



# Day One Biopharmaceuticals

Targeted Therapies for People of All Ages

October 2024



# Disclaimer

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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, cash equivalents and short-term investments to fund our operations, business plans and objectives, the anticipated gross proceeds of our private placement offering, timing and success of our commercialization and marketing efforts, 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 OJEMDA™ (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, potential instability in the global banking system, changes in the U.S. presidential administration, 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.

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# Cancer Therapies for People of All Ages








## 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



# Our Pipeline

Product Candidate	Therapeutic Area	Preclinical	Phase 1	Phase 2	Phase 3/ Registrational	Approved	Recent & Anticipated Milestones
<b>Tovorafenib<sup>3</sup></b> Type II RAF Inhibitor  OJEMDA brand name in U.S. <sup>1</sup>  Ex-U.S. Rights: 	BRAF-altered relapsed pLGG						<b>FDA approval</b> April 2024  <b>Ex-U.S. license agreement</b> July 2024
	Frontline RAF- altered pLGG						<b>First patient dosed</b> March 2023
<b>DAY301</b> PTK7 Targeted ADC	Adult and pediatric solid tumors						<b>U.S. IND cleared</b> April 2024  <b>First patient dosed expected</b> 4Q 2024 / 1Q 2025
<b>VRK1 Program</b> VRK1 Inhibitor	Adult and pediatric cancers						<b>In-licensed</b> August 2023

<sup>1</sup> OJEMDA has received accelerated approval by the U.S. Food and Drug Administration. <sup>2</sup> FIREFLY-1 is an open-label, pivotal Phase 2 trial. <sup>3</sup> Ex-U.S. license agreement with Ipsen to commercialize OJEMDA (tovorafenib) outside the U.S. DAY301 is a license agreement with MabCare Therapeutics for exclusive worldwide rights, excluding Greater China, for MTX-13/CB-002, a novel ADC targeting PTK7. pLGG, pediatric low-grade glioma. VRK1 Program is a research collaboration and license agreement with Sprint Bioscience AB for exclusive worldwide rights to a research-stage program targeting VRK1. The safety and efficacy of investigational agents and/or investigational uses of approved products have not been established.



# OJEMDA™ (tovorafenib)

Relapsed or Refractory BRAF-altered pLGG

# 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<sup>1</sup>

## 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<sup>2-6</sup>
- Despite surgery playing a significant role in treatment, the vast majority of patients still require systemic therapy<sup>7,8</sup>
- Due to high rate of disease recurrence, most patients will undergo multiple lines of systemic therapy over the course of their disease

# 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**

# 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<sup>2</sup> 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](https://dayonebio.com)

