Targeted Therapies for People of All Ages

November 2022

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This presentation and the accompanying oral commentary contain forward-looking statements that are based on our management's beliefs and assumptions and on information currently available to our management. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "could," "expect," "plan," anticipate," "believe," "estimate," "predict," "intend," "potential," "would," "continue," "ongoing" or the negative of these terms or other comparable terminology. Forward-looking statements include all statements other than statements of historical fact contained in this presentation, including information concerning our future financial performance, including the sufficiency of our cash and cash equivalents to fund our operations, business plans and objectives, timing and success of our planned nonclinical and clinical development activities, timing and results of nonclinical studies and clinical trials, efficacy and safety profile of our product candidates, the execution of the Phase 2 clinical trial for tovorafenib and the Phase 1b/2 clinical trial for tovorafenib and pimasertib as designed, any expectations about safety, efficacy, timing and ability to complete clinical trials and to obtain regulatory approvals for tovorafenib and other candidates in development, the ability of tovorafenib to treat pLGG or related indications, the potential therapeutic benefits and economic value of our product candidates, potential growth opportunities, competitive position, industry environment and potential market opportunities, our ability to protect intellectual property, and the impact of global business or macroeconomic conditions, including as a result of the COVID-19 pandemic, inflation, and rising interest rates, on our business and operations.

Forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. These factors, together with those that are described under the heading "Risk Factors" contained in our most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission ("SEC") and other documents we file from time to time with the SEC, may cause our actual results, performance or achievements to differ materially and adversely from those anticipated or implied by our forward-looking statements.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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

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

Mission That Creates Value

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

Tovorafenib (DAY101) Lead Program

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

Growing Portfolio and Runway Beyond Clinical Milestones

- Two clinical-stage MEKi assets, in-licensed for combination trials
- Projected cash runway into 2025
- Multiple key milestones
  - Top-line data from FIREFLY-1 trial in Q1 2023
  - NDA submission in 1H 2023, if data are supportive
  - First patient dosing in pivotal Phase 3 (FIREFLY-2 /LOGGIC), frontline trial expected Q4 2022

Pediatric Markets Create Opportunity for High Impact and Capital Efficiency

Regulatory and reimbursement tailwinds

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

Rapid clinical development

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

Enriched responder populations informed by underlying biology

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

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

Jeremy Bender, PhD, MBA

Chief Executive Officer

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

Samuel Blackman, MD, PhD

Chief Medical Officer & Founder

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

Charles York II, MBA

Chief Operating and Financial Officer

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

Mike Preigh, PhD

Chief Technical Officer

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

Davy Chiodin, PharmD

Chief Development Officer

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

Jaa Roberson

Chief People Officer

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

Adam Dubow

General Counsel

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

Our Pipeline

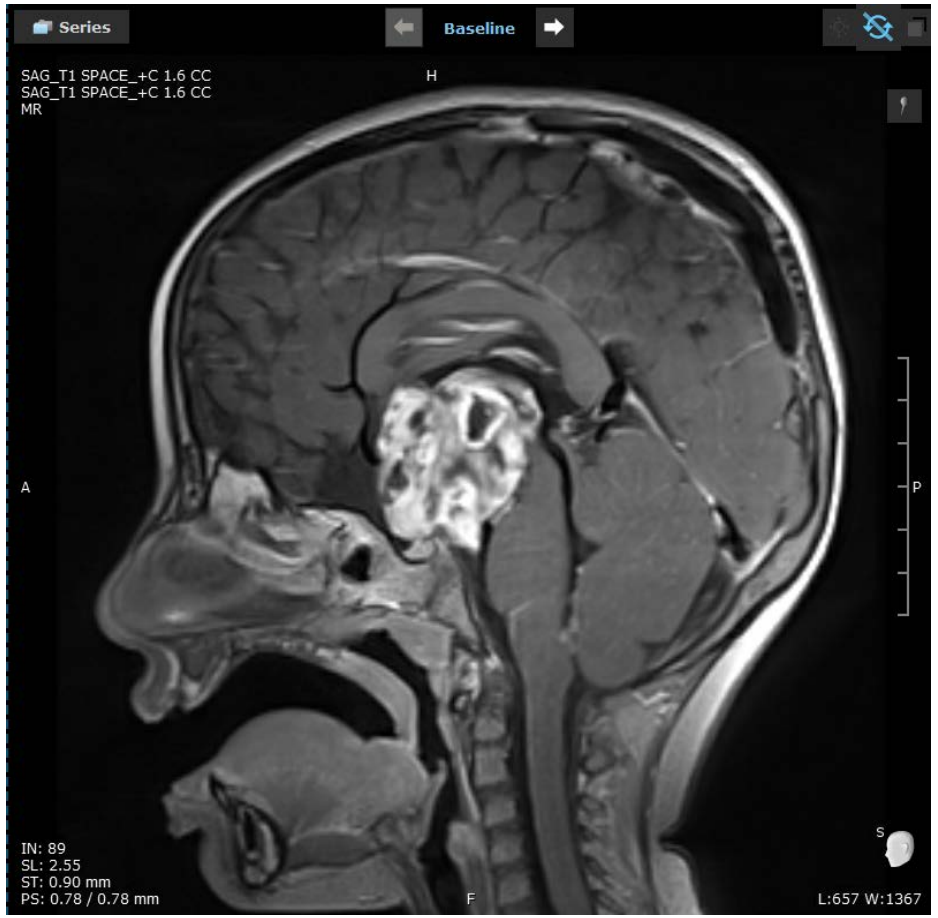
Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Recent & Anticipated Milestones
Tovorafenib (DAY101) Type II Pan-RAF Inhibitor ✓ FDA Breakthrough Therapy Designation for relapsed pLGG ✓ FDA Rare Pediatric Disease Designation (PRV Eligible) for pLGG ✓ FDA Orphan Drug Designation for gliomas ✓ EC Orphan Designation for gliomas	Relapsed pLGG	FIREFLY-1[1] (pivotal)				**Pivotal cohort enrollment complete:** May 2022 **Initial data presented:** June 2022 **Topline data expected:** Q1 2023
	Frontline pLGG	FIREFLY-2 (pivotal)				**Trial Initiation:** June 2022 **First patient dosing expected:** Q4 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*				**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)

Type II Pan-RAF Inhibitor

Pediatric Low-Grade Gliomas (pLGG)

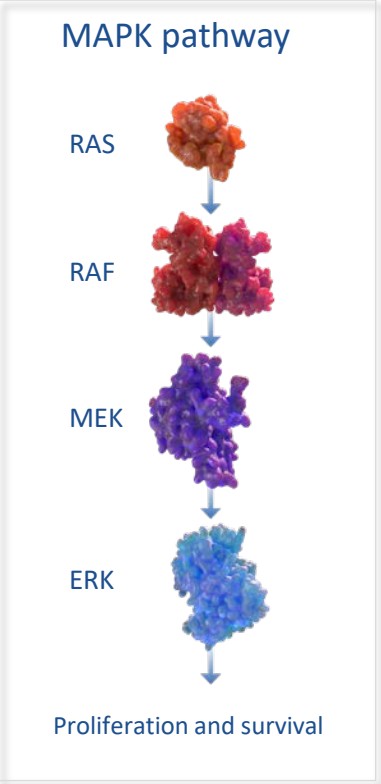


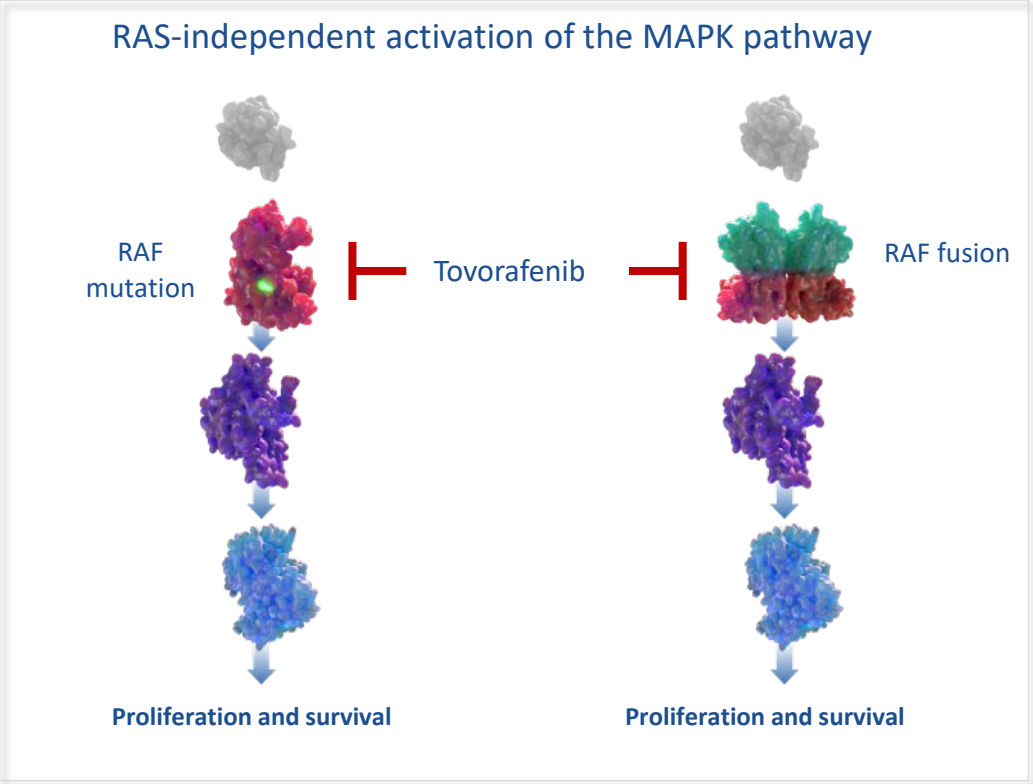
6 y/o with large relapsed BRAF fusion-positive optic pathway glioma

- **Despite being the most common brain tumor in children, there are no approved agents and no standard-of-care for the majority of patients with relapsed/progressive disease[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;

