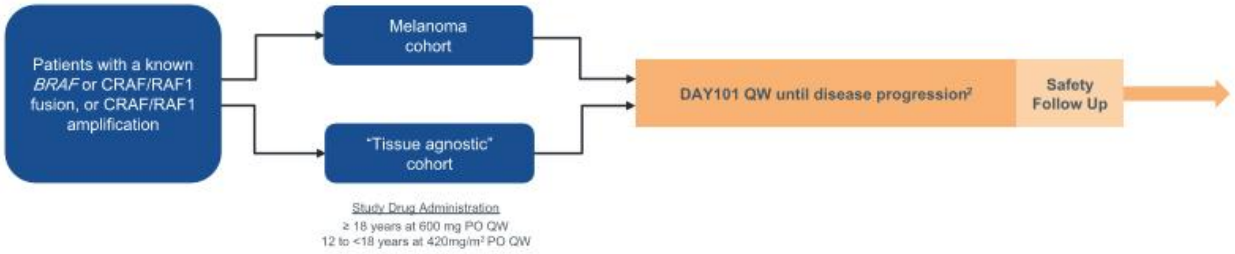
Phase 2 Study of Monotherapy DAY101 (tovorafenib) in Solid Tumors (FIRELIGHT-1)

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

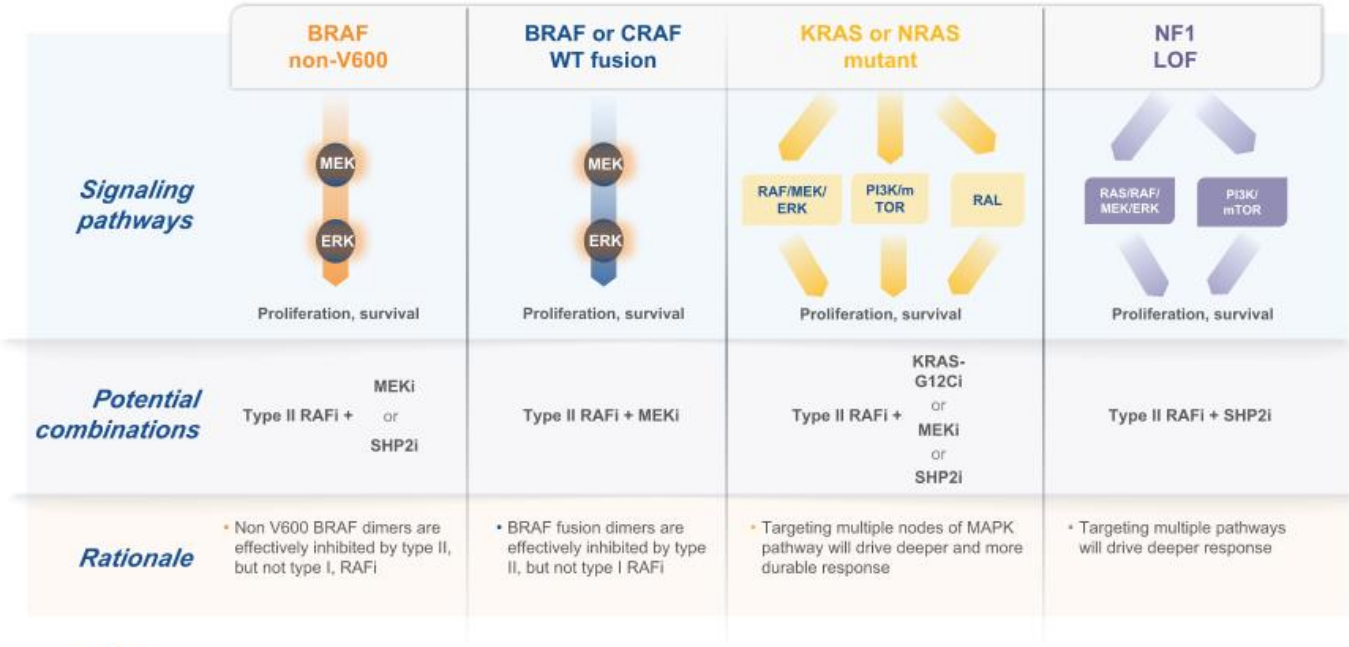
- Primary endpoint: ORR by RECIST version 1.1 for non-CNS solid tumors and RANO criteria for any CNS tumors
- Secondary endpoints: safety and additional efficacy parameters



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

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

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



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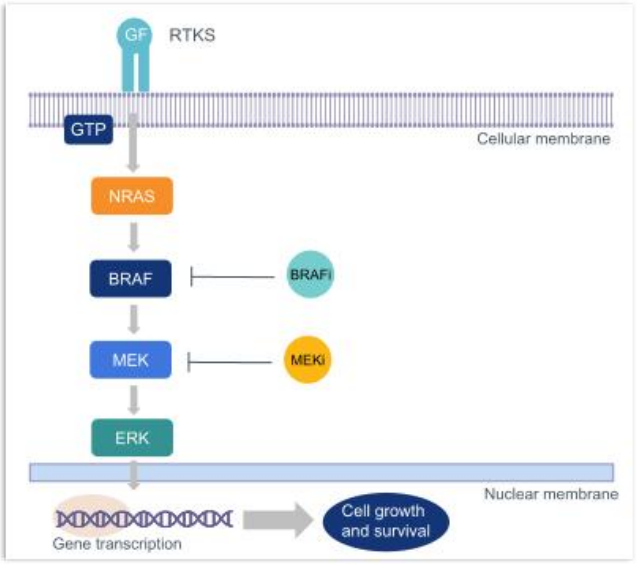
Pimasertib

