Day One
BIOPHARMACEUTICALS

Day One Biopharmaceuticals

Targeted Therapies for People of All Ages

April 2024

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 short-term investments to fund our operations, business plans and objectives, timing and success of our planned nonclinical and clinical development activities, the results of any of our strategic collaborations, including the potential achievement of milestones and provision of royalty payments thereunder, timing and results of nonclinical studies and clinical trials, efficacy and safety profiles of our products and product candidates, the ability of tovorafenib to treat pediatric low-grade glioma (pLGG) or related indications, the potential therapeutic benefits and economic value of our products and 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 inflation, changing interest rates, cybersecurity incidents, perceived instability in the global banking system, uncertainty with respect to the federal debt ceiling and budget and potential government shutdowns related thereto and global regional conflicts, 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 Annual Report on Form 10-K 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.

Cancer Therapies for People of All Ages

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Our Approach

- Develop medicines for genomically-defined cancers
- Establish first-in-class position through rapid registration pathways
- Expand to adolescent and adult populations in parallel and pursue those opportunities with the same commitment we do for children

Nasdaq: DAWN | IPO: 2021 | Founded: 2018 | Financial Position: Runway into 2026

Our Pipeline

Product Candidate	Therapeutic Area	Preclinical	Phase 1	Phase 2	Phase 3/ Registrational	Approved	Recent & Anticipated Milestones
Tovorafenib Type II RAF Inhibitor OJEMDA brand name in U.S.[1]	BRAF-altered Relapsed pLGG	FIREFLY-1 (pivotal Phase 2)				ojemda™ (tovorafenib)	**FDA approval:** April 2024
	Frontline RAF-altered pLGG	FIREFLY-2 (pivotal Phase 3)					**First patient dosed:** March 2023
Pimasertib MEK 1/2 Inhibitor	MAPK-altered solid tumors[†] (Combo w/ tovorafenib)	FIREFLIGHT-1[††]					**Recommended Phase 2 dose & schedule expected:** 2H 2024
VRK1 Program VRK1 Inhibitor	Pediatric and adult cancers						**In-licensed[§]:** August 2023

[1] OJEMDA has received accelerated approval by the U.S. Food and Drug Administration. [†] Pimasertib Phase 1 dose escalation and expansion trial previously completed. [††] Includes patients ≥12 years of age. [§] Research collaboration and license agreement with Sprint Bioscience AB for exclusive worldwide rights to a research-stage program targeting VRK1. pLGG, pediatric low-grade glioma.
The safety and efficacy of investigational agents and/or investigational uses of approved products have not been established.

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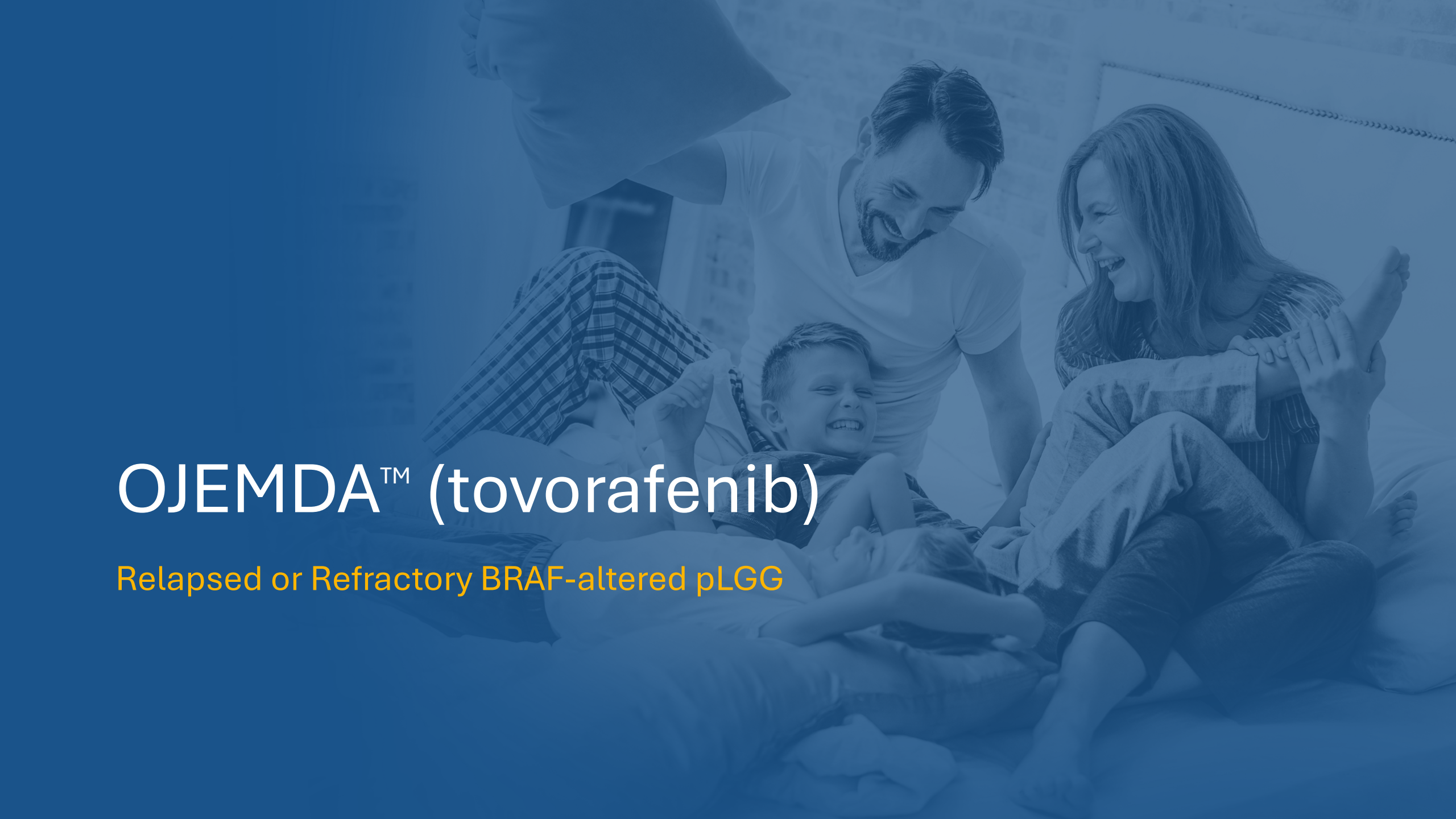
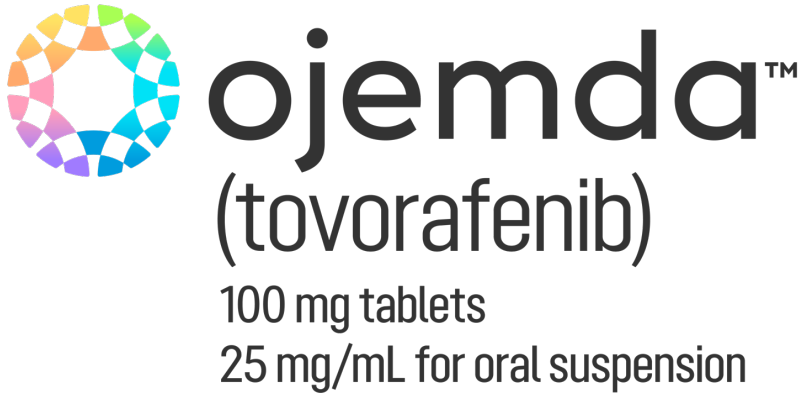


OJEMDA™ (tovorafenib)

Relapsed or Refractory BRAF-altered pLGG

OJEMDA Now Approved In The U.S.



OJEMDA is the **first and only FDA Approved therapy** for the treatment of pediatric patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma harboring a BRAF fusion or rearrangement, or BRAF V600 mutation

*This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial.

pLGG Impact On Patients' Lives

Lily was diagnosed with an operable brain tumor at 5 months of age

Pediatric Low-Grade Glioma: The Most Common Type Of Brain Tumor In Children

pLGGs are chronic and relentless, with patients suffering profound tumor and treatment-associated morbidity that can impact their life trajectory over the long term[1]

A Serious and Life-Threatening Disease

- For the majority of pLGG patients in the relapsed setting, there is no standard of care and no approved therapies
- Up to 75% of pLGGs have a BRAF alteration*, of those ~80% are BRAF fusions and ~20% are BRAF V600 mutations[2-6]
- Despite surgery playing a significant role in treatment, the vast majority of patients still require systemic therapy[7,8]
- Due to high rate of disease recurrence, most patients will undergo multiple lines of systemic therapy over the course of their disease

*Incidence of BRAF alterations varies across pLGG subtypes. [1] Sievert AJ, Fisher MJ. Pediatric low-grade gliomas. *J Child Neurol.* 2009;24(11):1397-1408. doi:10.1177/0883073809342005. [2] Penman CL et al. *Front Oncol.* 2015;5:54. [3] Cohen AR., *N Engl J Med.* 2020;386(20):1922-1931. [4] Lassaletta A, et al. *J Clin Oncol.* 2017;35(25):2934-2941. [5] Faulkner C, et al. J Neuropathol Exp Neurol. 2015;74(9):867-872. [6] Packer RJ, et al. Neuro Oncol. 2017;19(6):750-761. [7] Ostrum QT et al., Neuro Oncol. 2015; 16(Suppl 10):x1-x36; [8] De Blank P. et al., Curr Opin Pediatr. 2019 Feb; 31(1):21-27.

