Day One Biopharmaceuticals

Targeted Therapies for People of All Ages

41st Annual J.P. Morgan Healthcare Conference

January 2023

Disclaimer

This presentation and the accompanying oral commentary contain forward-looking statements that are based on our management's beliefs and assumptions and on information currently available to our management. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "could," "expect," "plan," anticipate," "believe," "estimate," "predict," "intend," "potential," "would," "continue," "ongoing" or the negative of these terms or other comparable terminology. Forward-looking statements include all statements other than statements of historical fact contained in this presentation, including information concerning our future financial performance, including the sufficiency of our cash, cash equivalents and investments to fund our operations, business plans and objectives, timing and success of our planned nonclinical and clinical development activities, timing and results of nonclinical studies and clinical trials, efficacy and safety profiles of our product candidates, execution of the Phase 2 clinical trial for tovorafenib and the Phase 1b/2 clinical trial for tovorafenib and pimasertib as designed, any expectations about safety, efficacy, timing and ability to complete clinical trials and to obtain regulatory approvals for tovorafenib and other candidates in development, the ability of tovorafenib to treat pediatric low-grade glioma (pLGG) or related indications, the potential therapeutic benefits and economic value of our product candidates, potential growth opportunities, competitive position, industry environment and potential market opportunities, our ability to protect intellectual property and the impact of global business or macroeconomic conditions, including as a result of 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.

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This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Cancer Drug Development for People of All Ages

Mission That Creates Value

- Day One's mission is to help children with cancer, from day one and every day after
- Develop medicines for genomically-defined cancers
- Establish first-in-class position through rapid pediatric registration
- Expand to adolescent and adult populations in parallel and pursue those opportunities with the same commitment we do for children

Tovorafenib (DAY101) Lead Program

- Investigational, oral, CNS-penetrant pan-RAF inhibitor
- Being studied as tablets and pediatric-friendly liquid suspension
- Breakthrough Therapy Designation
- Rare Pediatric Disease Designation
- Orphan Drug Designation (US/EU)

Growing Portfolio and Runway Beyond Clinical Milestones

- Two clinical-stage MEKi assets, in-licensed for combination trials
- Projected cash runway into 2025
- Upcoming key milestones
  - Planned NDA submission in 1H 2023
  - NDA data set will include additional follow up with data to be presented at a medical meeting in Q2 2023
  - First patient dosing in pivotal Phase 3 (FIREFLY-2 /LOGGIC), frontline trial expected Q1 2023

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

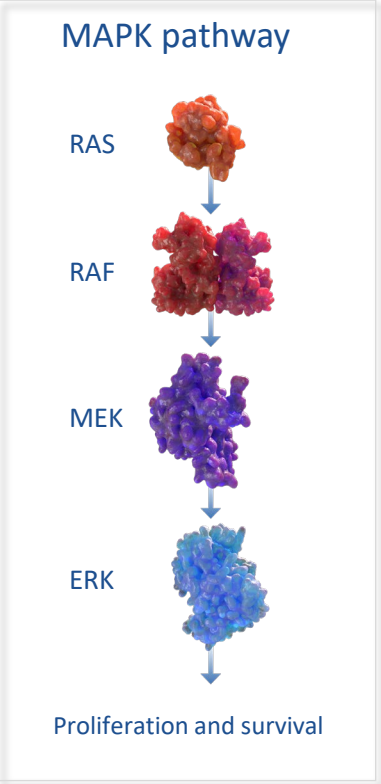
Chief Compliance & Ethics Officer at Bristol Myers Squibb (BMS); Legal leadership roles at BMS in the U.S., Asia and Europe; Partner at Sedgwick, Detert, Moran & Arnold