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 DAY101 (tovorafenib) and other targeted therapies may unlock the full value of pimasertib in advanced solid tumors

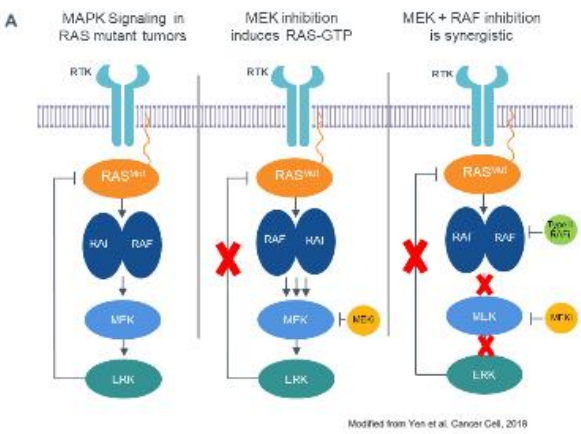


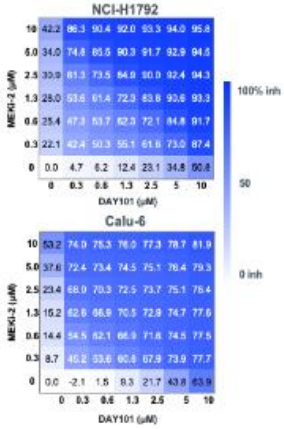
Source: Hepner, Salgues, Anjos, et al. 2017.

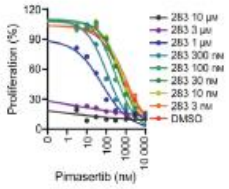
Sources: Pimasertib Investigator Brochure, v12, 2019; de Gooijer et al., Int J Cancer, 2018; Shaw et al., AACR LB-456, 2012; Lebbe et al., Cancers, 2020.

Vertical MAPK Pathway Inhibition with DAY101 (tovorafenib) 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)

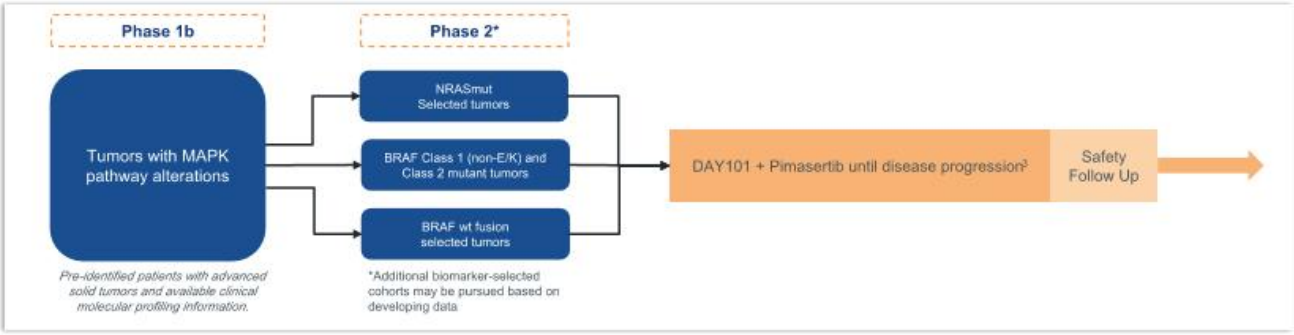
DAY101 (tovorafenib) /Pimasertib Combination to be Evaluated in Solid Tumors (FIRELIGHT-1)

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: 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 September 30, 2021: $297.2 million (no debt)
- IPO in May 2021: $184 million in gross proceeds, includes full exercise of underwriter's option
- 61.9 million shares of common stock outstanding

$ Millions	Three Months Ended 9/30/21	Nine Months Ended 9/30/21
R&D Expense	$9.8	$32.4
G&A Expense	$9.4	$18.4
Net Loss	$19.2	$50.8

Projected cash runway into 2024

- Initial clinical data for DAY 101 in pivotal FIREFLY-1 expected in first half 2022
- Anticipated NDA filing for DAY 101 in pLGG in 2023, if data from FIREFLY-1 are supportive
- DAY101 and pimasertib combination trial expected to initiate in first quarter 2022

Re-envisioning and Redefining Drug Development for People of All Ages – Starting at Day One

DAY101 (tovorafenib)

Oral, CNS-penetrant, pan-RAF

- pLGG: most common brain tumor in children, with no approved therapies
- Rapid and durable responses demonstrated in heavily pre-treated pLGG patients
- Well-tolerated as monotherapy; no Grade 4 AEs
- Worldwide rights to all indications
- IP: composition of matter to mid-2030s with PTE, potential exclusivity to late 2030s / early 2040s via broad patent portfolio

First Patient Dosed in Pivotal FIREFLY-1 May 2021, Initial Data 1H 2022

First Patient Dosed in Adult Solid Tumor Trial November 2021

PIMASERTIB

Oral, allosteric MEK inhibitor

- Combination with DAY101 (tovorafenib) in MAPK-altered solid tumors
- Clinical experience in over 800 patients
- Clear rationale for combo for pan-RAFi and MEKi
- Worldwide rights to all indications

Plan to Initiate Combination Trial with DAY101 (tovorafenib) 1Q 2022

SPECIALIZED TEAM

- Deep experience in the space and corporate development
- Strategy to aggressively pursue other assets and indications

Pursuing Fast-to-Market Pediatric and Adult Targeted Therapy Opportunities

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Thank you