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Conventional Treatments Can Be Disruptive To Childhood And Can Have Significant Long-Term Consequences

Surgery

- Significant recovery times
- Risks of complications
- Resection may be limited by location of tumor
- Potential for functional deficits based on location of tumor and extent of resection

Chemotherapy

- Requirement for indwelling catheter and weekly infusions
- Risk of neutropenia, hypersensitivity reactions, nausea and vomiting and peripheral neuropathy

Radiation

- Risk of secondary malignancy
- Risk of malignant transformation
- Risk of vascular proliferation and stroke
- Neurocognitive impact, depending on location of tumor and radiation field

Goal of therapy is to control the tumor, minimize the burden of surgery, chemotherapy, and radiation, and reduce the risk of life-long treatment and disease-related effects

Source: 1. Heitzer AM, Raghubar K, Ris MD, et al. Neuropsychological functioning following surgery for pediatric low-grade glioma: a prospective longitudinal study. J Neurosurg Pediatr. 2019;1-9. doi:10.3171/2019.9.PEDS19357. 2. Bryant R. Managing side effects of childhood cancer treatment. J Pediatr Nurs. 2003;18(2):113-125. doi:10.1053/jpdn.2003.11. 3. Zahnreich S, Schmidberger H. Childhood cancer: occurrence, treatment and risk of second primary malignancies. Cancers (Basel). 2021;13(11):2607. doi:10.3390/cancers/13112607. 4. National Cancer Institute. Fertility issues in girls and women with cancer. http://www.cancer.gov. Accessed June 13, 2022. 5. Alessi I., Caroleo A.M., de Palma L., Mastronuzzi A., Pro S., Colafati G.S., Boni A., Della Vecchia N., Velardi M., Evangelisti M., et al. Short and Long-Term Toxicity in Pediatric Cancer Treatment: Central Nervous System Damage. Cancers. 2022;14:1540. doi: 10.3390/cancers14061540.

Overview U.S. Prescribing Information For OJEMDA™ (tovorafenib)

Available in tablet formulation and pediatric-friendly powder for oral suspension

INDICATION

OJEMDA is indicated for the treatment of pediatric patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma harboring a BRAF fusion or rearrangement, or BRAF V600 mutation

RECOMMENDED DOSE

380 mg/m^2 administered orally once weekly (not to exceed a dose of 600mg once weekly); OJEMDA can be taken with or without food

For full prescribing information, visit dayonebio.com

*This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial.

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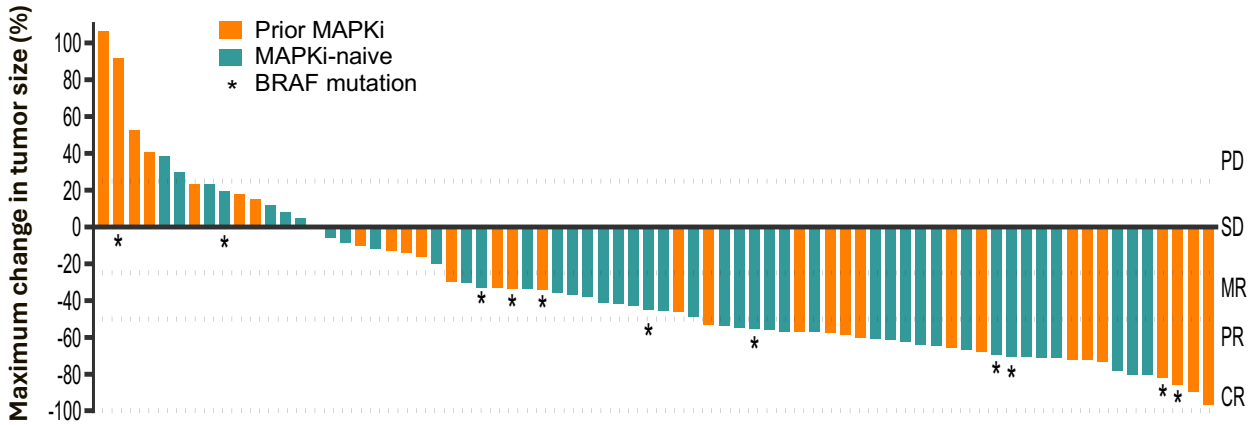
Efficacy Summary From OJEMDA™ (tovorafenib) Prescribing Information

51% **Overall response rate (RAPNO-LGG) in 76 evaluable patients**



Response (IRC)	RAPNO-LGG n	RAPNO-LGG n (%)	RAPNO-LGG 95% CI
ORR, n (%)	**76**	**39 (51)**	**40-63**
BRAF fusion or rearrangement	64	33 (52)	39-64
BRAF V600 mutation	12	6 (50)	21-79
Prior MAPKi use	45	22 (49)	31-64
MAPKi-naïve	31	17 (55)	36-73
Median DOR, months	**39**	**13.8**	**11.3-NR†**
Median TTR, months	**39**	**5.3**	
Range		1.6-11.2	

June 5, 2023 data cutoff. CI, confidence interval; DOR, duration of response; IRC, independent radiology review committee; LGG, low-grade glioma; NR, not reached; ORR, overall response rate; RAPNO, Response Assessment in Pediatric Neuro-Oncology; TTR, time to response; CR, complete response; PR, partial response; MR, minor response; SD, stable disease; PD, progressive disease. † As of the data cutoff, 66% remain on tovorafenib.

Safety Summary From OJEMDA™ (tovorafenib) Prescribing Information

Warnings and Precautions

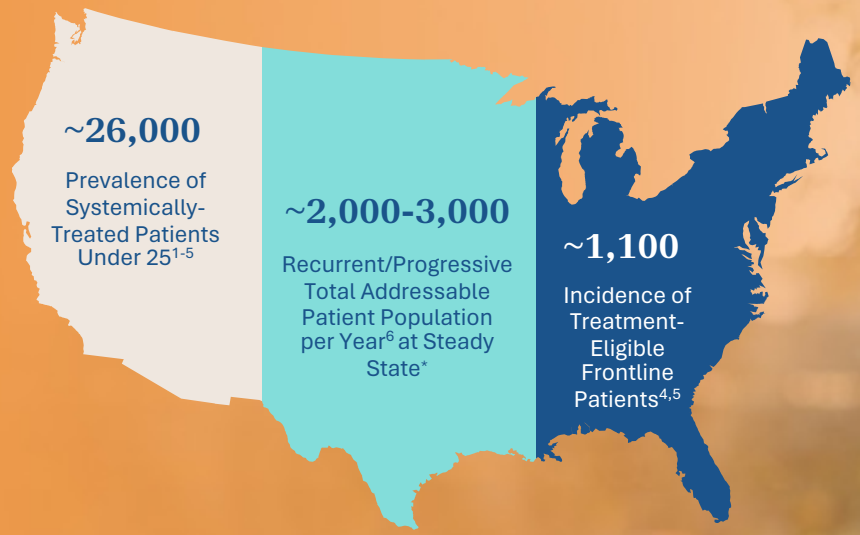
- Hemorrhage
- Skin toxicity, including photosensitivity
- Hepatotoxicity
- Effect on growth
- Embryo-fetal toxicity
- Use in NF1- associated tumors

No boxed warnings or contraindications

Preferred Term, n (%)	TEAEs (≥ 30% of patients [n=137])	
	Any Grade	Grade ≥3
Any AE	137 (100)	86 (63)
Hair color changes	104 (76)	0
Anemia	81 (59)	15 (11)
Elevated CPK	80 (58)	16 (12)
Fatigue	76 (55)	6 (4)
Vomiting	68 (50)	6 (4)
Hypophosphatemia	64 (47)	0
Headache	61 (45)	2 (1)
Maculo-papular rash	60 (44)	11 (8)
Pyrexia	53 (39)	5 (4)
Dry skin	49 (36)	0
Elevated LDH	48 (35)	0
Increased AST	47 (34)	4 (3)
Constipation	45 (33)	0
Nausea	45 (33)	0
Upper RTI	43 (31)	2 (1)
Dermatitis acneiform	42 (31)	1 (1)
Epistaxis	42 (31)	1 (1)

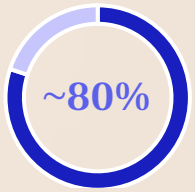
June 5, 2023 data cutoff. OJEMDA safety data (n=137). Treatment-emergent AEs ≥20% any grade in arms 1 & 2. AE, adverse event; AST, aspartate aminotransferase; CPK, creatine phosphokinase; LDH, lactate dehydrogenase; RTI, respiratory tract infection; TEAEs, treatment-emergent adverse events.