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

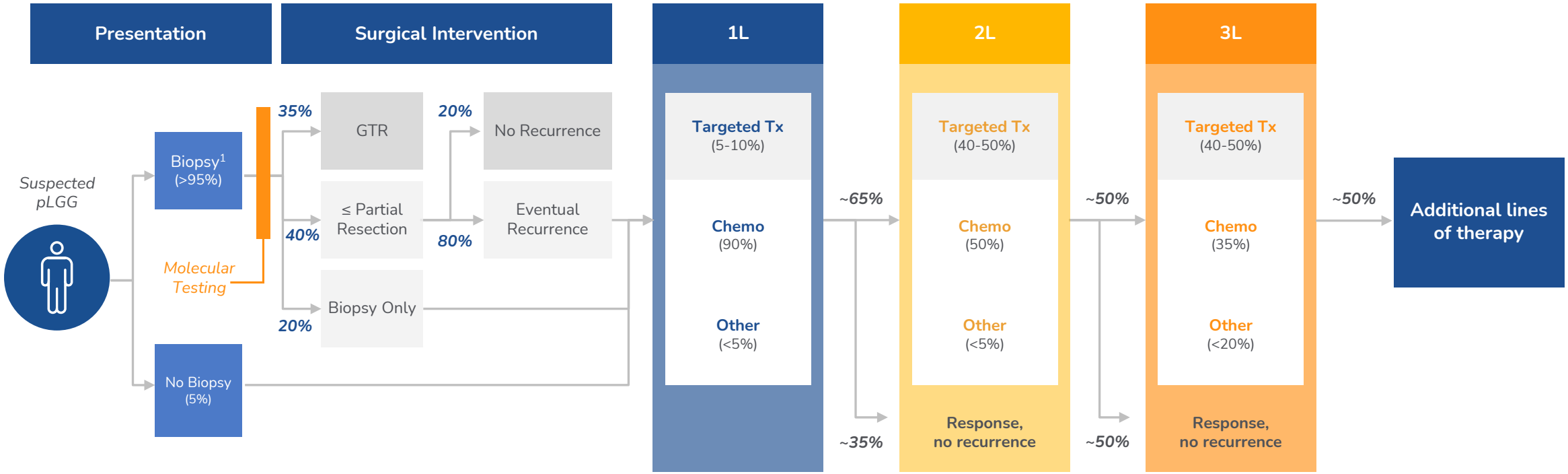




- **Tovorafenib (DAY101) is an investigational, oral, selective, CNS-penetrant, type II pan-RAF inhibitor that was designed to inhibit both monomeric and dimeric RAF kinase**
  - Activity in tumors driven by both RAF wild-type fusions and BRAF V600E mutations
  - Tablet and pediatric-friendly liquid suspension; once weekly dosing
- **Currently approved type I RAFi are indicated for use only in adults and patients 6+ with relapsed tumors harboring a BRAF V600 mutation**
  - Type I RAF inhibitors cause paradoxical MAPK activation in the setting of wild-type RAF, increasing the risk of tumor growth in *BRAF* fusion-driven and other non-V600 mutant cancers

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;

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

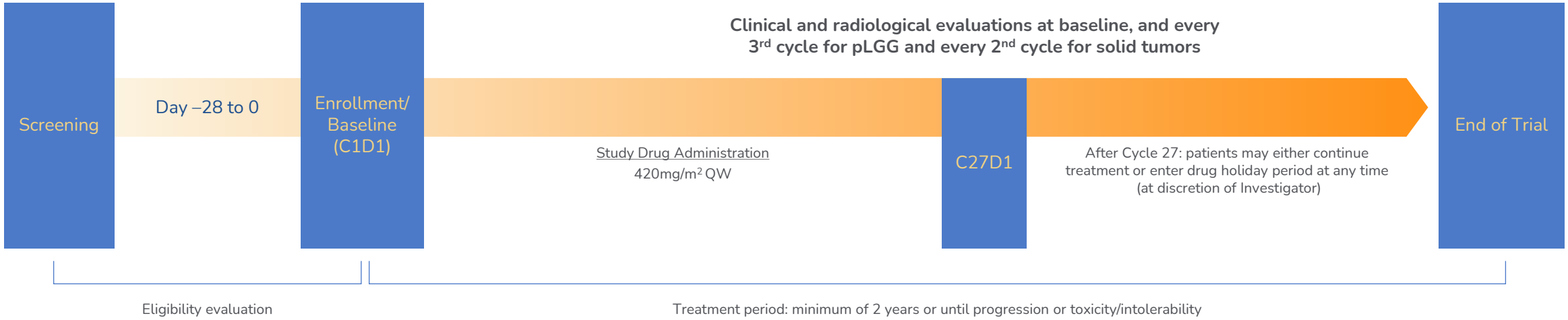
Pivotal Phase 2 Trial Of Monotherapy Tovorafenib (DAY101) In Relapsed Or Progressive pLGG (FIREFLY-1)

Trial Design

- Three arm, open-label, global registrational phase 2 trial
- Pivotal Arm 1 (recurrent/progressive LGG): n = ~ 60 RANO-evaluable patients aged 6 months to 25 years harboring a *KIAA1549-BRAF* fusion or BRAF V600 mutation
- Arm 2 (expanded access recurrent/progressive LGG): patients aged 6 months to 25 years harboring an activating RAF alteration
- Arm 3 (extracranial solid tumors): patients aged 6 months to 25 years harboring an activating RAF fusion

Endpoints (Pivotal Arm 1)

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

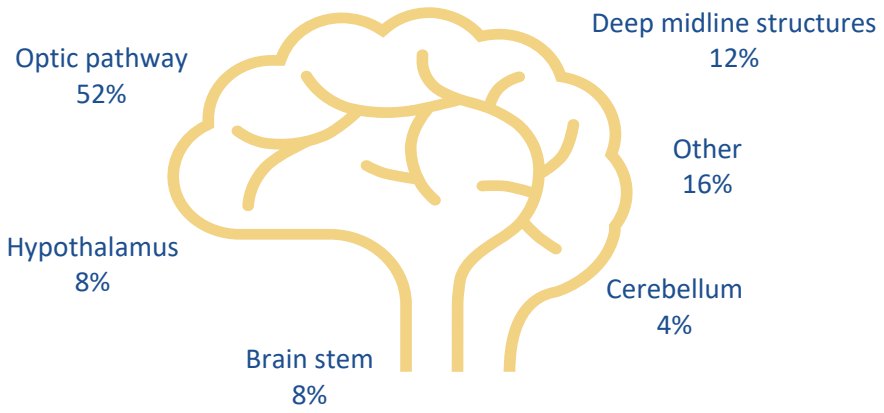


Abbreviations: C, cycle; D, day; LGG, low-grade glioma; ORR, objective response rate; PFS, progression-free survival.
NCT04775485

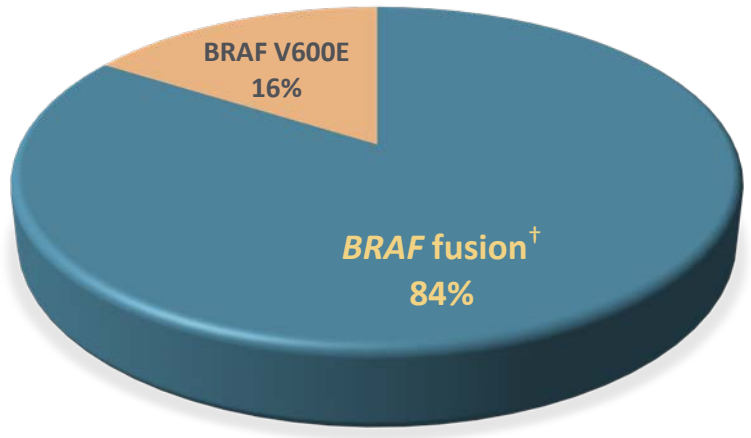
Baseline Characteristics

Characteristic	Arm 1 (N=25)
Median age, years (range)	8 (3-18)
Sex, n (%)	
Male	13 (52)
Female	12 (48)
Race, n (%)	
Black or African American	1 (4)
Asian	2 (8)
White	15 (60)
Other*	7 (28)
Karnofsky/Lansky performance status, n (%)	
50-70	1 (4)
80-100	24 (96)
Number of lines of prior therapy	
Median (range)	3 (1-9)
1, n (%)	5 (20)
2, n (%)	6 (24)
≥3, n (%)	14 (56)
Prior MAPK pathway targeted therapy, n (%)	
Yes	18 (72)
No	7 (28)

Location (n=25)