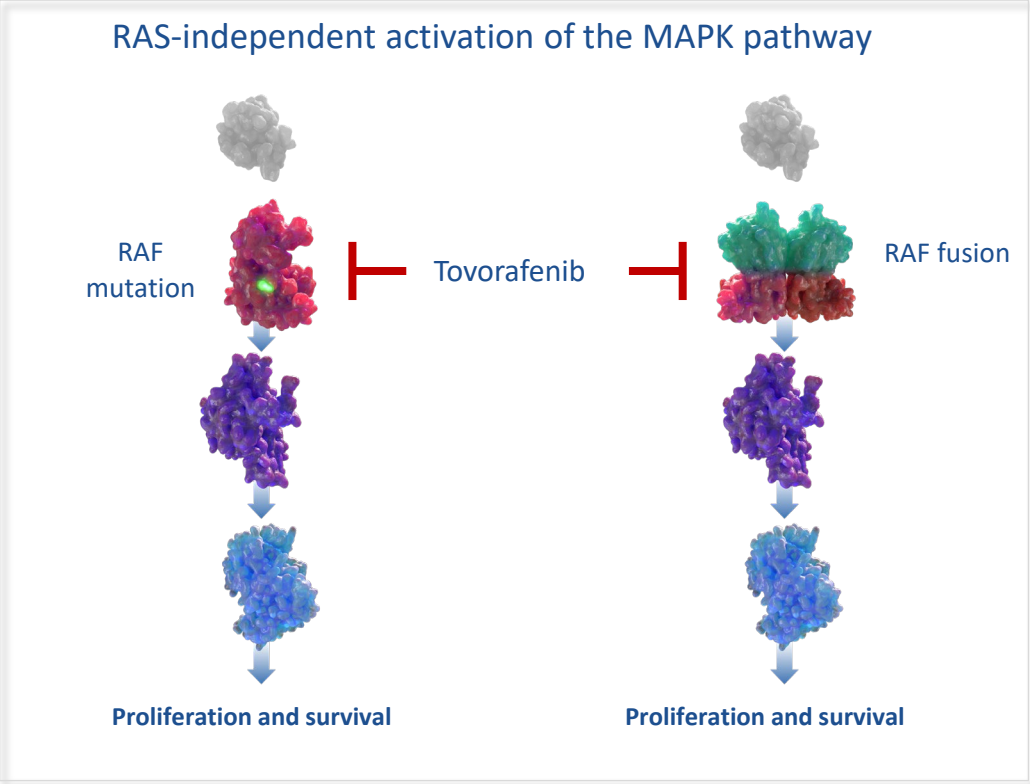
Our Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Recent & Anticipated Milestones
Tovorafenib (DAY101) Type II Pan-RAF Inhibitor ✓ FDA Breakthrough Therapy Designation for relapsed pLGG ✓ FDA Rare Pediatric Disease Designation (PRV Eligible) for pLGG ✓ FDA Orphan Drug Designation for malignant glioma ✓ EC Orphan Designation for glioma	Relapsed pLGG		FIREFLY-1[1] (pivotal)			**Topline data presented:** January 2023 **Pre-NDA meeting & NDA submission planned:** 1H 2023 **NDA data set presentation planned:** Q2 2023
	Frontline pLGG		FIREFLY-2 (pivotal)			**First patient dosing expected:** Q1 2023
	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*			**First patient dosed:** May 2022

*Includes patients ≥12 years of age. [1] FIREFLY-1 Arm 1 expected to support registration. [2] DAY101 adult monotherapy Phase 1 dose escalation and expansion trial previously completed. [3] Pimasertib Phase 1 dose escalation and expansion trial previously completed. pLGG, pediatric low-grade glioma. Tovorafenib and Pimasertib are investigational products. Safety and efficacy have not been established by any health authority.