Estimated *BRAF*-Altered pLGG Patient Population In The U.S.



Up to **75%** of pLGG cases are BRAF-altered[7-14]

Incidence of BRAF alterations varies across pLGG subtypes



of these cases have BRAF fusion, primarily KIAA1549-BRAF†

of these cases have BRAF point mutations, primarily BRAF V600††

[1] Selt F, van Tilburg CM, Bison B, et al. Response to trametinib treatment in progressive pediatric low-grade glioma patients. J Neurooncol. 2020;149(3):499-510. doi:10.1007/s11060-020-03640-3. [2] Ryall S, Tabori U, Hawkins C. Pediatric low-grade glioma in the era of molecular diagnostics. Acta Neuropathol Commun. 2020;8(1):30. doi:10.1186/s40478-020-00902-z. [3] SEER US complete prevalence counts of patients aged under 25 with Brain and Other Nervous Systems tumors as of January 1, 2017. [4] CBTRUS, Qaddoumi et al 2009, Schreck et al 2019, ClearView Analysis. [5] US Census. Estimated annual incidence, estimated prevalence, and estimated recurrent/progressive total addressable patient population are Day One calculations based on publicly available data. [6] Source: Internal market research conducted by EpidStrategies, A Division of ToxStrategies, Inc. on behalf of Day One. [7] Ryall S, et al. *Acta Neuropathol Commun.* 2020;8(1):30. [8] Behling F, et al. *Cancers (Basel).* 2019;11(6):794. [9] Penman CL, et al. *Front Oncol.* 2015;5:54. [10] Packer RJ, et al. *Neuro Oncol.* 2017;19(6):750-761. [11] Cohen AR, et al. *N Engl J Med.* 2022;386(20):1922-1931. [12] Ryall S, et al. *J Neuropathol Exp Neurol.* 2017;76(7):562-570. [13] Lassaletta A, et al. *J Clin Oncol.* 2017;35(25):2934-2941. [14] Faulkner C, et al. *J Neuropathol Exp Neurol.* 2015;74(9):867-872. * The estimated addressable pool of recurrent or progressive pLGG patients is based on progression free survival curves modeled from published literature. † Predominantly seen in pilocytic astrocytomas. †† May vary across pLGG subtypes. BRAF, V-Raf murine sarcoma viral oncogene homolog B; MAPK, mitogen-activated protein kinase; pLGG, pediatric low-grade glioma.

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What Physicians & Caregivers Are Looking For In A Therapy

What HCP's are Seeking

Effective in stopping or shrinking tumors
Manageable safety profile
Minimal disruption to child's life

"The goal is not interfering with the child's life."
– Ped Onc, Chicago Ad Board

What Caregivers are Seeking

Live as normal of a childhood as possible
Minimal impact from the disease
Minimal disruption to child's life

"Our time with our kids is precious and not guaranteed, so the less time with meds and doctors the better."
– Caregiver for a child under 5 yrs

Product Profile Aligns With What Physicians Are Looking For In A Therapy

ojemda™
(tovorafenib)
100 mg tablets
25 mg/mL for oral suspension

Efficacy	Meaningful tumor stabilization or shrinkage may be possible with OJEMDA. In the clinical trial: • 51% of children experienced tumor shrinkage by at least 25% • 82% of children saw their tumors shrink or remain stable
Safety	Generally well-tolerated therapy, with 9 out of 10 patients staying on treatment in the clinical trial Most common grade 3 / 4 adverse events include: anemia, elevated CPK, maculo-papular rash, fatigue & vomiting
Dosing	Once-weekly, taken with or without food conveniently from home can mean fewer daily interruptions

OJEMDA is indicated for the treatment of patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma (LGG) harboring a BRAF fusion, rearrangement, or BRAF V600 mutation.

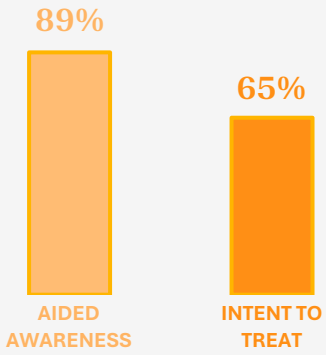
Data from Pivotal Phase 2 FIREFLY-1 trial.

Comprehensive Approach For A Successful Launch

ojemda™ (tovorafenib)
100 mg tablets
25 mg/mL for oral suspension

Physicians

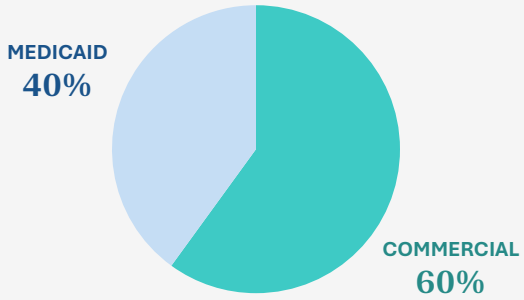
Objective: Establish OJEMDA™ as 1st choice in relapsed / refractory *BRAF*-altered pLGG patients



- Dedicated & experienced sales team to engage HCPs

Payers

Objective: Rapidly establish coverage



- Pre-launch engagement to establish Day One & provide background information
- Plans in place for rapid engagement post-approval

Patients & Families

Objective: Provide a positive & supportive experience when initiating therapy

Biologics By McKesson | Onco360® ONCOLOGY PHARMACY

- SP distribution enables consistent patient experience
- Comprehensive patient support programs address patient needs and accelerates access to drug

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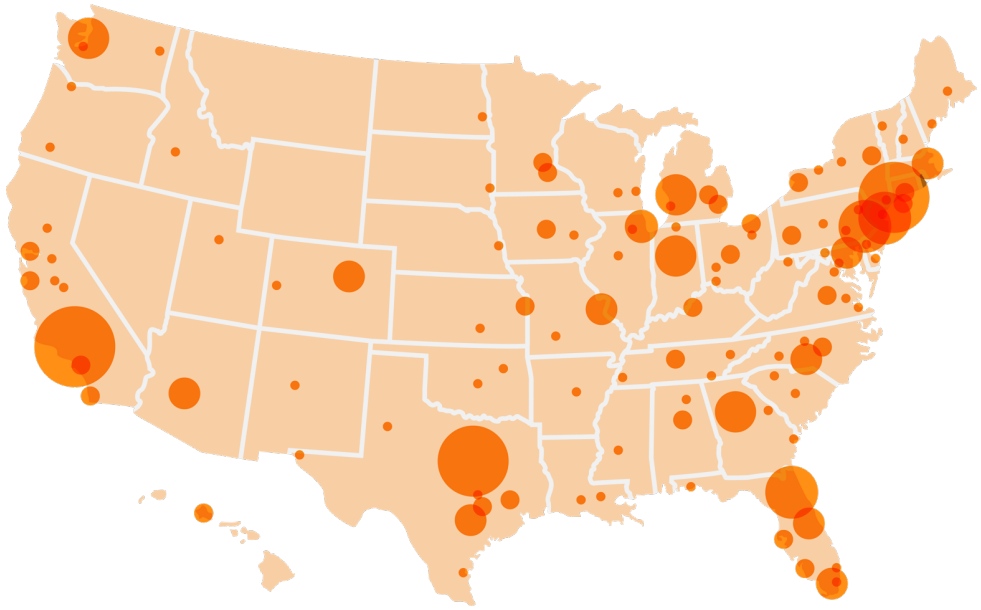
Targeted Launch With Highly Experienced Field Team

ojemda™
(tovorafenib)
100 mg tablets
25 mg/mL for oral suspension

Targeting ~200 centers where 90% of pLGG patients receive treatment



Deep oncology experience with relationships at top-tier accounts

18 Account Managers fully-dedicated to OJEMDA

Average experience:

13 years of oncology

4 years of rare disease

2 years of pediatric oncology clinical experience

Institutional experience and existing relationships with key accounts

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Patient Support Program Supporting Access

ojemda™
(tovorafenib)
100 mg tablets
25 mg/mL for oral suspension

EveryDay Support.