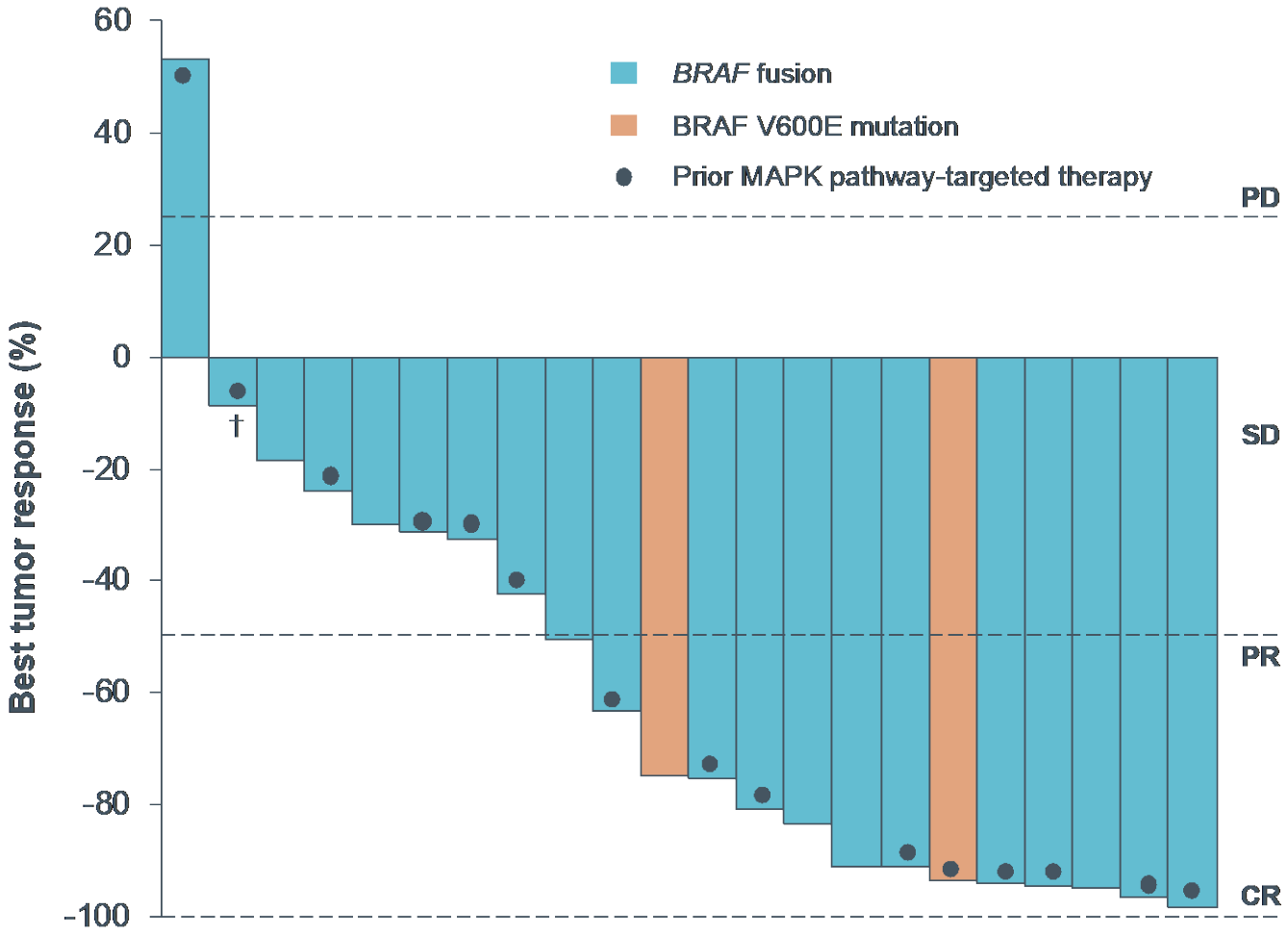


BRAF alteration (n=25)



Apr 14, 2022 data cutoff; *Includes 4 patients with race not specified. †Includes 2 patients with BRAF duplication and 1 with BRAF rearrangement per fluorescence in situ hybridization. MAPK, mitogen-activated protein kinase; prior MAPK pathway targeted therapy indicates either prior MEKi and/or prior type I RAFi therapy.

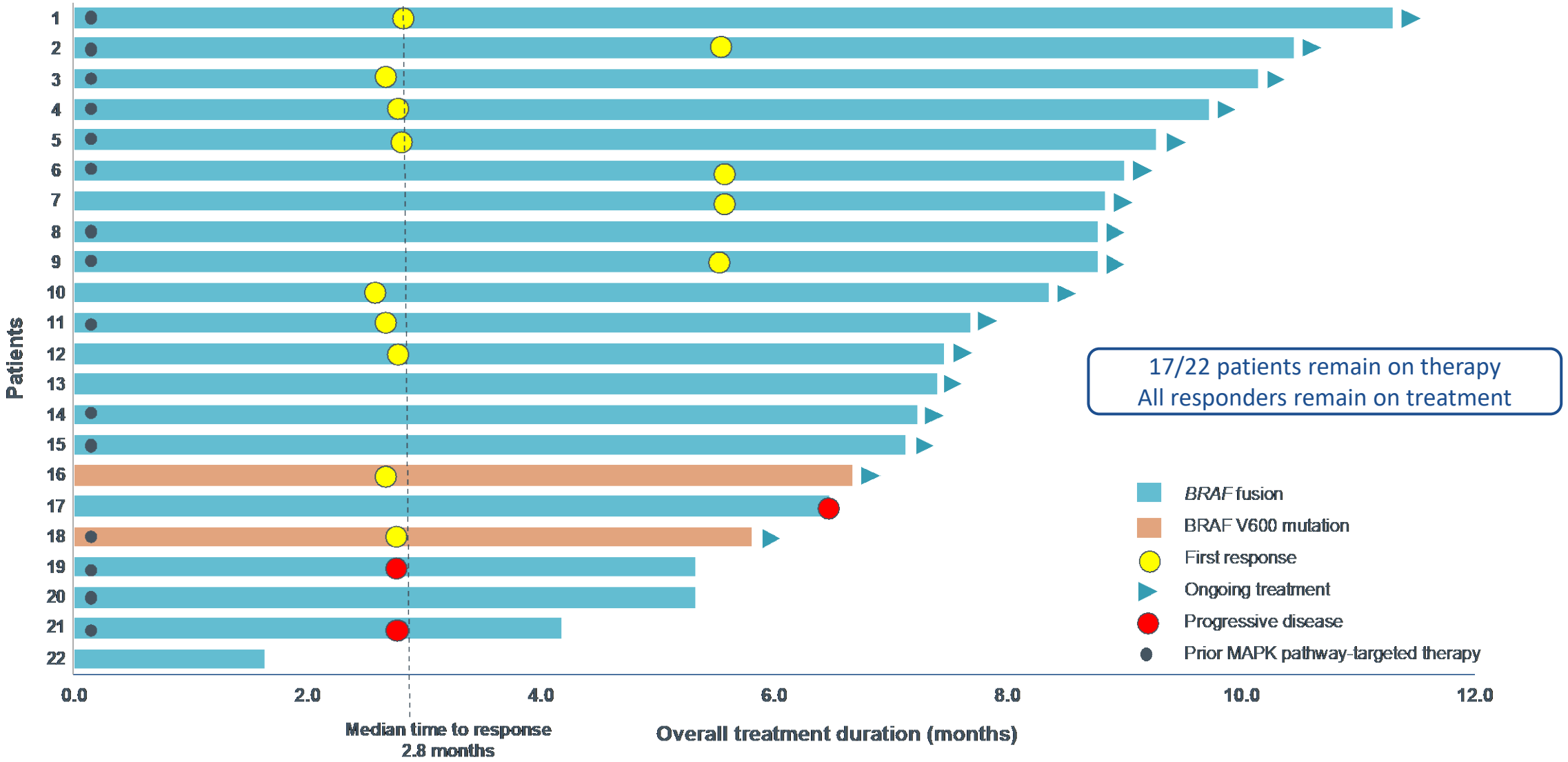
Tumor Response To Tovorafenib (DAY101) For All Patients With RANO-Evaluable Lesions (n=22)*



Response (IRC)	RANO Evaluable N=22*
ORR (95% CI)	64% (41-83)
BRAF fusion (n=20)	60%
BRAF V600E (n=2)	100%
CBR#	91%
Best overall response	
PR (13/22)	59%
uPR (1/22)	5%
SD (6/22)	27%

Apr 14, 2022 data cutoff. Total % of response maybe may be different than the sum of the individual overall response due to rounding. *3/25 patients lacked evaluable lesions per RANO criteria based on IRC evaluation. †Progressive disease due to presence of new lesions. #patients with best overall response of CR, PR/uPR and SD. CBR, clinical benefit rate; IRC, independent radiological review committee; ORR, overall response rate; MAPK, mitogen-activated protein kinase; PR, partial response; SD, stable disease; uPR, unconfirmed partial response

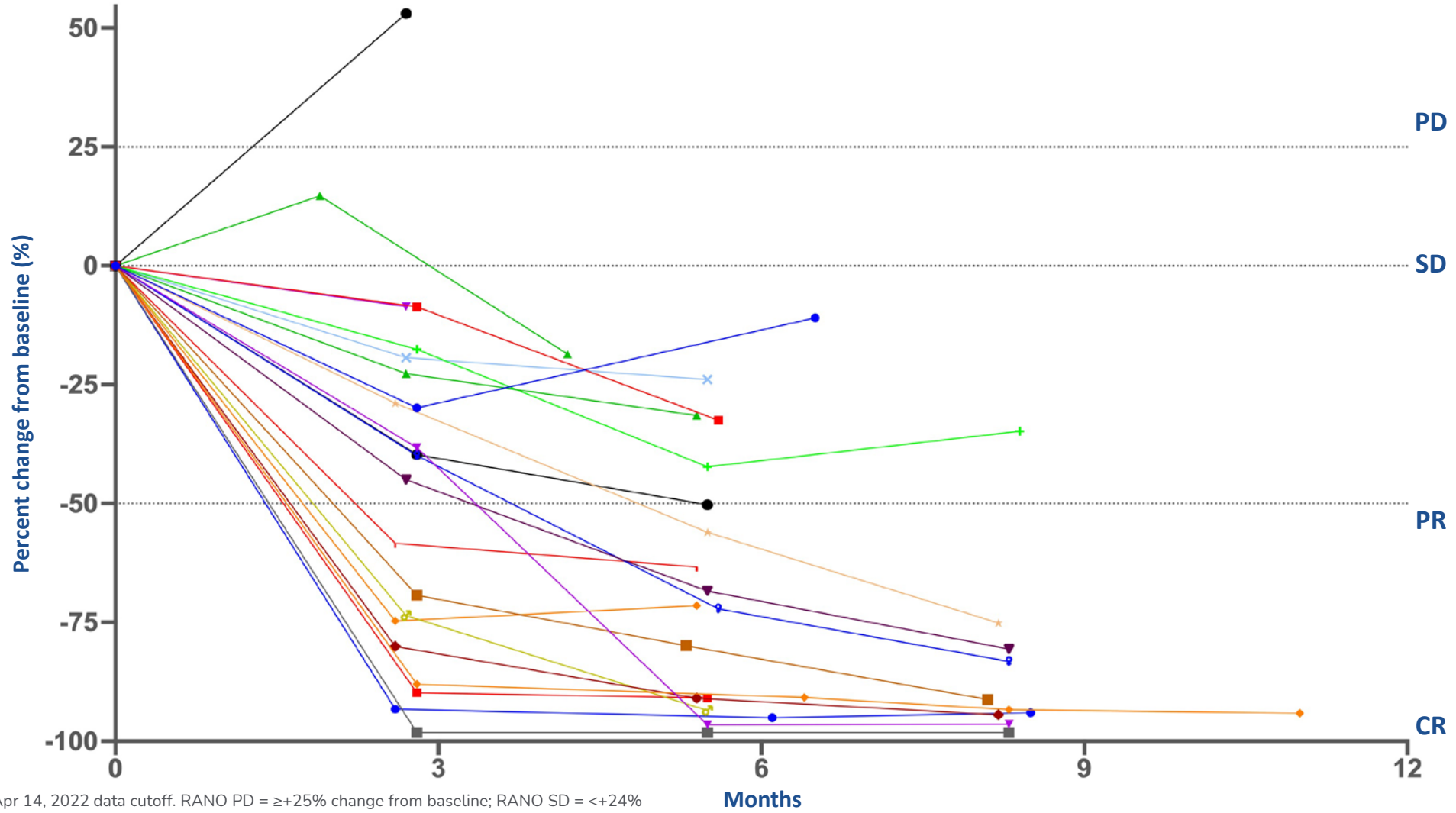
Duration of Tovorafenib (DAY101) Therapy For All Patients with RANO-Evaluable Lesions (n=22)