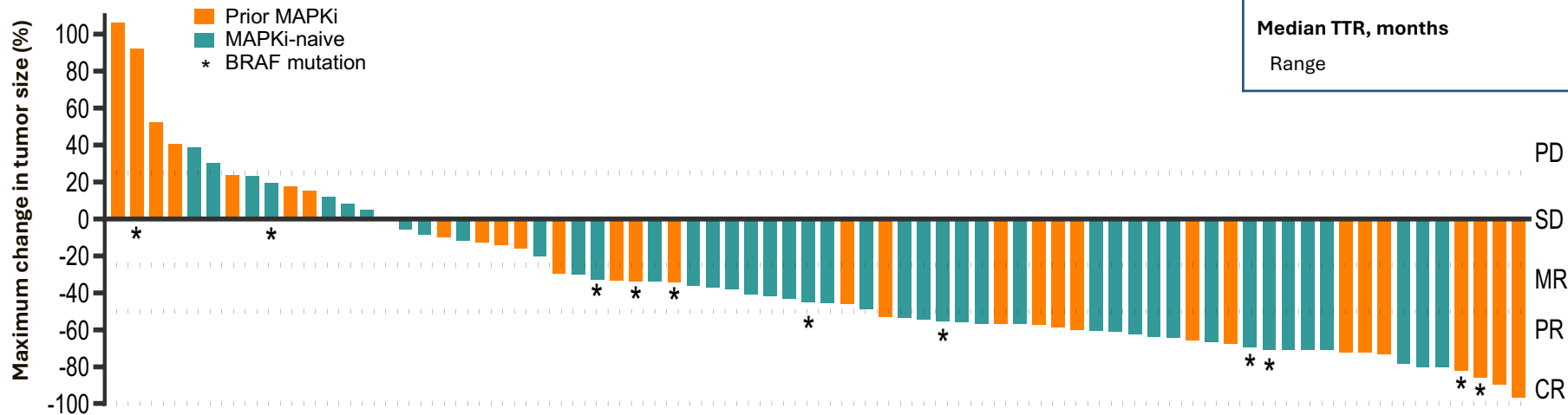


# Efficacy Summary From OJEMDA™ (tovorafenib) Prescribing Information



51%

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



Response (IRC)	RAPNO-LGG		
	n	n (%)	95% CI
<b>ORR, n (%)</b>	<b>76</b>	<b>39 (51)</b>	<b>40-63</b>
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
<b>Median DOR, months</b>	<b>39</b>	<b>13.8</b>	<b>11.3-NR<sup>†</sup></b>
<b>Median TTR, months</b>	<b>39</b>	<b>5.3</b>	
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. <sup>†</sup>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

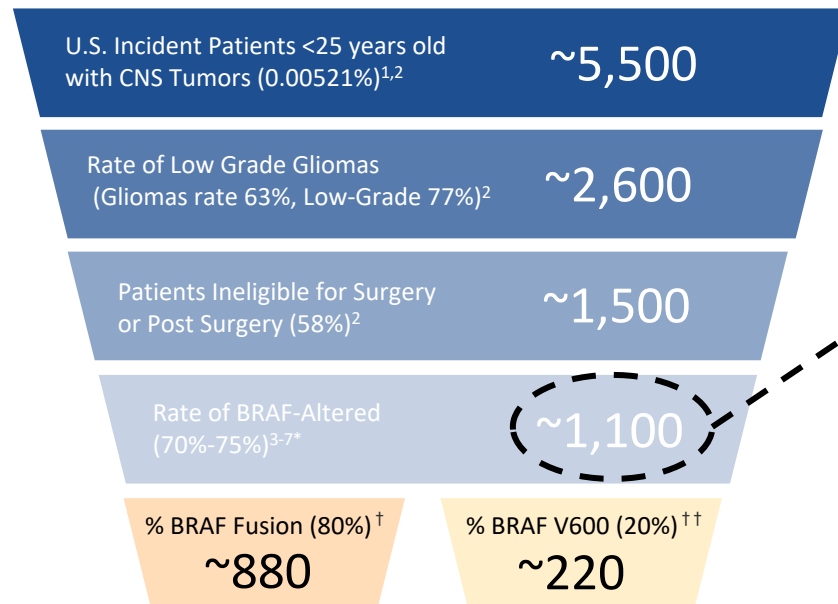
Preferred Term, n (%)	TEAEs (≥ 30% of patients [n=137])	
	Any Grade	Grade ≥3
Any AE	137 (100)	86 (63)
Hair color changes	104 (76)	0
Anemia	81 (59)	15 (11)
Elevated CPK	80 (58)	16 (12)
Fatigue	76 (55)	6 (4)
Vomiting	68 (50)	6 (4)
Hypophosphatemia	64 (47)	0
Headache	61 (45)	2 (1)
Maculo-papular rash	60 (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)