FROM DAY ONE

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FIREFLY-2 / LOGGIC

Pivotal Phase 3 Trial of Tovorafenib in Frontline pLGG

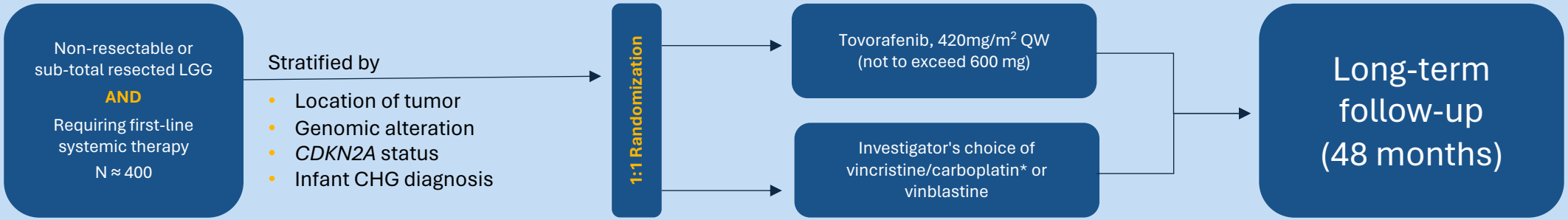
FIREFLY-2/LOGGIC Pivotal Phase 3 Trial Of Tovorafenib In Frontline pLGG

Trial Design

- Randomized, global, registrational Phase 3 trial of monotherapy tovorafenib vs SoC chemotherapy
- Eligibility: Patients aged 6 months to <25 years with LGG harboring a RAF alteration and requiring first-line systemic therapy
- Tovorafenib available as tablets and pediatric-friendly liquid suspension
- Patients who progress after stopping tovorafenib 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-LGG 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.

FIRELIGHT-1

Phase 1b/2 Trials Evaluating Tovorafenib as a Combination with Pimasertib

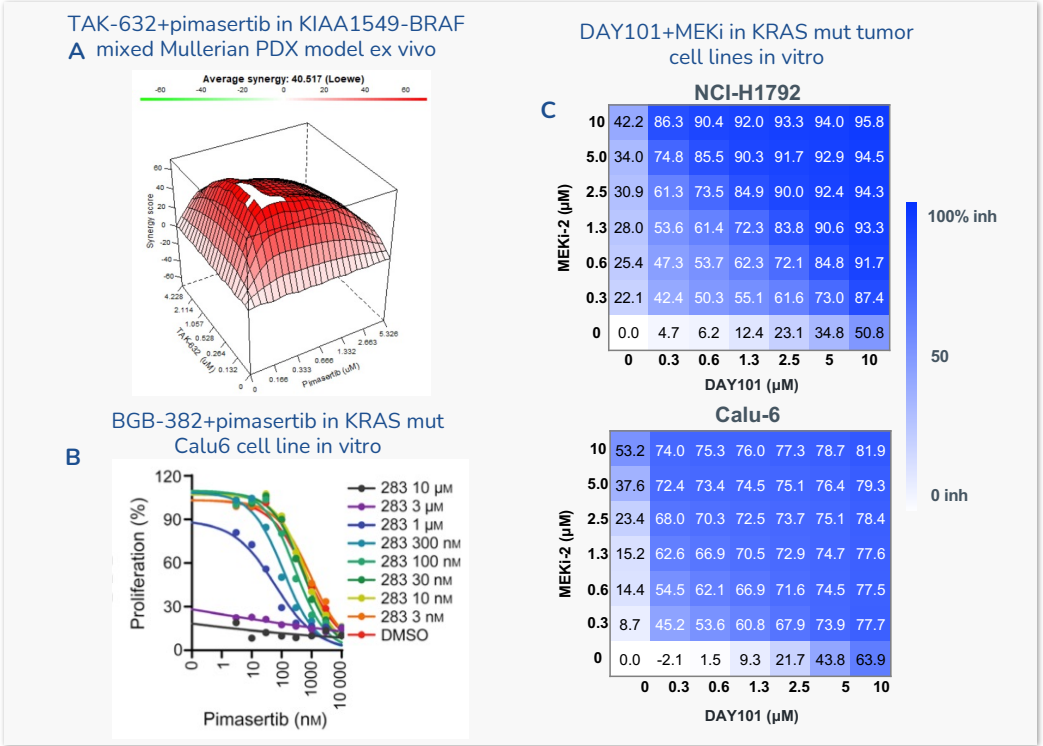
Pimasertib: Investigational Allosteric MEK1/2 Inhibitor With Demonstrated Activity In MAPK-Driven Solid Tumors

- 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 and other targeted therapies may unlock the full value of pimasertib in advanced solid tumors

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 And Pimasertib May Unlock Potential Synergy For Adult Solid Tumors

BRAF non-V600 mutant	KRAS or NRAS mutant
MEK ERK	RAF/ MEK/ERK PI3K/m TOR PI3K/m TOR
Proliferation, survival	Proliferation, survival
Type II RAFi + MEKI	Type II RAFi + MEKI
Non V600 BRAF dimers are effectively inhibited by type II RAFi , but not type I BRAFi	Targeting multiple nodes of MAPK pathway will drive deeper and more durable response



A Type II RAFi + MEKi is synergistic in BRAF fusion melanoma PDX model ex vivo (internal data)

B Sensitivity of KRAS Q61 mutant cells to pimasertib is enhanced when cells are treated with the type II BRAF inhibitor BGB-283 (Yuan et al., Mol Onc 2020)

C Tovorafenib + MEK inhibitor is synergistic in KRAS G12C and Q61 mutant tumor cells (Venetsanakos et al., 2021 AACR poster presentation)

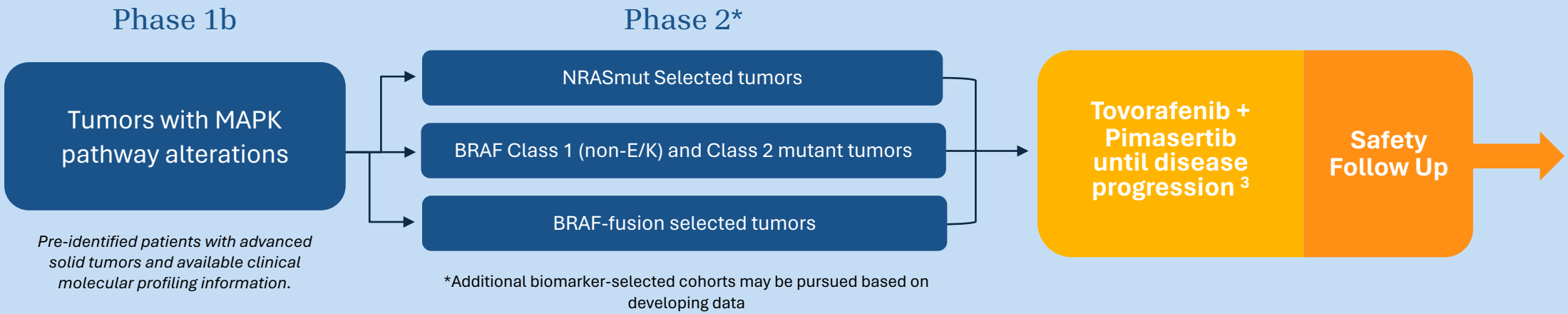
Tovorafenib / Pimasertib Combination In Solid Tumors (FIRELIGHT-1)

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 December 31, 2023: $366.3 million (no debt)

~87.4 million shares of common stock outstanding as of February 21, 2024

$ Millions	Twelve Months Ended 12/31/23	Twelve Months Ended 12/31/22
R&D Expense	$130.5	$85.6
G&A Expense	$75.5	$61.3
Net Loss	$188.9	$142.2

Projected Cash Runway into 2026

FIREFLY-1: Pivotal Phase 2 clinical trial of tovorafenib

- Data published in *Nature Medicine* and oral presentations at SNO in November 2023
- OJEMDA™ (tovorafenib) approved in the U.S. and received PRV in April 2024

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

- First patient dosed in March 2023

All financial and share information is unaudited. [1]NDA data set includes analysis of primary (ORR by RANO-HGG) and secondary (ORR by RAPNO, PFS) efficacy endpoints, safety, and exploratory analyses (including ORR by RANO-LGG). PRV, Priority Review Voucher.