Apr 14, 2022 data cutoff.

Individual Patient Tumor Change From Baseline

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



Apr 14, 2022 data cutoff. RANO PD = ≥+25% change from baseline; RANO SD = <+24% to > -50% change from baseline; RANO PR = ≤ -50% change from baseline; RANO CR = -100% change from baseline.

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

	Treatment-emergent AEs		Treatment-related AEs	
Preferred term, n (%)	Any grade	Grade ≥3	Any grade	Grade ≥3
Blood creatine phosphokinase increased	20 (80)	2 (8)	18 (72)	2 (8)
Hair color changes	17 (68)	-	17 (68)	-
Anemia	14 (56)	3 (12)	10 (40)	2 (8)
Aspartate aminotransferase increased	14 (56)	-	12 (48)	-
Vomiting	14 (56)	2 (8)	6 (24)	1 (4)
Rash*	13 (52)	3 (12)	13 (52)	3 (12)
Blood lactate dehydrogenase increased	12 (48)	-	9 (36)	-
Headache	10 40)	-	3 (12)	-
Dry skin	9 (36)	-	7 (28)	-
Epistaxis	9 (36)	-	4 (16)	-
Constipation	8 (32)	-	5 (20)	-
Hypocalcemia	8 (32)	-	6 (24)	-
Nausea	8 (32)	-	3 (12)	-
Alanine aminotransferase increased	7 (28)	1 (4)	4 (16)	1 (4)
Fatigue	7 (28)	-	7 (28)	-

- Most treatment-emergent AEs were grade 1 or 2 (96%)
- Other important treatment-emergent AEs included:
  - Decreased weight (24%)
  - Decreased appetite (16%)
  - Hyponatremia (16%)
- 7 patients (28%) required dose modifications due to treatment-related AEs
- No patient discontinued treatment due to AEs

Apr 14, 2022 data cutoff. AE, adverse event. TEAE, treatment-emergent adverse event.
*Includes maculopapular and erythematous rash

Key Takeaways

- **Encouraging initial efficacy data from FIREFLY-1 for pediatric patients with relapsed LGG harboring *BRAF* fusion or BRAF V600 mutation, for whom there is no standard-of-care and no approved agents for the majority of patients**
  - 64% ORR and 91% clinical benefit rate (partial response/unconfirmed partial response + stable disease) in the 22 RANO-evaluable patients:
    - 14 partial responses (13 confirmed responses and 1 unconfirmed response)
    - 6 patients with stable disease
  - All patients with stable disease (n=6) were noted to have tumor shrinkage, ranging between 19% and 43%
  - Responses were observed in patients with both BRAF fusions and BRAF V600E mutations who received prior MAPK-targeted therapy
  - The median-time-to-response was 2.8 months
  - A heavily-pretreated population, with a median of 3 prior lines of therapy (range: 1-9)
  - All patients who responded remain on therapy (n=14) and no patients have discontinued treatment due to treatment-related adverse events
- **Initial safety data, based on the first 25 patients, indicated monotherapy tovorafenib (DAY101) to be generally well-tolerated**
  - Majority of AEs were grade 1 or 2; most common treatment-related AEs were CPK elevation, rash, and hair color changes
  - Treatment-related AEs of grade 3 or greater occurred in nine patients (36%)
- **Plan to present additional initial study results from FIREFLY-1 at the Society for Neuro-Oncology (SNO) annual meeting**
- **Topline results from the full registrational cohort (n=~60) of FIREFLY-1 expected to be available 1Q 2023, with NDA submission planned for 1H 2023**
- **Early results from FIREFLY-1 support plan to evaluate tovorafenib (DAY101) in parallel with a pivotal Phase 3 frontline pLGG study (FIREFLY-2)**
  - Primary endpoint of ORR based on RANO criteria, assessed by blinded independent central review

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

	2020 Estimated Incidence Under 25	2017 Estimated SEER Prevalence Under 25
US Population[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 (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.

FIREFLY-2/LOGGIC

Pivotal Phase 3 Trial of Tovorafenib (DAY101) in Newly Diagnosed pLGG

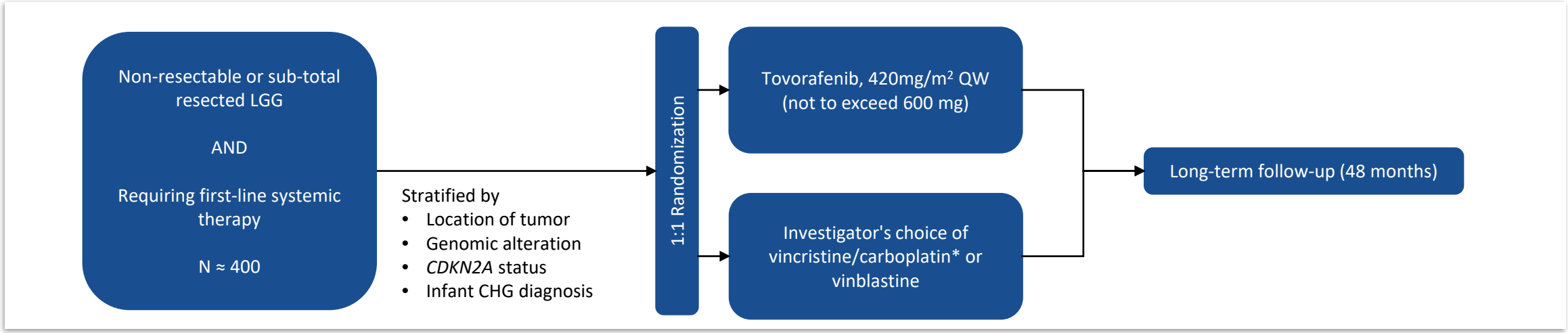
FIREFLY-2/LOGGIC Pivotal Phase 3 Trial Of Tovorafenib (DAY101) In Newly Diagnosed pLGG

Trial Design

- Randomized, global, registrational Phase 3 trial of monotherapy tovorafenib (DAY101) vs SoC chemotherapy
- Eligibility: Patients aged 6 months to <25 years with LGG harboring a RAF alteration and requiring first-line systemic therapy
- Tovorafenib (DAY101) available as tablets and pediatric-friendly liquid suspension
- Patients who progress after stopping tovorafenib (DAY101) may be re-challenged
- Patients who progress in the SoC arm during or post-treatment may cross-over to receive tovorafenib

Endpoints

- **Primary endpoint: ORR based on RANO criteria, assessed by blinded independent central review**
- Key secondary endpoints: PFS and DoR by RANO criteria, ORR by RAPNO criteria
- Other secondary endpoints: changes in neurological and visual function, safety, and tolerability
- Key exploratory objectives: QoL and health utilization measures



* COG or SIOPe-LGG regimen

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

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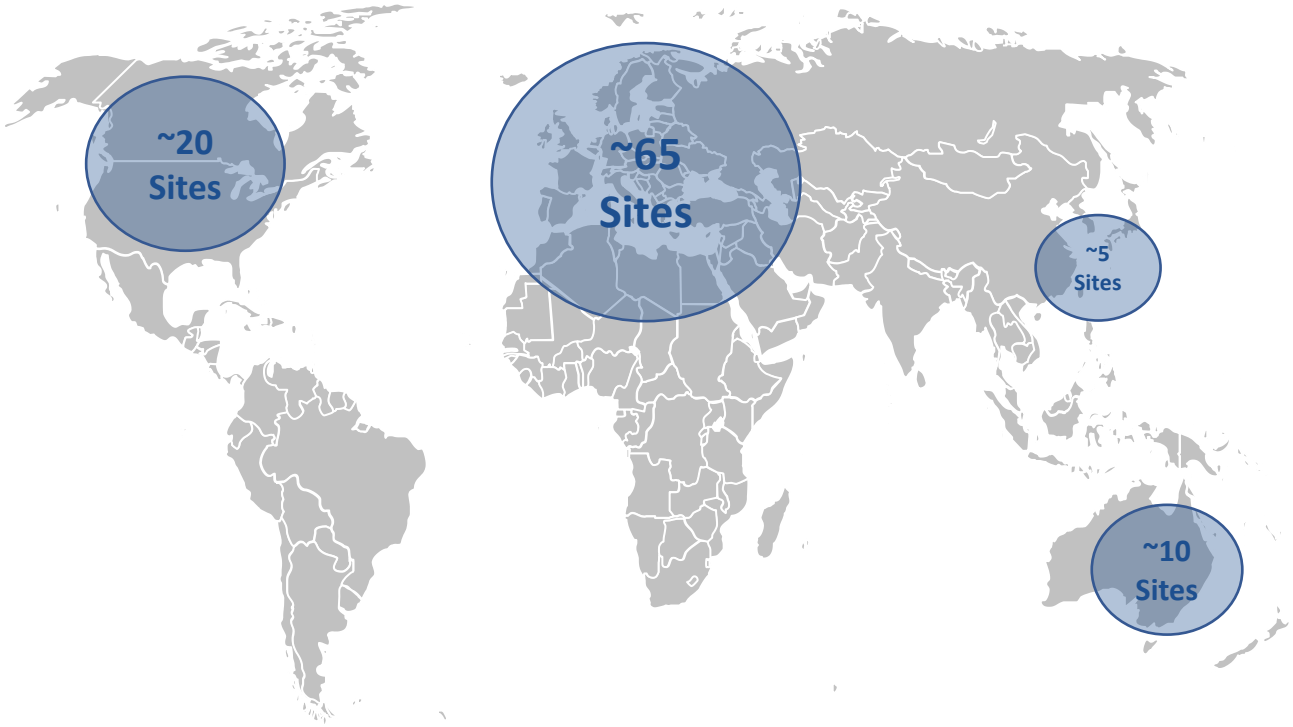
FIREFLY-2/LOGGIC: Pivotal Phase 3 Study Of Tovorafenib (DAY101) In Newly Diagnosed pLGG