# Addressable U.S. Opportunity of OJEMDA Estimated to be ~2,000-3,000 Patients

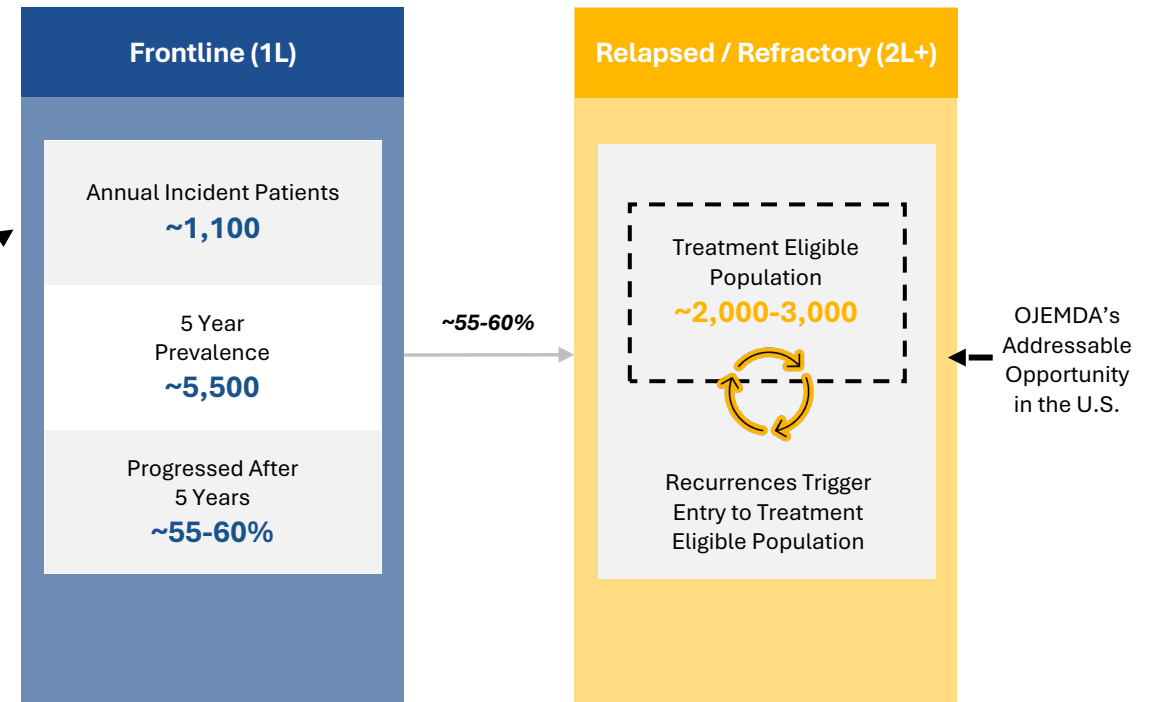
## Illustrative pLGG Patient Flow<sup>§</sup>

Prevalence of Systemically-Treated Patients Under 25 Years ~26,000

### Incident Therapeutic Build for New pLGG Patients to be Treated in Frontline Setting



1L BRAF-Altered pLGG Patients Eligible for Systemic Therapy



Majority of pLGG patients will progress within 5 years

<sup>1</sup>. US Census. <sup>2</sup> CBTRUS, Qaddoumi et al 2009, Schreck et al 2019, ClearView Analysis. <sup>3</sup> Penman CL et al. *Front Oncol.* 2015;5:54. <sup>4</sup> Cohen AR., *N Engl J Med.* 2020;386(20):1922-1931. <sup>5</sup> Lassaletta A, et al. *J Clin Oncol.* 2017;35(25):2934-2941. <sup>6</sup> Faulkner C, et al. *J Neuropathol Exp Neurol.* 2015;74(9):867-872. <sup>7</sup> Packer RJ, et al. *Neuro Oncol.* 2017;19(6):750-761. \* Incidence of BRAF alterations varies across pLGG subtypes. <sup>†</sup> Predominantly seen in pilocytic astrocytomas. <sup>††</sup> May vary across pLGG subtypes. BRAF, V-Raf murine sarcoma viral oncogene homolog B; MAPK, mitogen-activated protein kinase; pLGG, pediatric low-grade glioma. <sup>§</sup> Estimated annual incidence, estimated prevalence, estimated progression rates, and estimated recurrent/progressive total addressable opportunity are Day One calculations based on publicly available data. The estimated recurrent/progressive total addressable opportunity is based on progression free survival curves modeled from published literature and internal market research conducted by EpidStrategies, A Division of ToxStrategies, Inc. on behalf of Day One.

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

## 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, maculopapular 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.