Priorities as a Commercial-Stage Company

Launch OJEMDA™ (tovorafenib)

- Expand awareness amongst physicians and establish broad coverage to enable patient access
- Establish OJEMDA as the standard of care for relapsed or refractory pLGG harboring a BRAF alteration
- Provide a positive and supportive experience when initiating OJEMDA therapy for patients and families

Advance Portfolio

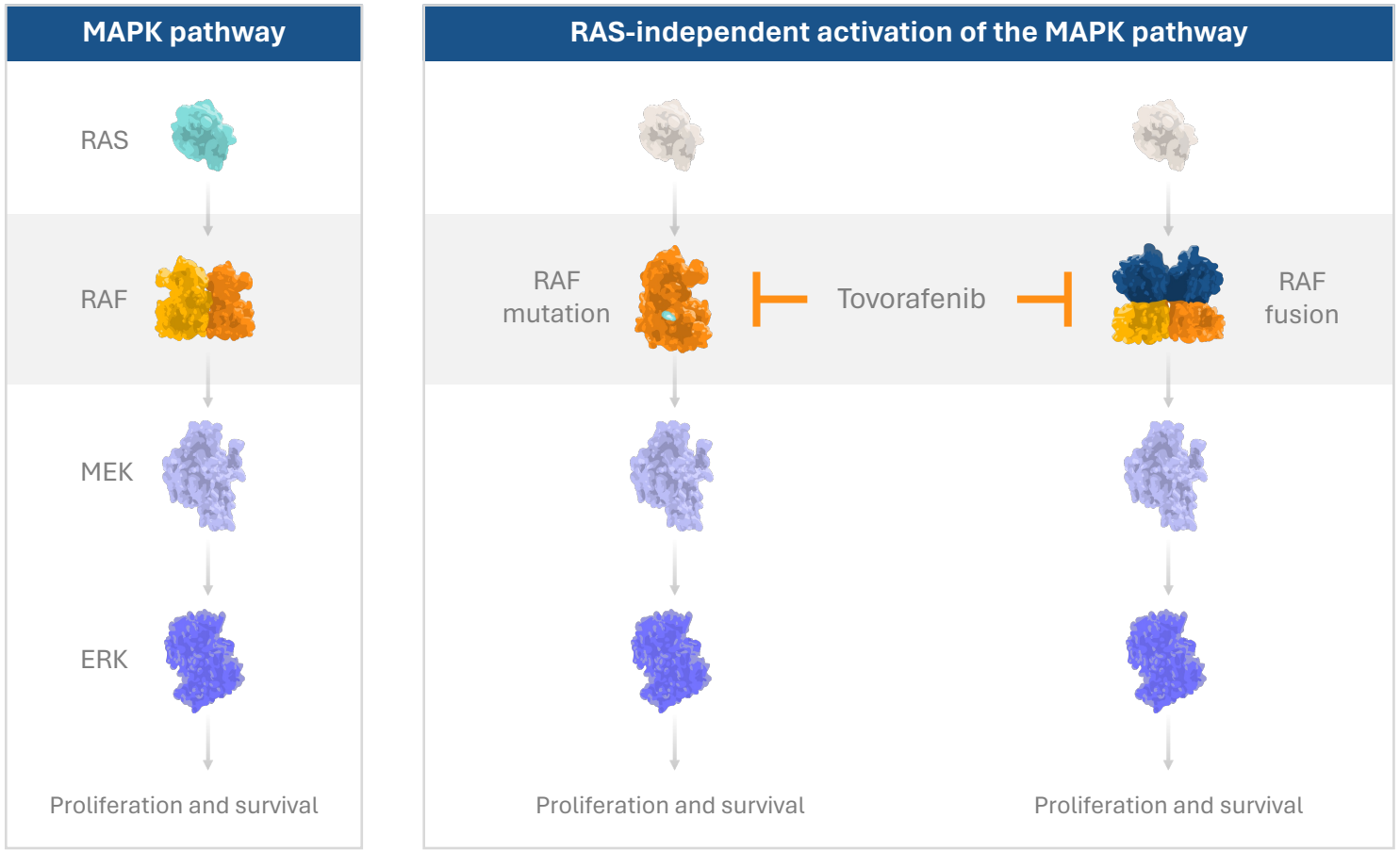
- FIREFLY-2: Study tovorafenib as a frontline therapy for treatment-naive patients with pLGG
- FIRELIGHT-1: Evaluate tovorafenib in combination with pimasertib in adolescent and adult populations
- Advance early stage VRK1 program to clinical development

Expand Pipeline

- Grow Day One into a leading, biopharmaceutical company that is the partner of choice for oncology drug development
- Explore selective partnerships as a source of capital and risk sharing
- Further invest in business development activities to expand our multiple asset portfolio for both children and adults

Appendix

Tovorafenib Inhibits Both BRAF Fusions And BRAF V600 Mutations



Tovorafenib is an investigational, oral, selective, CNS-penetrant, type II RAF inhibitor that was designed to inhibit both monomeric and dimeric RAF kinase

- Activity in tumors driven by both RAF fusions and BRAF V600E mutations
- Tablet and pediatric-friendly liquid suspension
- Once weekly dosing

Currently approved type I BRAF inhibitors are indicated for use in patients with tumors bearing BRAF V600 mutations

- Type I BRAF inhibitors cause paradoxical MAPK activation in the setting of wild-type RAF, increasing the risk of tumor growth in BRAF fusion-driven

Source: 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.

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

Trial Design

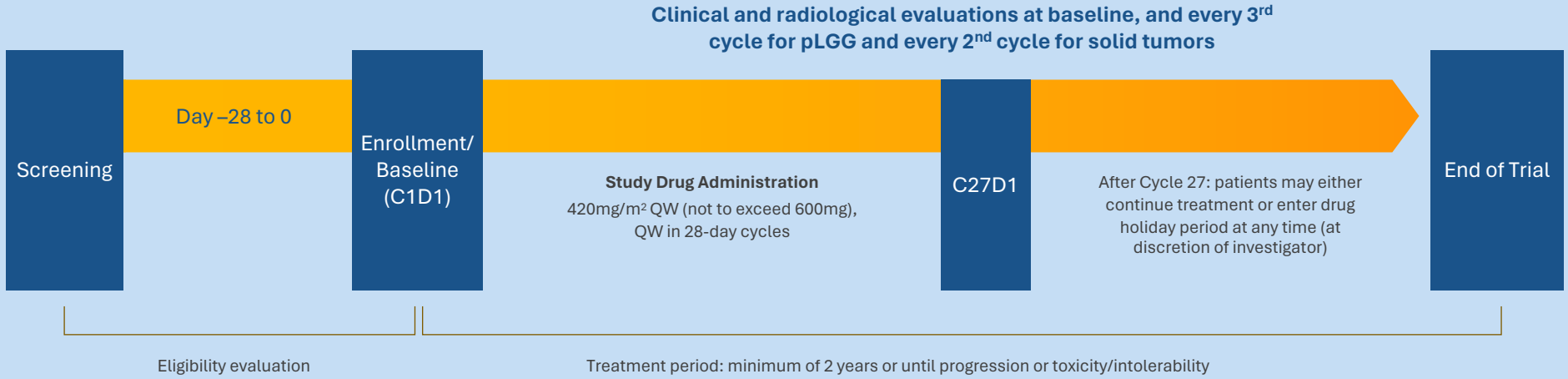
- Three arm, open-label, global registrational phase 2 trial
  - **Pivotal Arm 1 (recurrent/progressive pLGG, n=77): harboring a KIAA1549-BRAF fusion or BRAF V600E mutation**
  - Arm 2 (expanded access recurrent/progressive LGG, n=60): harboring an activating RAF alteration
  - Arm 3 (extracranial solid tumors): harboring an activating RAF fusion

Endpoints (Pivotal Arm 1)

- **Primary endpoint: ORR based on RANO-HGG[1], assessed by blinded independent central review**
- Secondary endpoints: ORR by RAPNO-LGG[2] assessed by blinded independent central review; PFS, DoR; TTR, CBR; safety
- Exploratory analyses: ORR and CBR by RANO-LGG[3] assessed by blinded independent central review

Key Inclusion Criteria

- 6 months – 25 years of age
- RAF-altered tumor
- ≥1 prior line of systemic therapy with radiographic progression
- Prior use of MAPK pathway targeted therapy was permitted



June 5, 2023 data cutoff. [1] Wen PY, et al. *J Clin Oncol*. 2010;28(11):1963-1972. [2] Fangusaro J, et al. Lancet Oncol. 2020;21(6):e305–316. [3] van den Bent MJ, et al. Lancet Oncol. 2011;12(6):583-593. Abbreviations: CBR, clinical benefit rate; IRC, independent review committee; C, cycle; D, day; LGG, low-grade glioma; ORR, objective response rate; PFS, progression-free survival; DoR, duration of response; QW, once weekly; TTR, time to response; RANO, Response Assessment in Neuro-Oncology; RAPNO, Response Assessment in Pediatric Neuro-Oncology; MAPK, mitogen-activated protein kinase. For more information, please refer to NCT04775485