- **Collaboration between Day One and the LOGGIC consortium, internationally recognized experts in pLGG research**
  - Coupled with the LOGGIC-CORE molecular diagnostic program
  - Worked jointly on the study design and discussions with the U.S. and EU regulatory authorities
- **Approximately 100 potential sites (~65 from the LOGGIC consortium)**

LOGGIC EUROPE

LOGGIC: LOw Grade Glioma In Children

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



Our Pipeline

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	Frontline pLGG		FIREFLY-2 (pivotal)			**Trial Initiation:** June 2022 **First patient dosing expected:** Q4 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*			**First patient dosed:** May 2022

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Tovorafenib (DAY101) is Active as a Monotherapy in Patients with RAF-altered Adult Solid Tumors and Has Shown Strong Synergy Preclinically in Combination

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

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

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

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

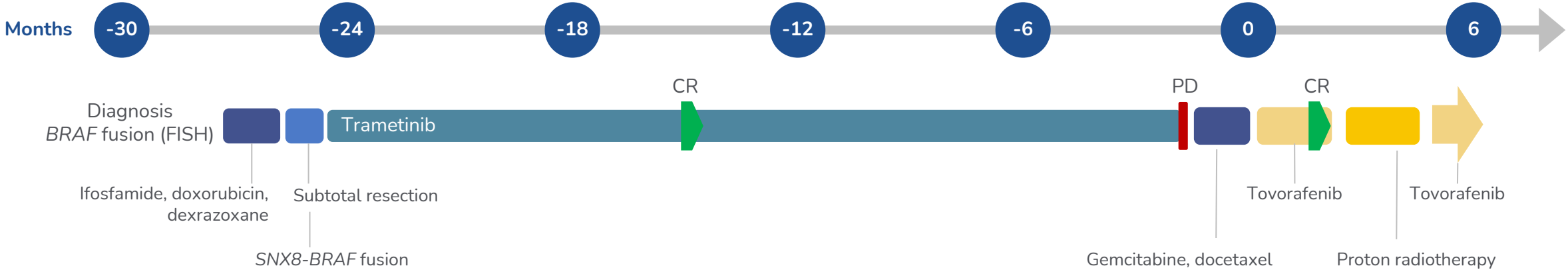
We ***initiated*** an adult solid tumor ***study*** to further evaluate monotherapy tovorafenib (DAY101) in patients with RAF altered tumors for which there are no currently approved therapies

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

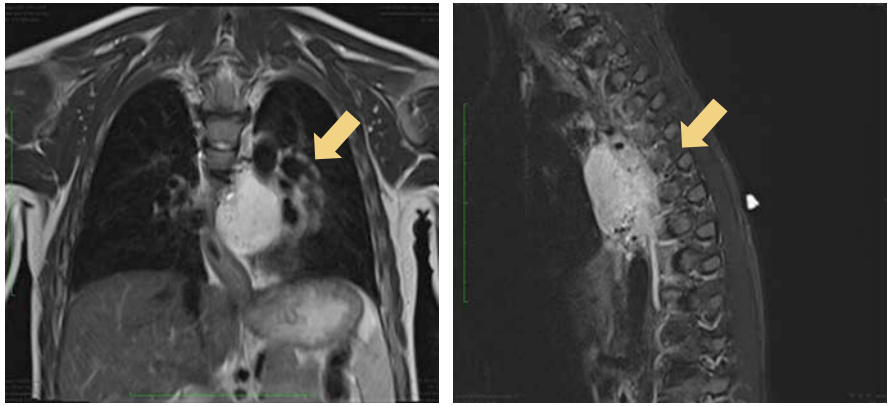
Source: Olszanski AJ et. al. European Society for Medical Oncology Congress; Poster #410P, 2017
Unpublished clinical study results

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

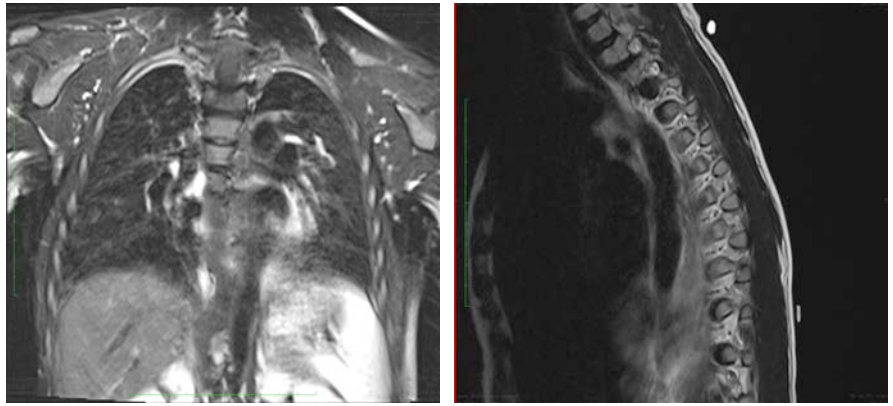
A male child spindle cell sarcoma, 5-years of age at diagnosis



Baseline



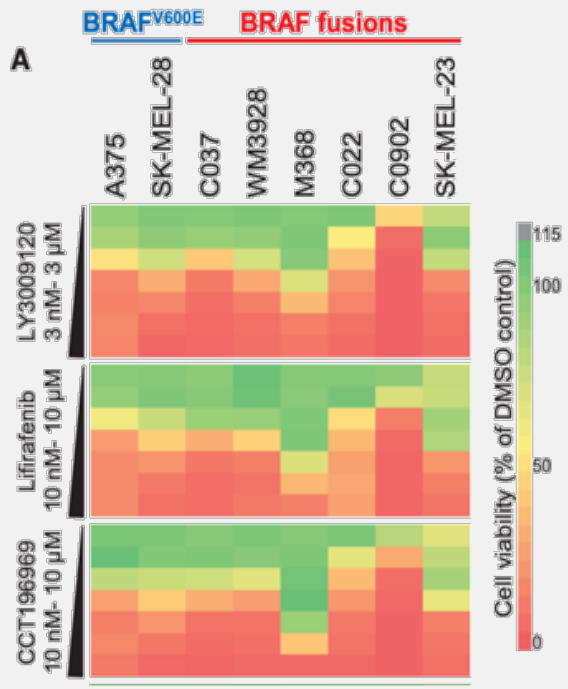
After 2 cycles of tovorafenib



- 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

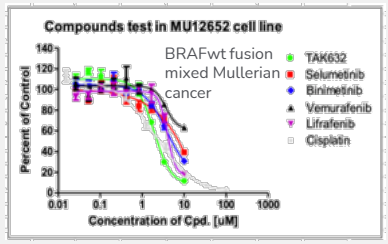
Data cut off: September 30, 2021

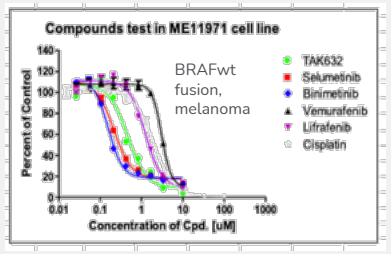
Next-generation RAF Inhibitors are Unique in Their Ability to Address Adult Cancers Associated with RAF Wild-type Fusions



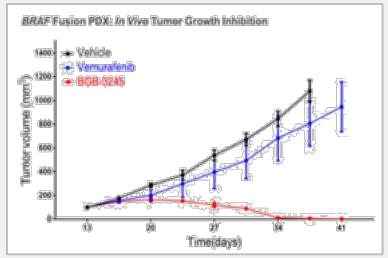
Botton T et al, Cell Reports, 2019

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





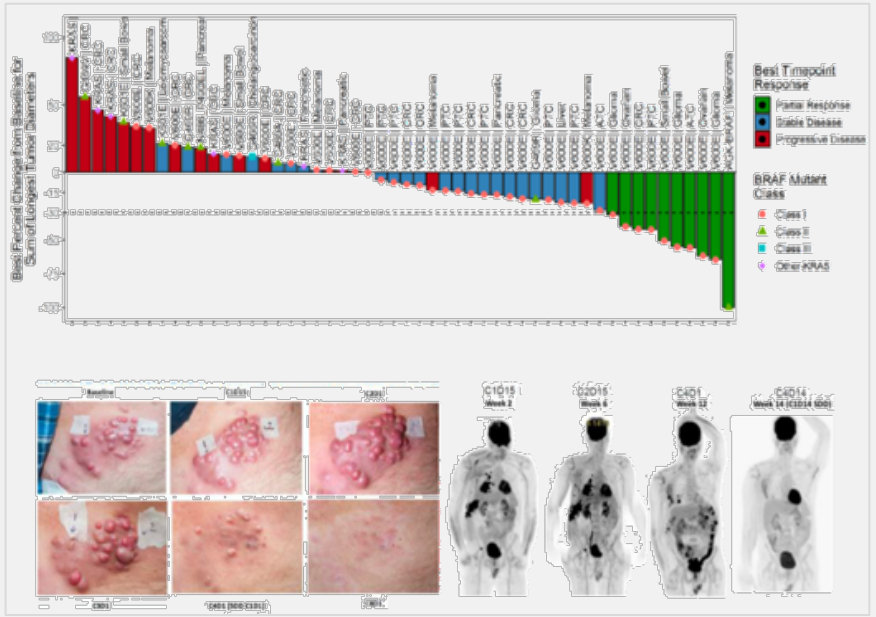
Day One/CrownBio internal data E5251-U2001 (Sep 2020)