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

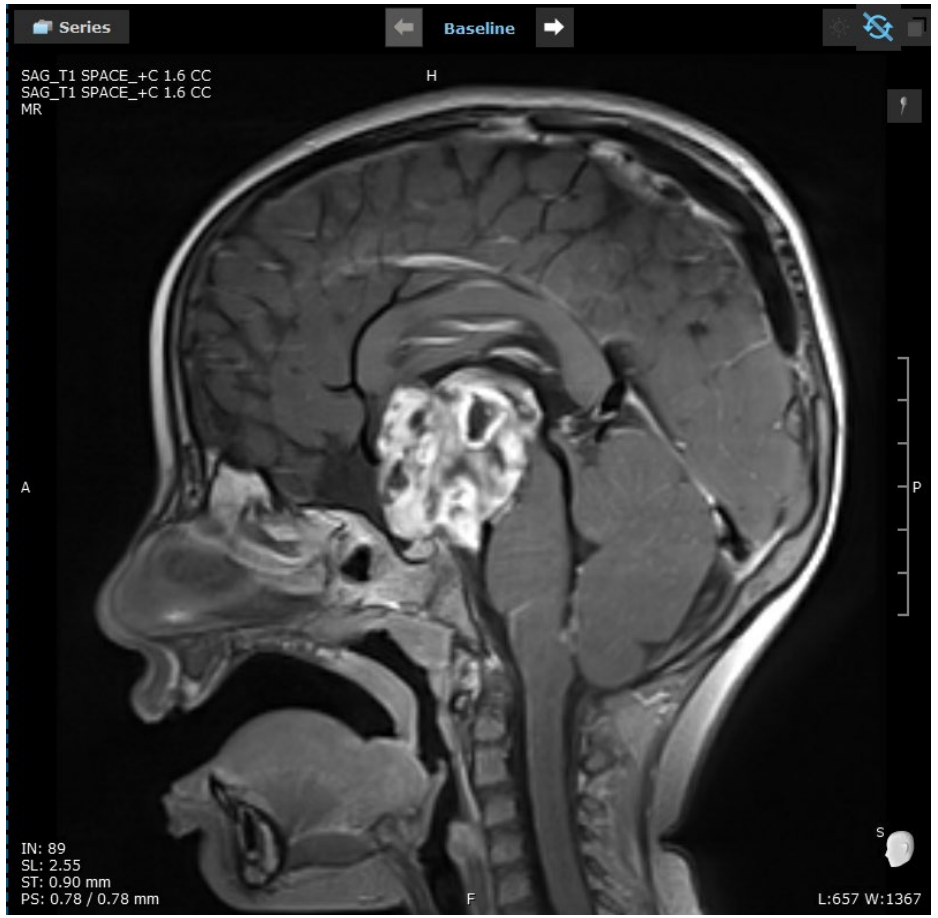




- **Tovorafenib (DAY101) is an investigational, oral, selective, CNS-penetrant, type II pan-RAF inhibitor that was designed to inhibit both monomeric and dimeric RAF kinase**
  - Activity in tumors driven by both RAF wild-type fusions and BRAF V600E mutations
  - Tablet and pediatric-friendly liquid suspension
  - Once weekly dosing
- **Currently approved type I RAFi are indicated for use only in adults and patients 6+ years of age 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

1. Sun Y et al., Neuro Oncol. 2017; 19: 774–85; 2. Sievart AJ et al., PNAS. 2013; 110:5957-62; 3. Karajannis MA et al., Neuro Oncol 2014;16(10):1408-16;

Pediatric Low-Grade Gliomas (pLGG)