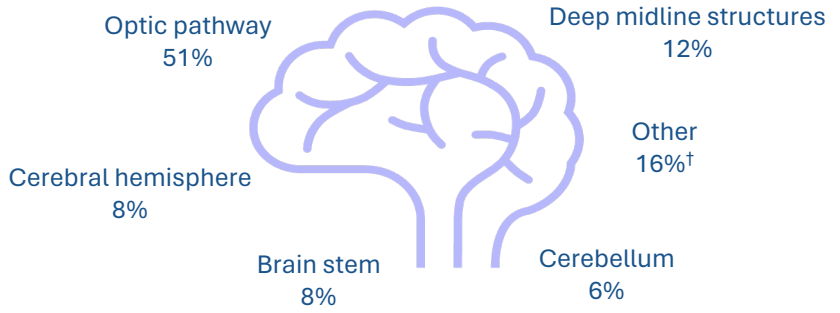
Data from Pivotal Phase 2 FIREFLY-1 Trial

June 5, 2023 data cutoff

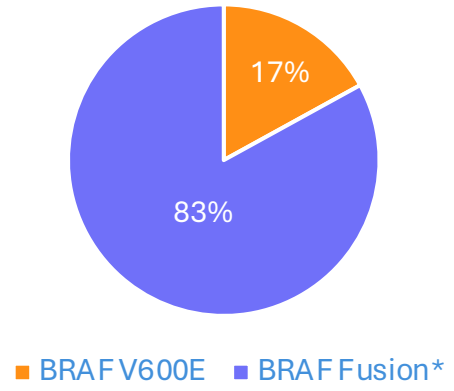
FIREFLY-1 Baseline Patient Characteristics

Characteristic	Arm 1 (n=77)
Median age, years (range)	8 (2-21)
Sex, n (%) Male Female	 40 (52) 37 (48)
Race, n (%) White Asian Black Multiple Other Not specified	 41 (53) 5 (6) 2 (3) 3 (4) 6 (8) 20 (26)
Number of lines of prior systemic therapy Median (range) 1, n (%) 2, n (%) ≥3, n (%)	 3 (1-9) 17 (22) 21 (27) 39 (51)
Prior MAPK pathway targeted therapy, n (%) Prior MEK inhibitor Prior BRAF inhibitor Prior BRAF and MEK inhibitors‡ Any MAPK inhibitor	 43 (56) 8* (10) 5 (7) 46 (60)

Location (n=77)

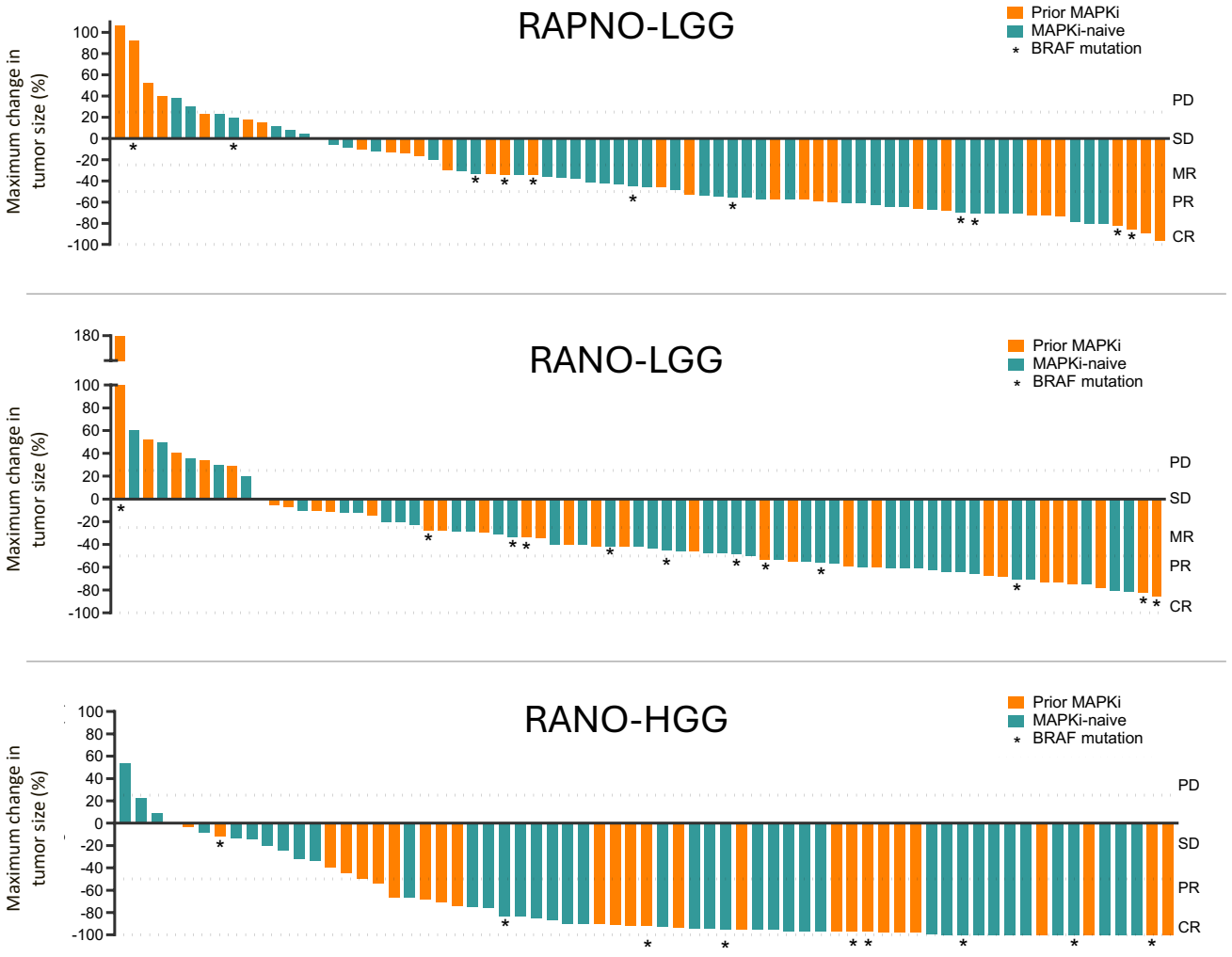


***BRAF* alteration (n=77)**



June 5, 2023 data cutoff. *Includes 6 patients with BRAF duplication and 2 with BRAF rearrangement per fluorescence in situ hybridization or in situ hybridization. †Includes tumors that were extending into multiple regions of the brain, leptomeningeal disease, and/or spinal disease. ‡The 5 patients that had previously received both a MEK inhibitor and also a BRAF inhibitor are recorded in both the "Prior MEK inhibitor" and "Prior BRAF inhibitor" groups. MAPK, mitogen-activated protein kinase.