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

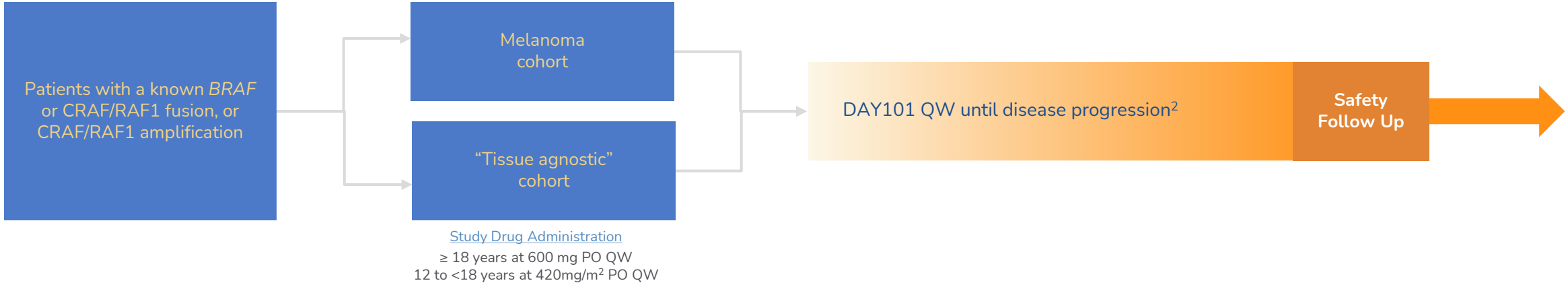
Phase 2 Study of Monotherapy Tovorafenib (DAY101) in Solid Tumors (FIRELIGHT-1)

Trial Design[1]

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

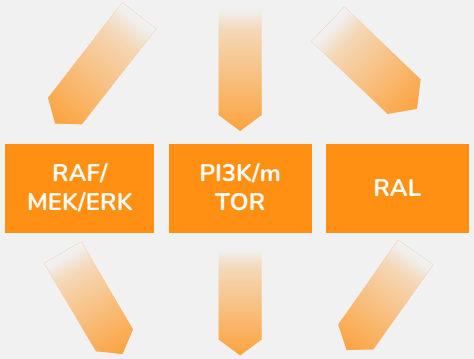
Endpoints

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



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

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

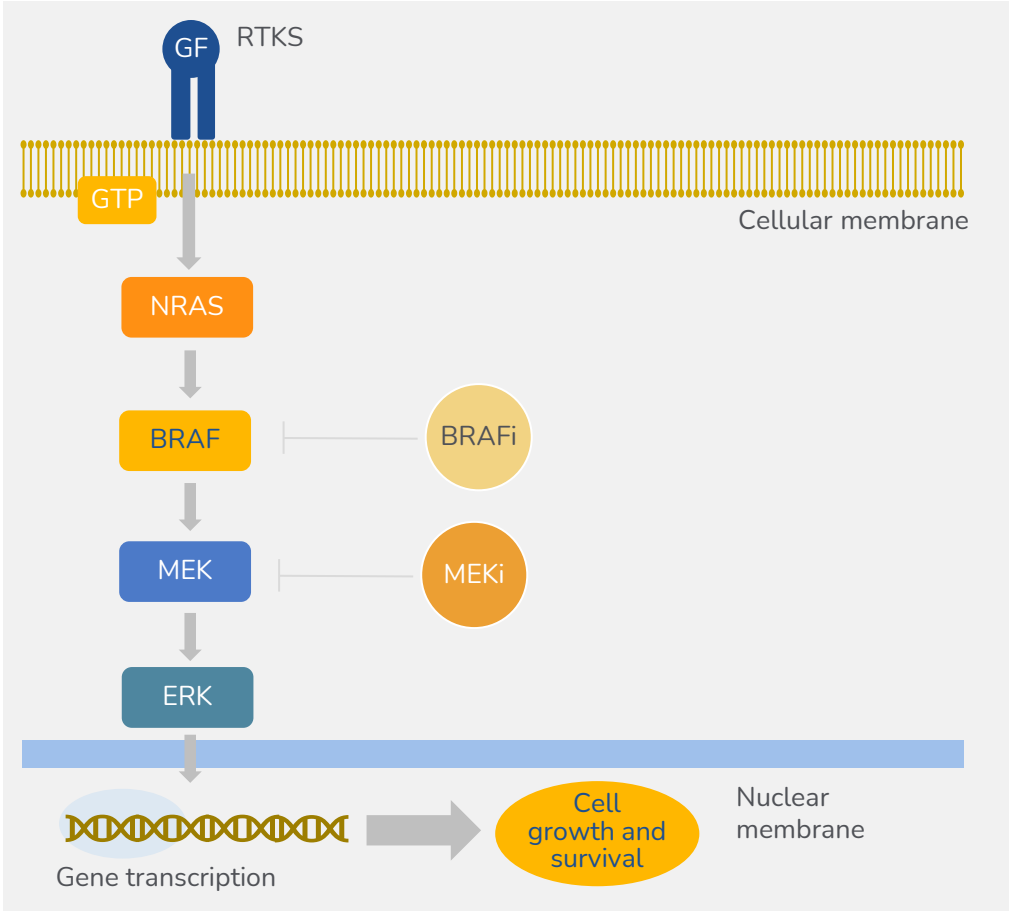
	BRAF non-V600	BRAF or CRAF WT fusion	KRAS or NRAS mutant	NF1 LOF
Signaling pathways	 Proliferation, survival	 Proliferation, survival	 Proliferation, survival	 Proliferation, survival
Potential combinations	Type II RAFi + MEKi or SHP2i	Type II RAFi + MEKi	Type II RAFi + KRAS - G12Ci or MEKi or SHP2i	Type II RAFi + SHP2i
Rationale	Non V600 BRAF dimers are effectively inhibited by type II, but not type I, RAFi	BRAF fusion dimers are effectively inhibited by type II, but not type I RAFi	Targeting multiple nodes of MAPK pathway will drive deeper and more durable response	Targeting multiple pathways will drive deeper response

Pimasertib

MEK1/2 Inhibitor

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

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



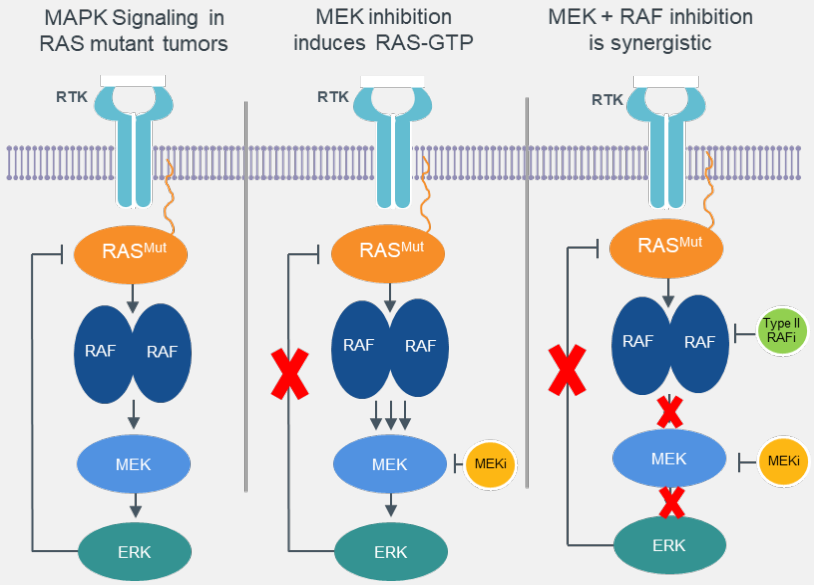
Source: Hepner, Salgues, Anjos, et al. 2017.