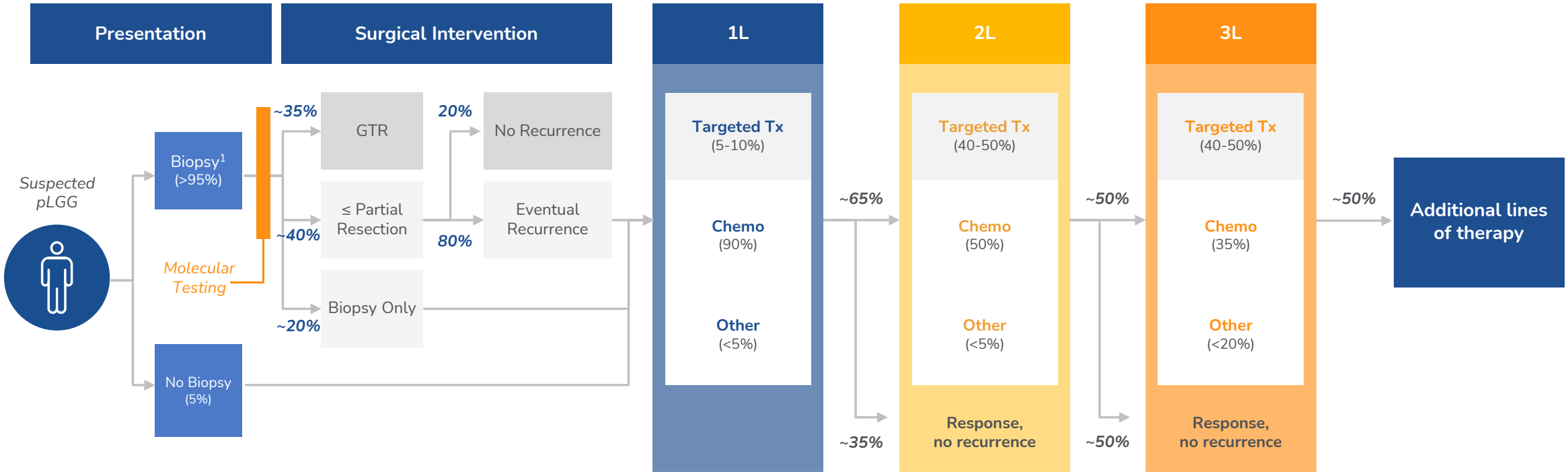


6 y/o with large relapsed BRAF fusion-positive optic pathway glioma

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

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

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

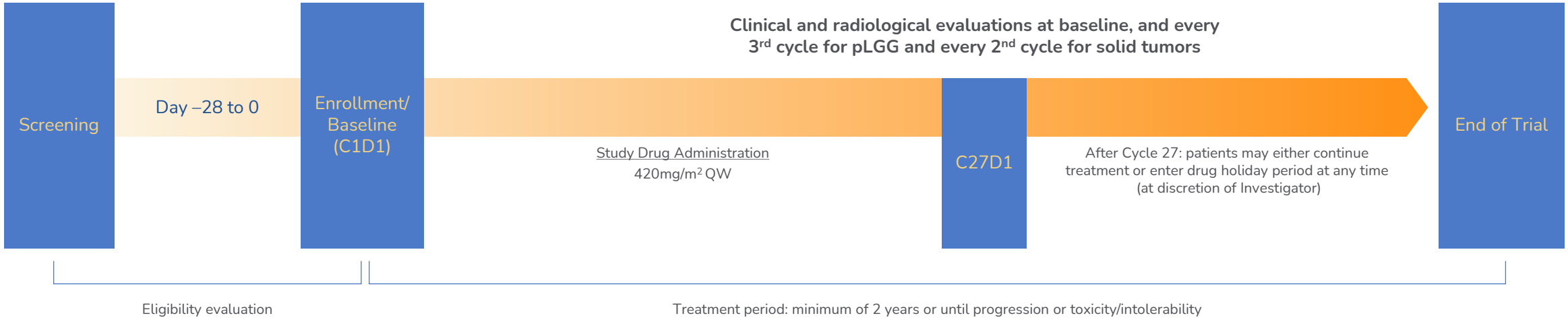
Pivotal Phase 2 Trial Of Monotherapy Tovorafenib (DAY101) in Relapsed or Progressive pLGG (FIREFLY-1)

Trial Design

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

Endpoints (Pivotal Arm 1)

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

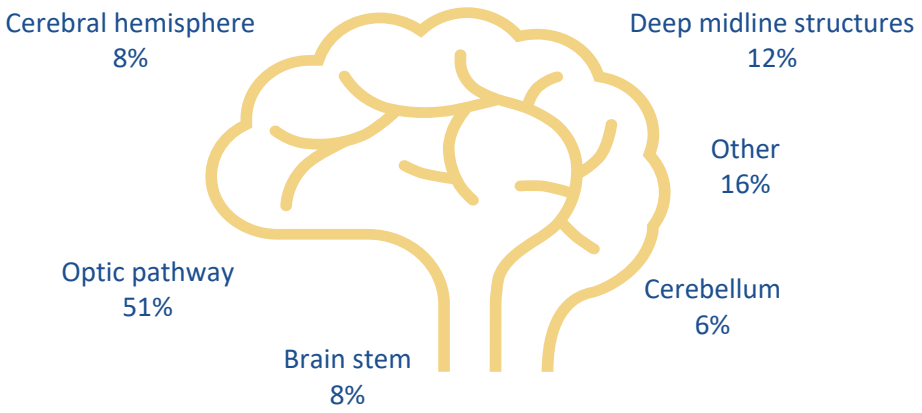


Abbreviations: C, cycle; D, day; LGG, low-grade glioma; ORR, objective response rate; PFS, progression-free survival.
NCT04775485

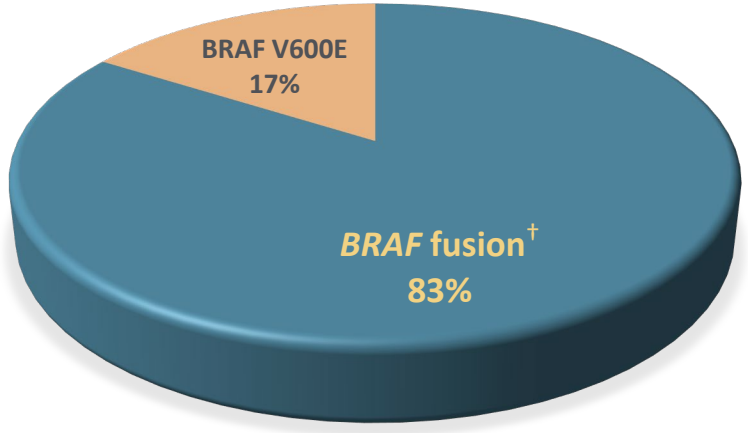
FIREFLY-1 Baseline Patient Characteristics

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

Location (n=77)



BRAF alteration (n=77)



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

Topline Data from Ongoing Pivotal Phase 2 FIREFLY-1 Trial

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

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

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

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

Among a total of 77 treated patients:

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

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

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

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

~1,100
Estimated Annual Incidence

~26,000
Estimated Prevalence

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

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

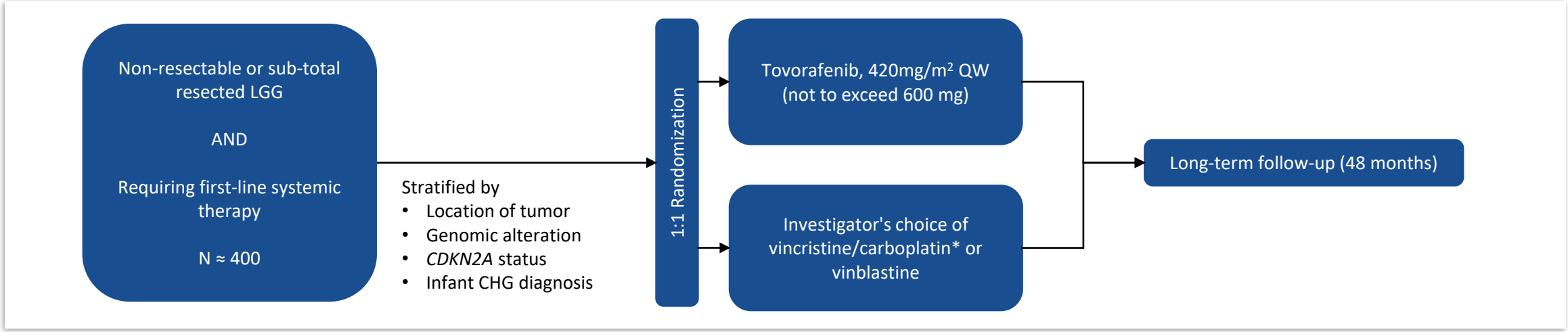
FIREFLY-2/LOGGIC Pivotal Phase 3 Trial of Tovorafenib (DAY101) in Newly Diagnosed pLGG

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**
  - The ORR primary analysis is expected to occur ~12 months after the last patient randomized
- Key secondary endpoints: PFS and DoR by RANO criteria, ORR by RAPNO criteria
- Other secondary endpoints: changes in neurological and visual function, safety, and tolerability
- Key exploratory objectives: QoL and health utilization measures



* COG or SIOPe-LGG regimen

Abbreviations: CHG, chiasmatic, hypothalamic glioma; DoR, duration of response; LGG, low-grade glioma; ORR, objective response rate; QoL, quality of life; QW, once weekly; SoC, standard of care

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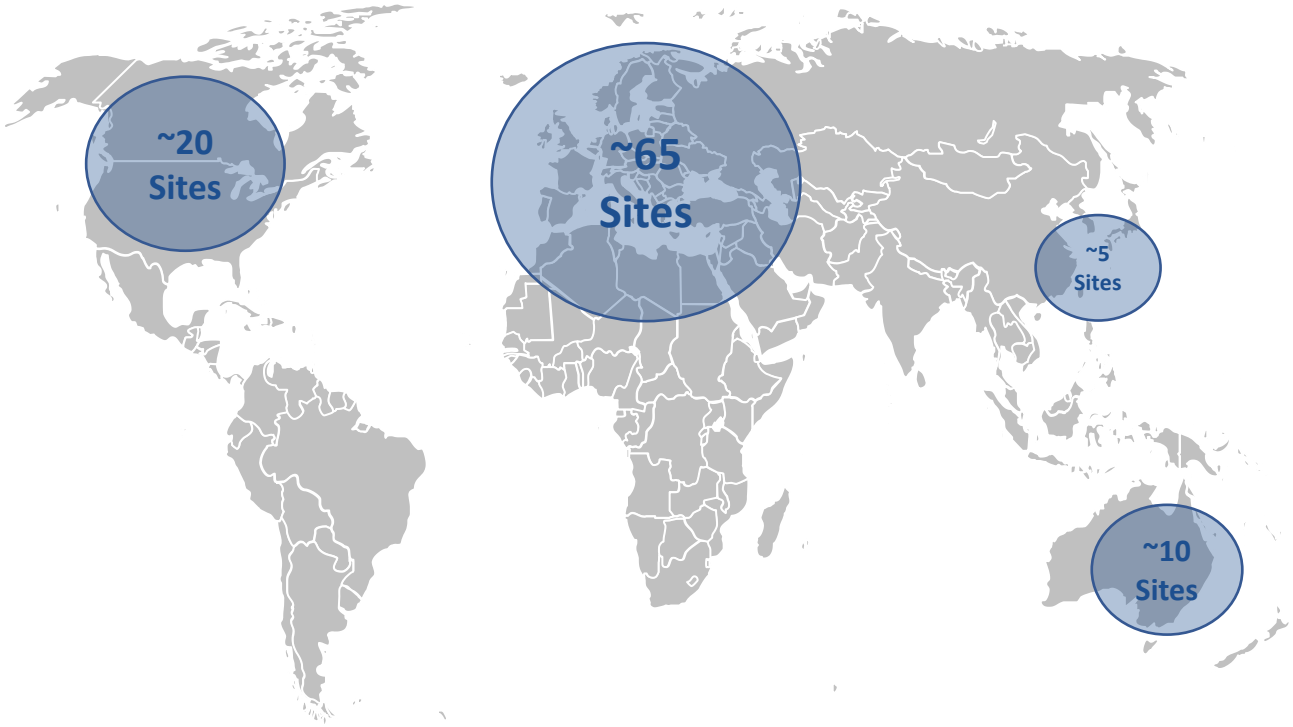
FIREFLY-2/LOGGIC: Pivotal Phase 3 Study Of Tovorafenib (DAY101) In Newly Diagnosed pLGG