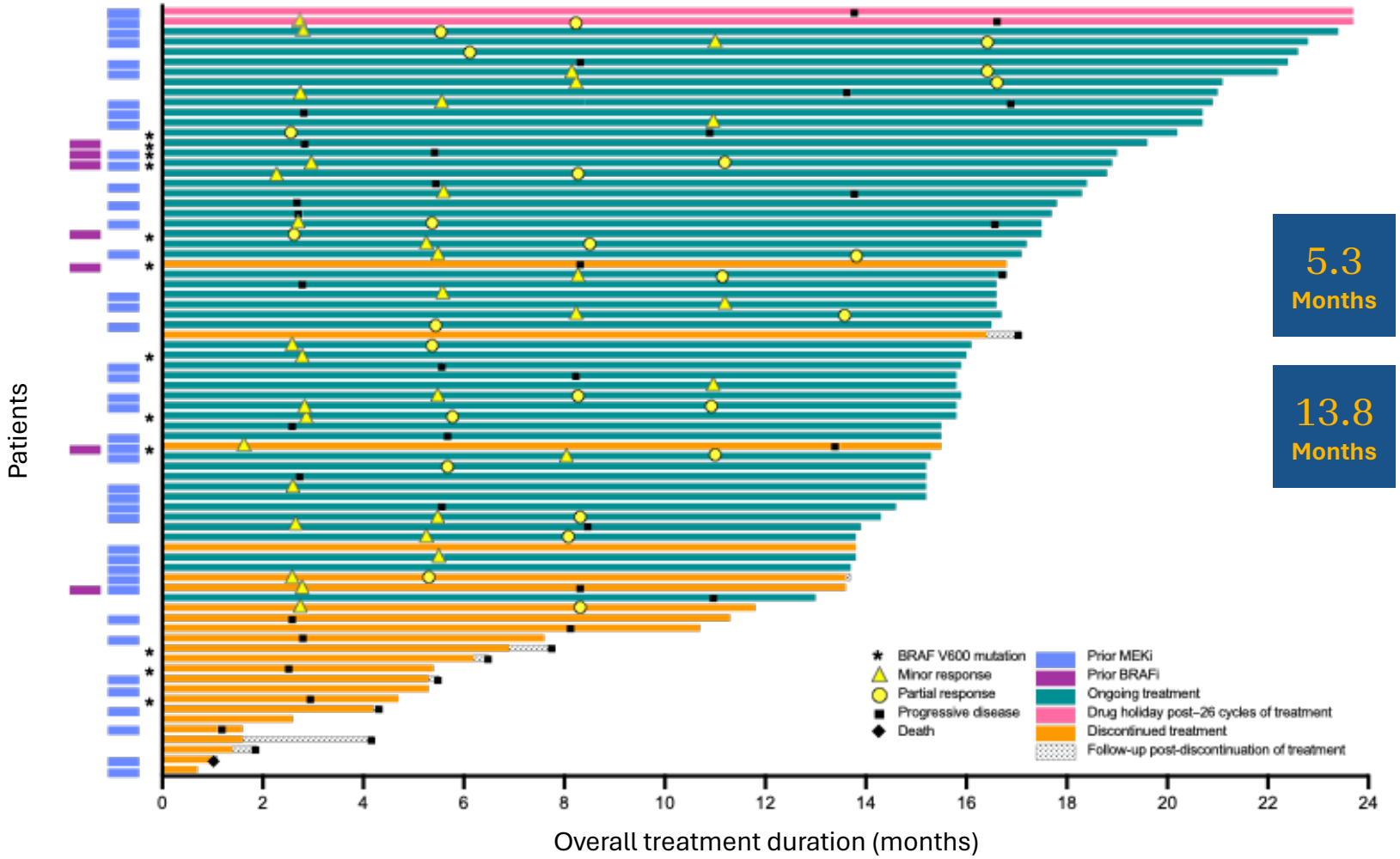
Tumor Response To Tovorafenib Using RAPNO-LGG, RANO-LGG and RANO-HGG



Response (IRC)	RAPNO-LGG n=76	RANO-LGG N=76	RANO-HGG N=69
ORR,* n (%)	**39 (51)**	**40 (53)**	**46 (67)**
95% CI	40-63	41-64	54-78
CBR,* n (%)			
SD of any length of time	62 (82)	63 (83)	64 (93)
SD ≥12 months	43 (57)	46 (61)	54 (78)
BOR,* n (%)			
CR	0	0	12 (17)
PR	28 (37)	20 (26)	34 (49)
MR	11 (14)	20 (26)	n/a
SD	23 (30)	23 (30)	18 (26)
SD <12 months	19 (25)	17 (22)	10 (14)
SD ≥12 months	4 (5)	6 (8)	8 (12)
PD	13 (17)	11 (14)	4 (6)
NE	1 (1)	2 (3)	1 (1)
Median DOR, months	**13.8**	**14.4**	**16.6**
95% CI	11.3-NR	11.0-NR	11.6-NR
Median TTR, months	**5.3**	**5.5**	**3.0**
Range	1.6-11.2	1.6-11.3	2.6-16.6

June 5, 2023 data cutoff. BOR, best overall response; CBR, clinical benefit rate; CI, confidence interval; CR, complete response; DOR, duration of response; HGG, high-grade glioma; IRC, independent radiology review committee; LGG, low-grade glioma; MR, minor response; n/a, not applicable; NE, not evaluable; NR, not reached; ORR, overall response rate; PD, progressive disease; PR, partial response; RANO, Response Assessment in Neuro-Oncology; RAPNO, Response Assessment in Pediatric Neuro-Oncology; SD, stable disease; TTR, time to response. * ORR, CBR and BOR for RAPNO-LGG and RANO-LGG included MRs.

Duration Of Tovorafenib Therapy For All Patients With RAPNO-LGG Evaluable Lesions

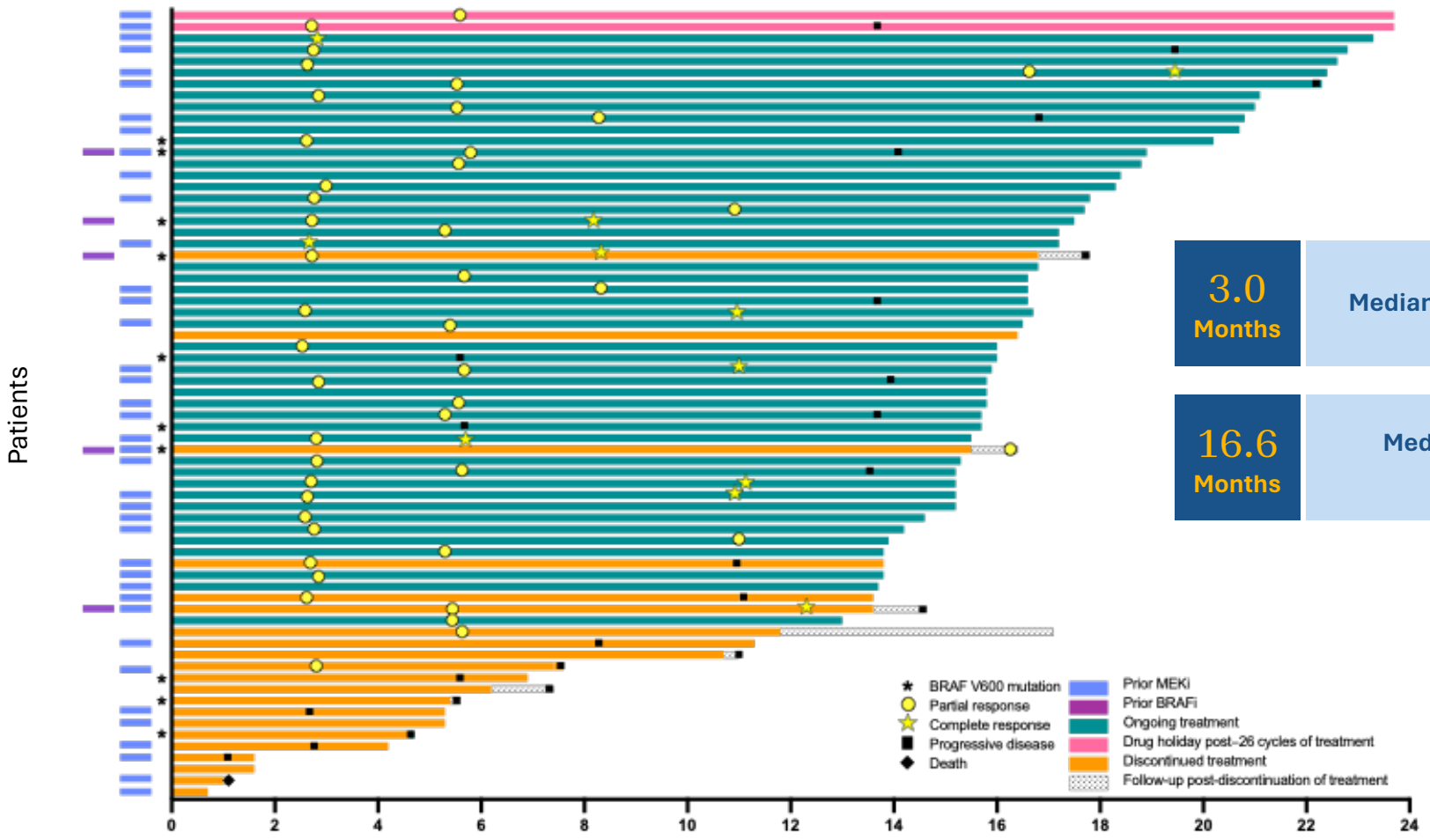


5.3 Months — Median time to response

13.8 Months — Median duration of treatment

June 5, 2023 data cutoff.