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

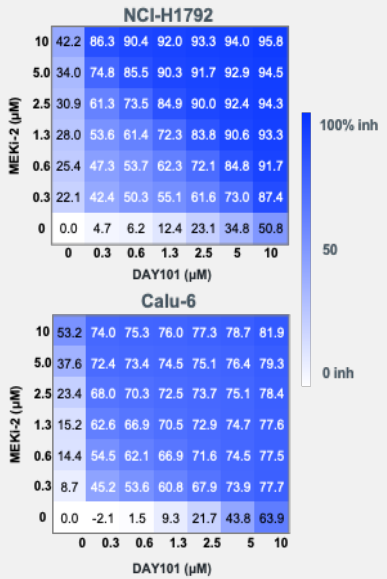
- The MAPK pathway normally has multiple feedback loops that negatively regulate upstream (RAS/RAF) activation to ensure optimal signaling
- Monotherapy MEK inhibition disables these feedback loops and induces RAS signaling as well as RAF dimerization and activation
- Combination therapy with a MEK inhibitor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

A

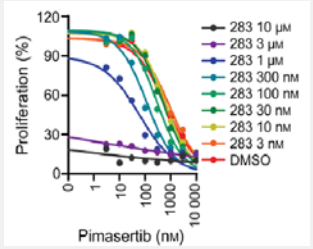


Modified from Yen et al. Cancer Cell, 2018

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)

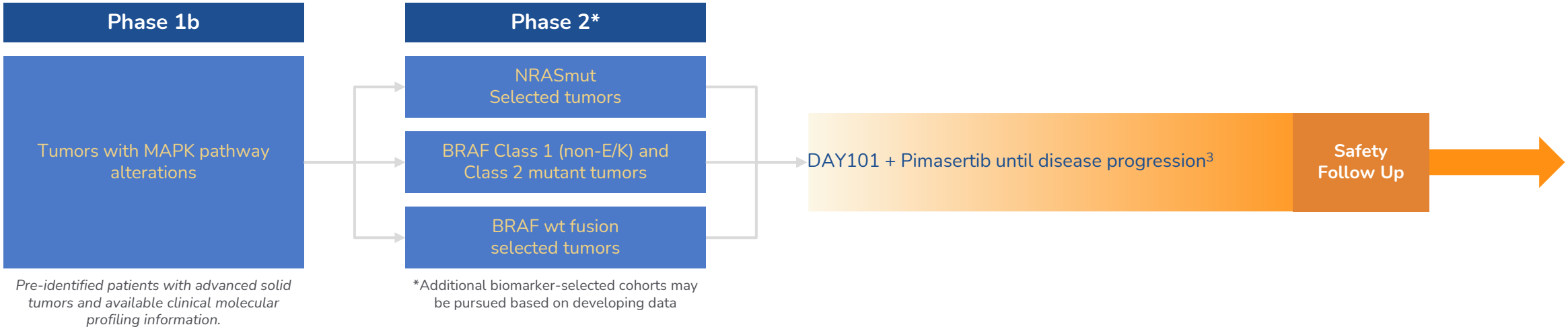
Tovorafenib (DAY101) / Pimasertib Combination to be Evaluated in Solid Tumors (FIRELIGHT-1)

Trial Design[1]

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



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

Summary

Financial Summary: DAWN

Cash, cash equivalents and short-term investments as of September 30, 2022: $374.3 million (no debt)

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

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

Projected cash runway into 2025

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

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

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

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

FIRELIGHT-1: Tovorafenib (DAY101) and pimasertib combination

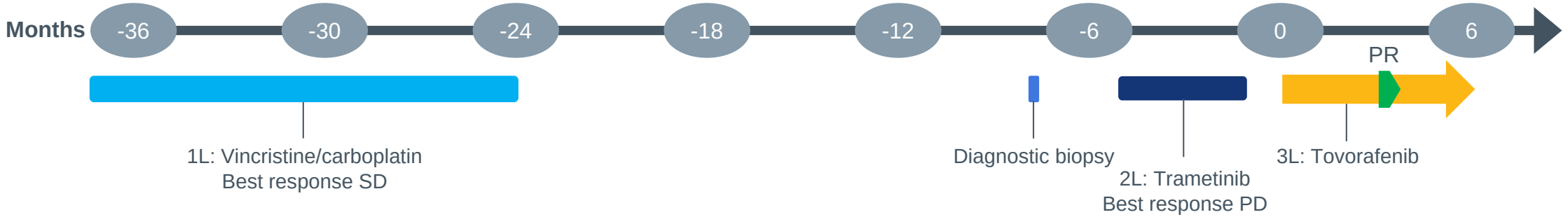
- First patient dosed in May 2022

All financial and share information is unaudited

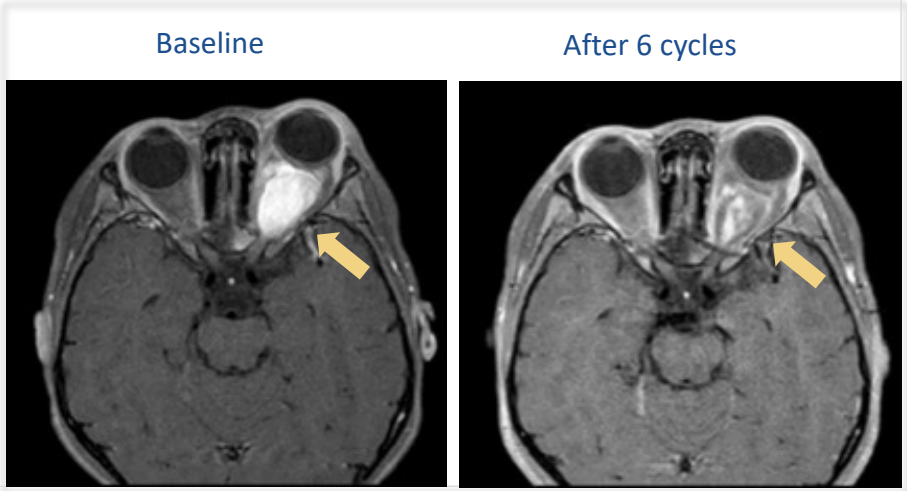
Appendix

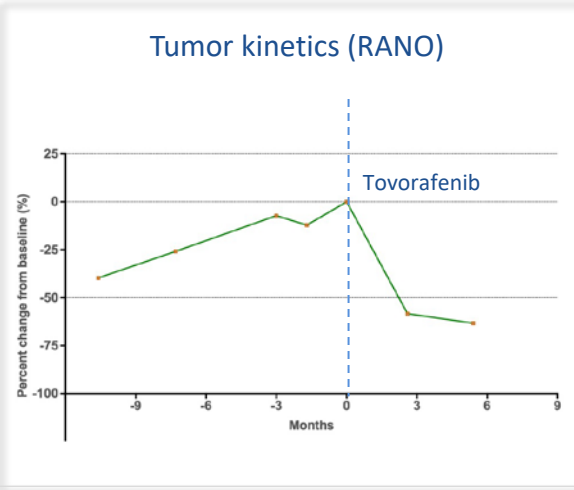
Case Study: Activity Of Tovorafenib (DAY101) In KIAA1549-BRAF Fusion Optic Pathway Glioma

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



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

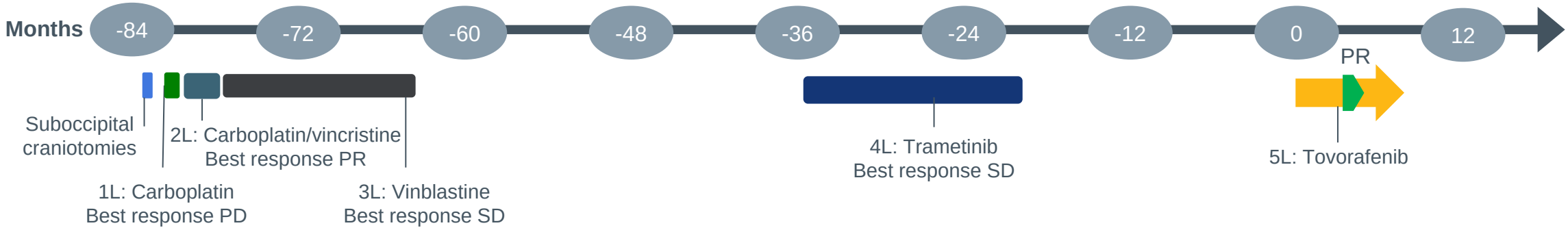




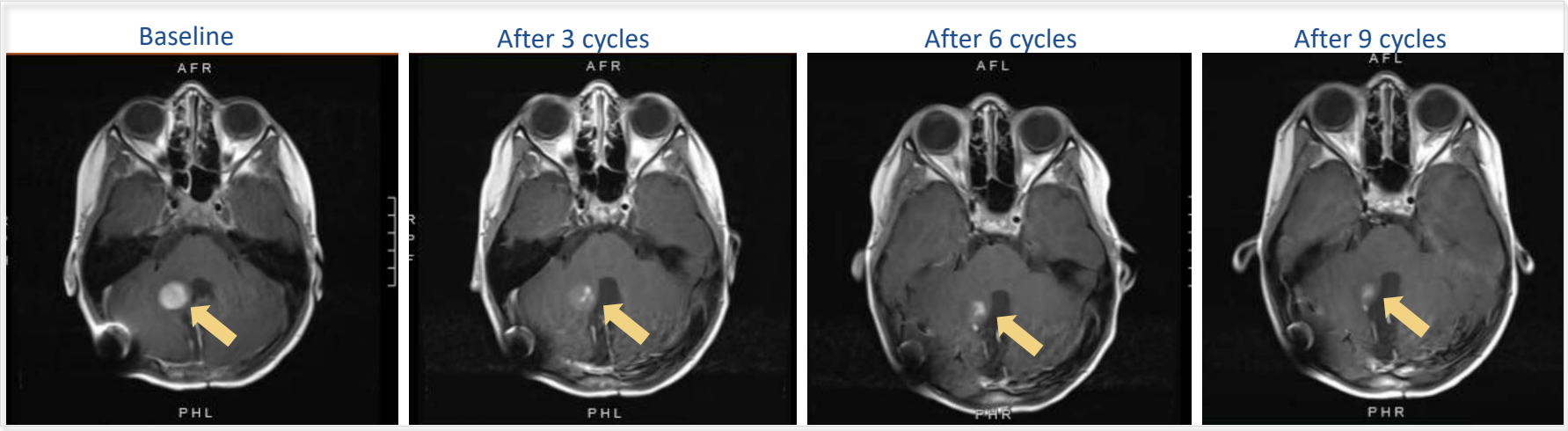
Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