- **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)**

LO GIC
EUROPE

LOGGIC: LOw Grade Glioma In Children

KiTZ
Hopp Children's Cancer Center Heidelberg
German Cancer Research Center (DKFZ)
Heidelberg University Hospital
Heidelberg University



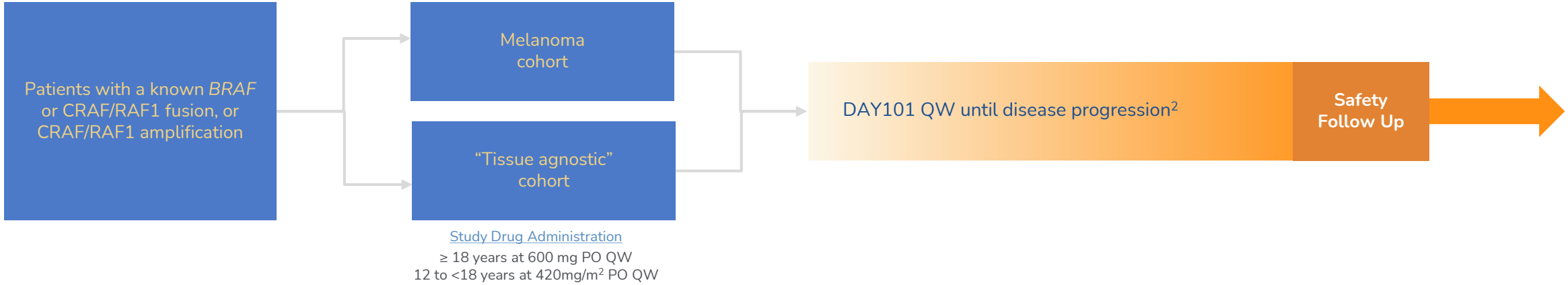
Phase 2 Study of Monotherapy Tovorafenib (DAY101) in Solid Tumors (FIRELIGHT-1)

Trial Design[1]

- Single arm, open-label, global phase 1b/2a trial
- n = 40 patients (approximately)
- Eligibility: Patients aged 12 years and older with non-hematologic tumor with an activating BRAF fusion, CRAF/RAF1 fusion, or CRAF/RAF1 amplification

Endpoints

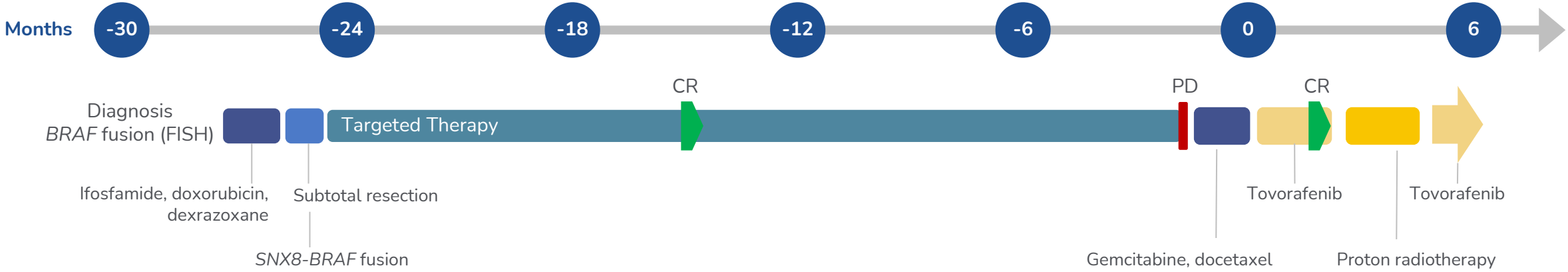
- Primary endpoint: ORR by RECIST version 1.1 for non-CNS solid tumors and RANO criteria for any CNS tumors
- Secondary endpoints: safety and additional efficacy parameters