Duration Of Tovorafenib Therapy For All Patients With RANO-HGG Evaluable Lesions

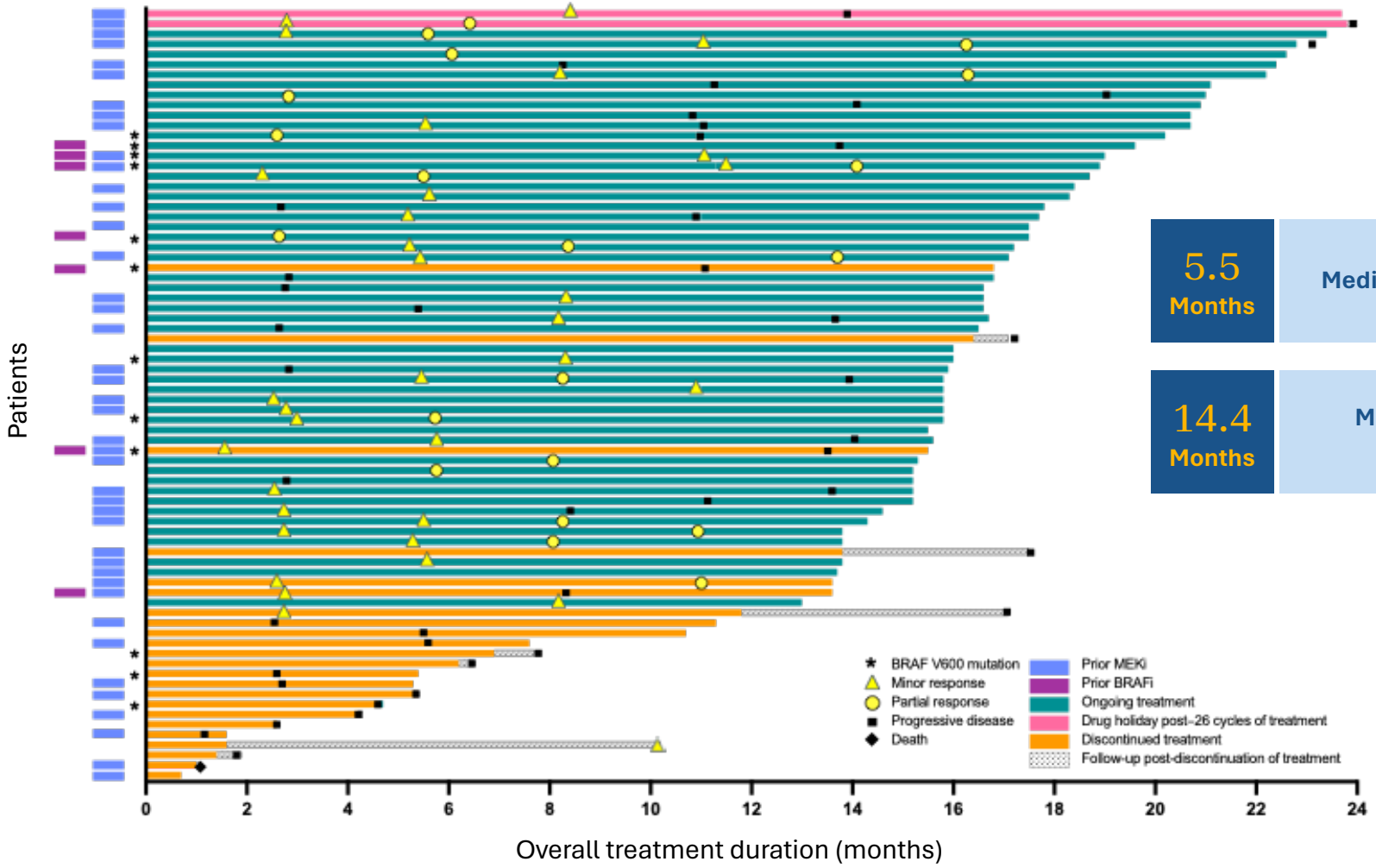


3.0 Months — Median time to response

16.6 Months — Median duration of treatment

June 5, 2023 data cutoff.

Duration Of Tovorafenib Therapy For All Patients With RANO-LGG Evaluable Lesions



5.5 Months — Median time to response

14.4 Months — Median duration of treatment

June 5, 2023 data cutoff.

Tumor Response To Tovorafenib Across Three Assessment Criteria Were Consistent Across BRAF Fusion And Mutation Patients, and Patients With Prior MAPK Treatment

Response (IRC)	RAPNO-LGG[2] n		RANO-LGG[3,4] n		RANO-HGG[1] n	
ORR,* n (%)	**76**	**39 (51)**	**76**	**40 (53)**	**69**	**46 (67)**
BRAF fusion	64	33 (52)	64	33 (52)	59	41 (69)
BRAF mutation	12	6 (50)	12	7 (58)	10	5 (50)
Prior MAPKi	45	22 (49)	45	23 (51)	41	29 (71)
MAPKi-naive	31	17 (55)	31	17 (55)	28	17 (61)
CBR,* n (%) (SD of any length of time)	**76**	**62 (82)**	**76**	**63 (83)**	**69**	**64 (93)**
BRAF fusion	64	53 (83)	64	53 (83)	59	55 (93)
BRAF mutation	12	9 (75)	12	10 (83)	10	9 (90)
Prior MAPKi	45	38 (84)	45	38 (84)	41	37 (90)
MAPKi-naive	31	24 (77)	31	25 (81)	28	27 (96)
CBR,* n (%) (SD ≥12 months)	**76**	**43 (57)**	**76**	**46 (61)**	**69**	**54 (78)**
BRAF fusion	64	37 (58)	64	39 (61)	59	49 (83)
BRAF mutation	12	6 (50)	12	7 (58)	10	5 (50)
Prior MAPKi	45	25 (56)	45	26 (58)	41	33 (80)
MAPKi-naive	31	18 (58)	31	20 (65)	28	21 (75)
Median DOR, months (95% CI)**	**39**	**13.8 (11.3-NR)**	**40**	**14.4 (11.0-NR)**	**46**	**16.6 (11.6-NR)**
BRAF fusion	33	13.8 (11.3-NR)	33	16.3 (11.0-NR)	41	16.8 (11.6-NR)
BRAF mutation	6	NR (8.4-NR)	7	12.0 (8.4-NR)	5	15.1 (8.3-NR)
Prior MAPKi	22	13.8 (11.3-NR)	23	12.0 (8.5-NR)	29	15.1 (9.0-16.8)
MAPKi-naive	17	NR (8.4-NR)	17	16.3 (8.4-NR)	17	NR (11.6-NR)

June 5, 2023 data cutoff. [1] Fangusaro J, et al. *Lancet Oncol.* 2020;21(6):e305–316. [2] Fangusaro J, et al. *Lancet Oncol.* 2020;21(6):e305–316. [3] van den Bent MJ, et al. *Lancet Oncol.* 2011;12(6):583-593. 4. Wen PY, et al. *J. Clin Oncol.* 2017;35(21),2439-2449. * ORR, CBR for RAPNO-LGG and RANO-LGG included MRs. ** the 95% CI were calculated using Kaplan-Meier method.

Tovorafenib Safety Data (n=137)

Preferred Term, n (%)	TEAEs		TRAEs	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any AE	137 (100)	86 (63)	134 (98)	58 (42)
Hair color changes	104 (76)	0	104 (76)	0
Anemia	81 (59)	15 (11)	67 (49)	14 (10)
Elevated CPK	80 (58)	16 (12)	77 (56)	16 (12)
Fatigue	76 (55)	6 (4)	60 (44)	6 (4)
Vomiting	68 (50)	6 (4)	28 (20)	3 (2)
Hypophosphatemia	64 (47)	0	48 (35)	0
Headache	61 (45)	2 (1)	29 (21)	0
Maculo-papular rash	60 (44)	11 (8)	56 (41)	11 (8)
Pyrexia	53 (39)	5 (4)	17 (12)	1 (1)
Dry skin	49 (36)	0	45 (33)	0
Elevated LDH	48 (35)	0	42 (31)	0
Increased AST	47 (34)	4 (3)	41 (30)	4 (3)
Constipation	45 (33)	0	31 (23)	0
Nausea	45 (33)	0	25 (18)	0
Upper RTI	43 (31)	2 (1)	2 (1)	0
Dermatitis acneiform	42 (31)	1 (1)	41 (30)	1 (1)
Epistaxis	42 (31)	1 (1)	27 (20)	0
Decreased appetite	39 (28)	5 (4)	28 (20)	4 (3)
Paronychia	36 (26)	2 (1)	32 (23)	2 (1)
Pruritus	35 (26)	1 (1)	32 (23)	1 (1)
COVID-19	34 (25)	0	0	0

- The most common reasons for discontinuation were tumor hemorrhage (3 patients) and decrease in growth velocity (2 patients)
- 33 patients (24%) had TRAEs leading to dose reduction; 50 patients (37%) had TRAEs leading to dose interruption
- Median duration of dose interruption was 2 weeks
- 9 patients (7%) had TRAEs leading to discontinuation

June 5, 2023 data cutoff. Treatment-emergent AEs ≥25% any grade in arms 1 & 2. AE, adverse event; ALT, Alanine transaminase; AST, aspartate aminotransferase; COVID-19, Coronavirus disease 2019; CPK, creatine phosphokinase; LDH, lactate dehydrogenase; RTI, respiratory tract infection; TEAEs, treatment-emergent adverse events; TRAEs, treatment-related adverse events.