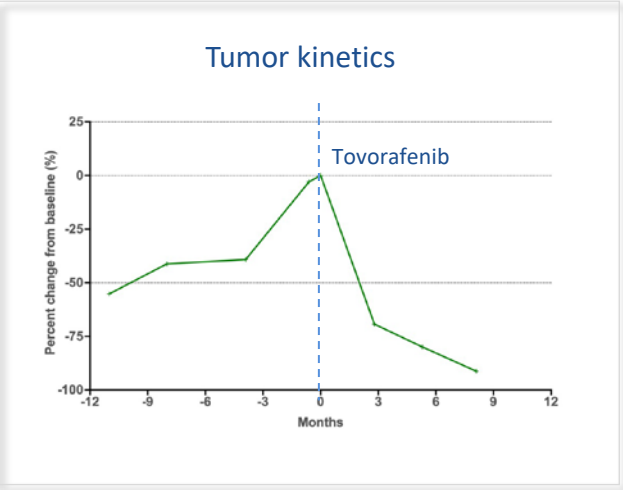
Case Study: Activity Of Tovorafenib (DAY101) In KIAA1549-BRAF Fusion Posterior Fossa Pilocytic Astrocytoma

An 8-years-old female child with a posterior fossa pilocytic astrocytoma, eczema, nausea and constipation



- PR (-69%) at cycle 3 with 500 mg QW tovorafenib, with a deepening of response (80% and 91% in cycles 6 and 9, respectively) over time
- AEs included grade 2 decrease in neutrophil count, pustular rash, and upper respiratory infection
- Patient continues to receive weekly tovorafenib



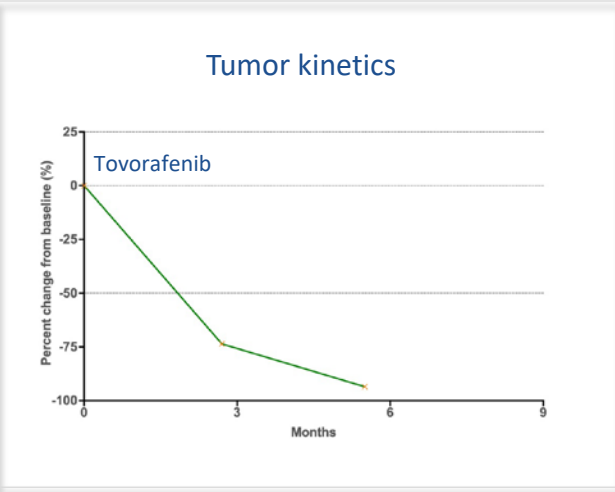


Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

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

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

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

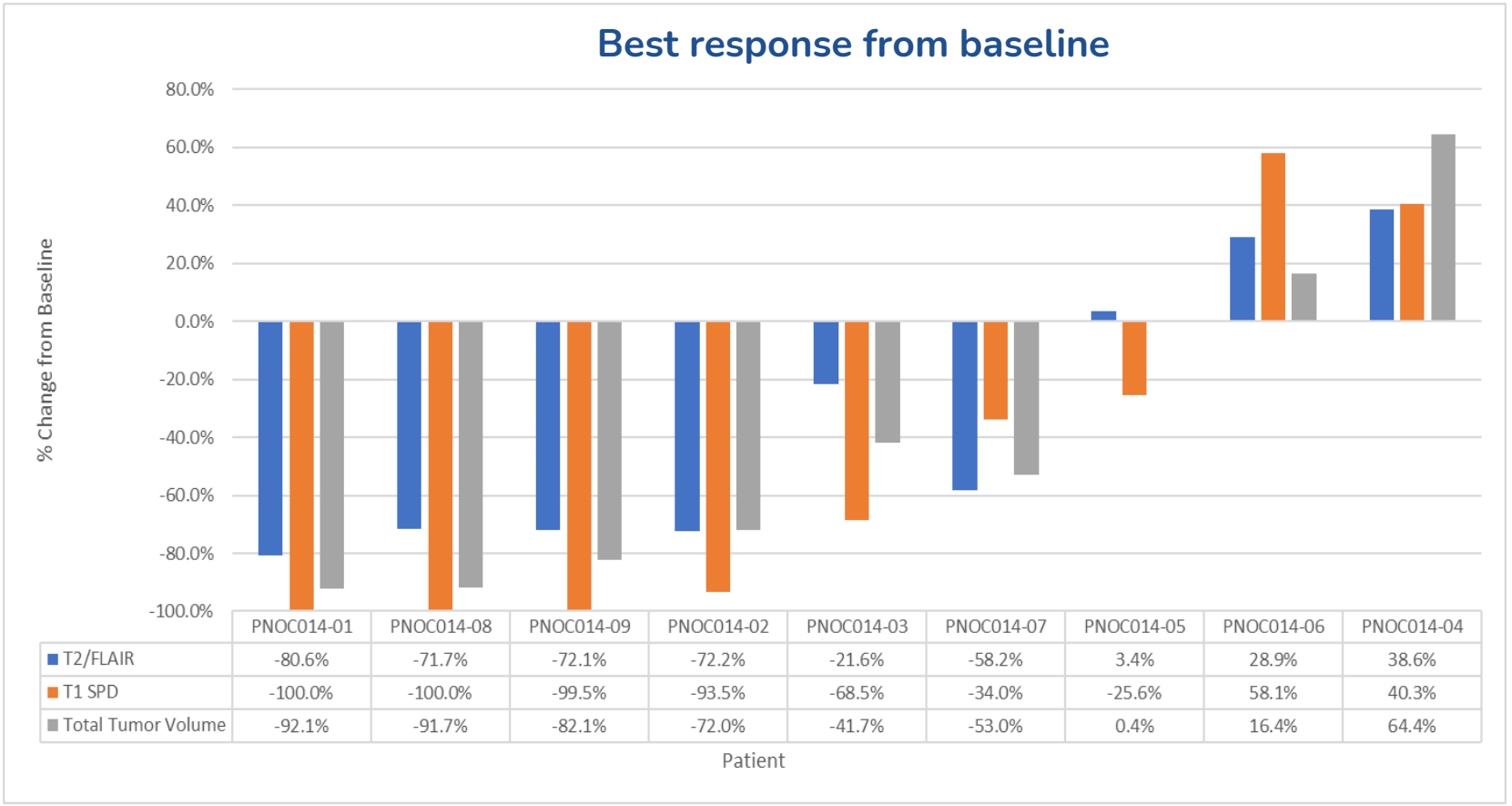


Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

FIREFLY-1 Study Status

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

Results from Independent Radiology Review of PNOC014



	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%	-34.0%	-25.6%	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%

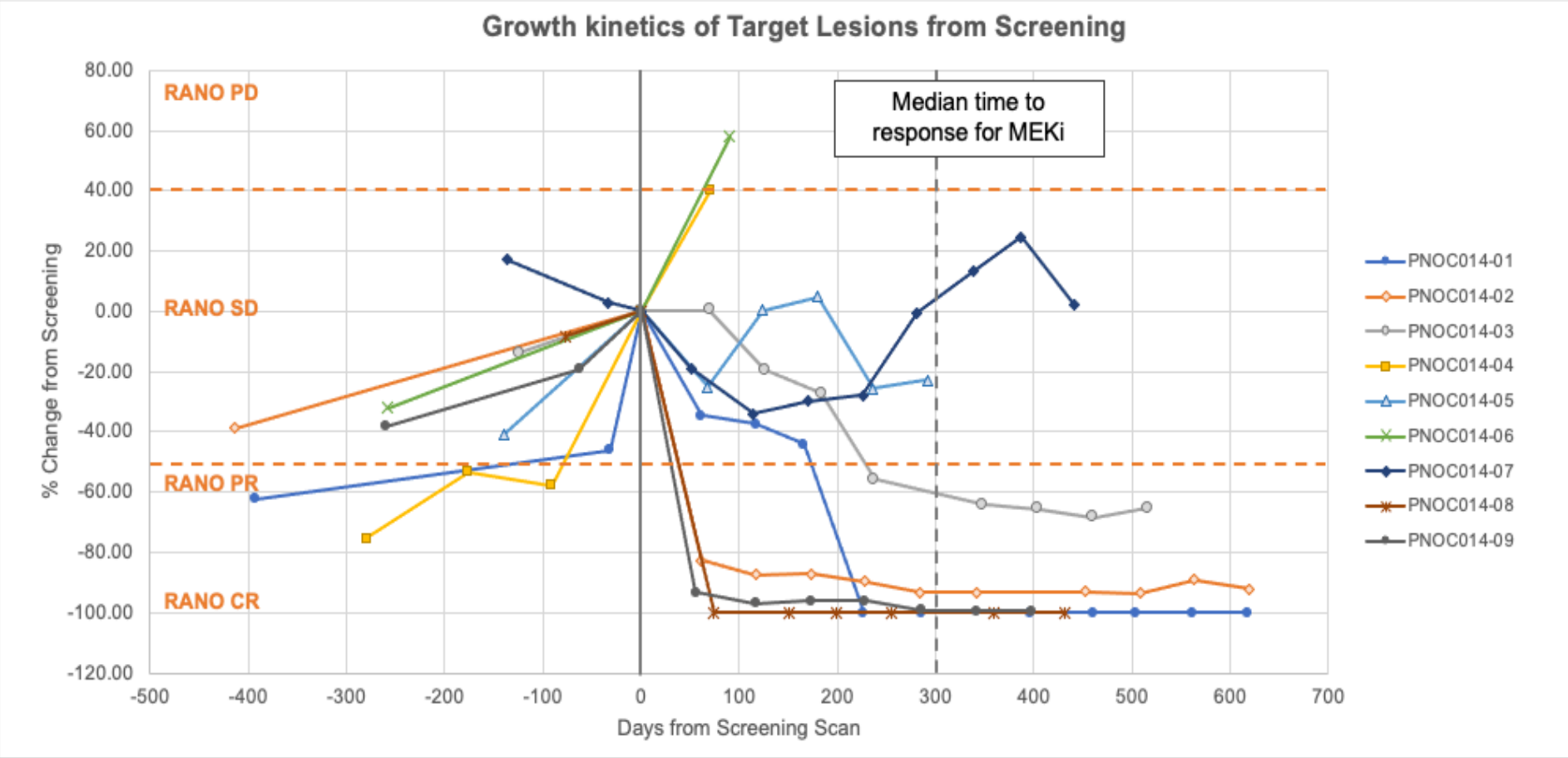
RANO: Response assessment for neuro-oncology (FDA standard)

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 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