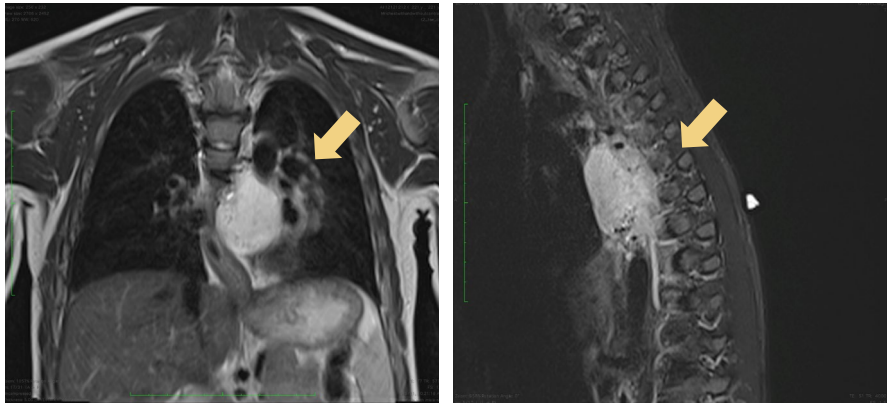
Abbreviations: ORR, objective response rate; QW, once weekly ; PO, by mouth; BRAF, B-Raf proto-oncogene.0
1. Umbrella master study – DAY101-102 (main protocol) DAY101 and MAPK pathway aberration, Sub-study 1 monotherapy (DAY101-102a), Sub-study 2 MEK combo (DAY101-102b).
2. DAY101 QW until disease progression, intolerable toxicity, withdrawal of consent, or death

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

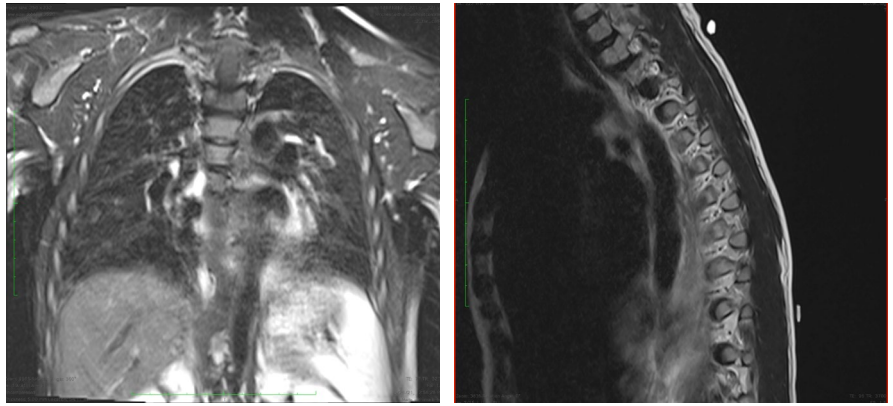
A male child spindle cell sarcoma, 5-years of age at diagnosis



Baseline



After 2 cycles of tovorafenib

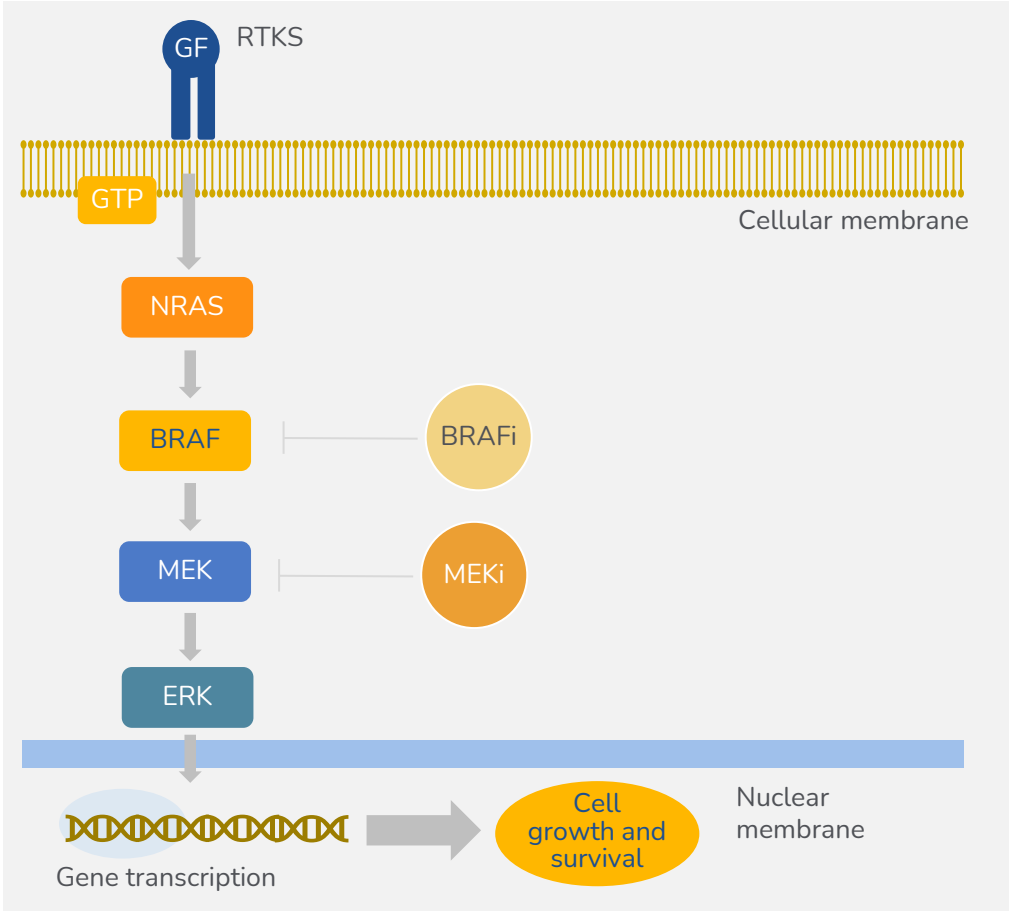


- After the first dose of tovorafenib (DAY101), the patient experienced grade 2 rash, which resolved in a day following a dose of diphenhydramine
- Radiotherapy-related adverse events included hyperpigmentation overlying the spine on the upper back with no skin breaks, and mild dysphagia

Data cut off: September 30, 2021

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

- Pimasertib is an investigational orally-bioavailable, selective, non-competitive MEK1/2 inhibitor in-licensed from Merck KGaA in February 2021
- Extensive non-clinical and clinical development work through Phase 2, including a solid tumor trial in Japan and combinations with other MOAs
- Main AEs typical for all in-class allosteric MEK inhibitors (GI, CPK elevation, skin rash, visual disturbances)
- Nearly three-fold higher CNS penetration than other MEKi inhibitors (trametinib or selumetinib)
- Pimasertib showed monotherapy clinical activity, including an improvement in median PFS versus dacarbazine in NRAS mutant melanoma
- Combination with tovorafenib (DAY101) and other targeted therapies may unlock the full value of pimasertib in advanced solid tumors



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.

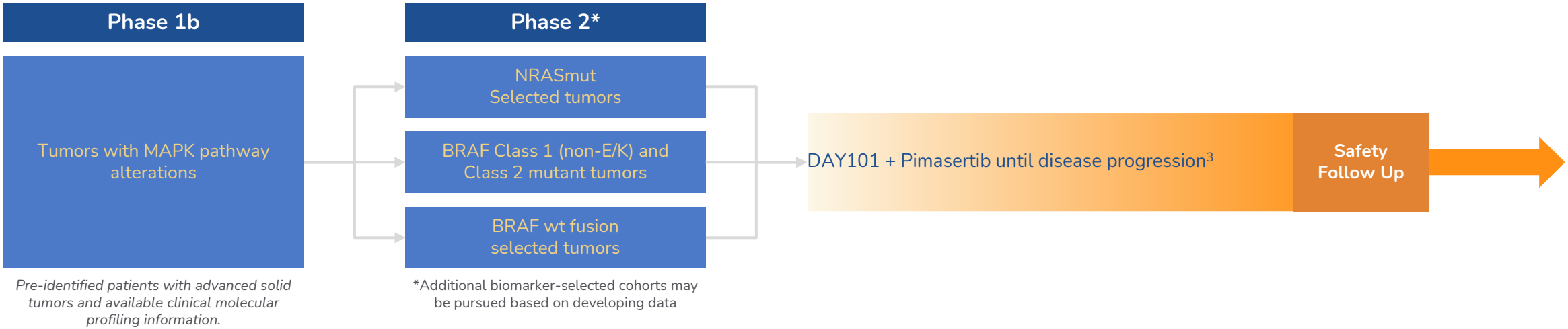
Tovorafenib (DAY101) / Pimasertib Combination to be Evaluated in Solid Tumors (FIRELIGHT-1)

Trial Design[1]

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

Endpoints

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



Pre-identified patients with advanced solid tumors and available clinical molecular profiling information.

*Additional biomarker-selected cohorts may be pursued based on developing data

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

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)

- Topline results presented in January 2023
- Pre-NDA meeting and NDA submission planned in 1H 2023
- NDA data set will include additional follow up with data to be presented at a medical meeting in Q2 2023

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

- First patient dosing expected in Q1 2023

All financial and share information is unaudited

Next Steps

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

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

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

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

FIREFLY-1

- Present NDA data set at medical meeting in Q2 2023
- Pre-NDA meeting and NDA submission planned for 1H 2023

FIREFLY-2

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

FIRELIGHT-1

- Evaluate tovorafenib in combination and as monotherapy in adolescent and adult populations

Commercial

- Continue investment in market and launch preparation activities

Business Development

- Further investment in business development activities to expand our multiple asset portfolio

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

Thank you