# Strong Q3 Patient Demand Continues to Drive Performance

## Revenue Drivers

Strong and steady patient demand & high continuation rates were primary growth drivers in Q3 2024

## Breadth & Depth of Prescribers

- Nearly doubled the number of HCPs who prescribed OJEMDA in Q3
- HCPs treating more than 1 patient continues to increase



**\$20.1M** in net product revenue in 3Q 2024

## Growing Utilization

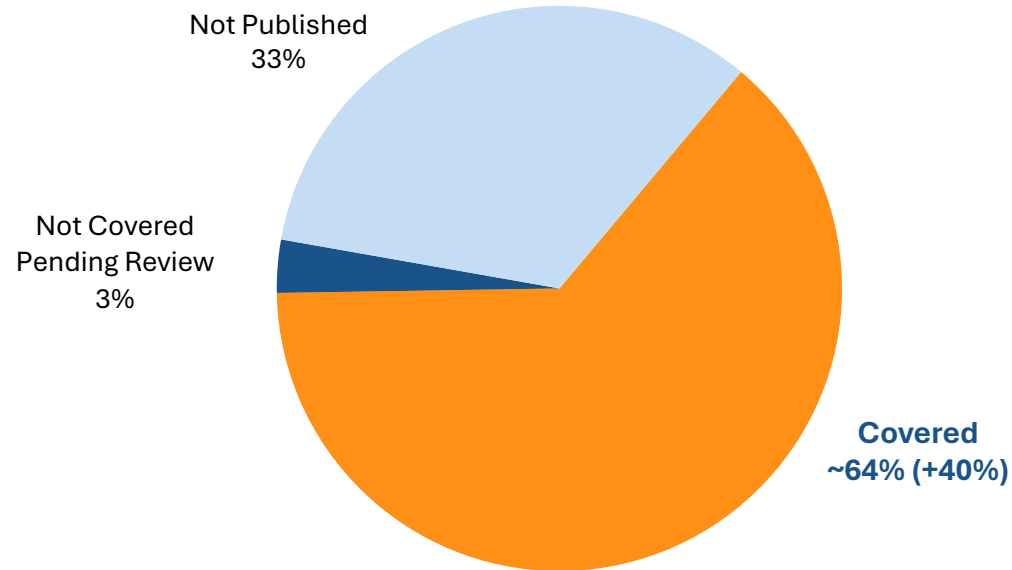
616 prescriptions in Q3 2024,  
**158% growth vs Q2 2024\***

## Payer Coverage

High payer approval rate enabling a high percentage of patients on paid drug

# Coverage Approval Rates are High Across both Commercial and Medicaid Payers Despite Limited Published Coverage

**Reported Coverage<sup>1,2</sup>**  
Percent of Covered Lives



## Payer Mix

- ~60% commercial patients
- ~40% Medicaid patients

**~80% Patients Approved for Coverage, Despite Lower Reported Coverage<sup>3</sup>**

# Well-Positioned For Commercial Execution And Sustained Growth

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## Continuing Launch Trajectory

**Increase breadth & depth of prescribers**

**Position OJEMDA as the standard of care in 2nd line**

**Establish remaining payer coverage policies**



# FIREFLY-2 / LOGGIC

Pivotal Phase 3 Trial of Tovorafenib in  
Frontline pLGG



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

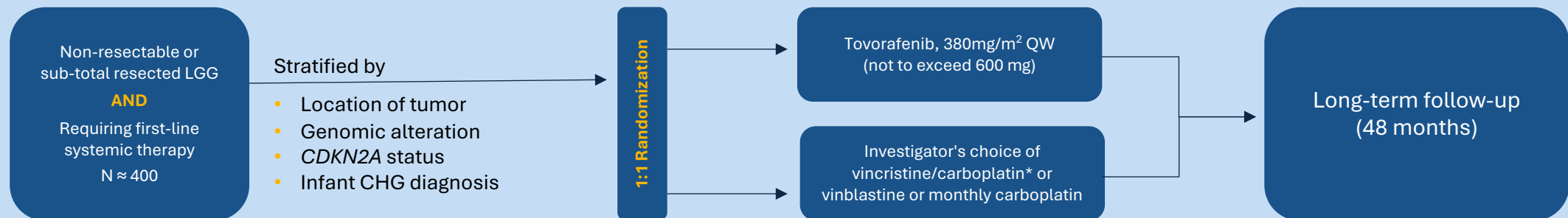


## Trial Design

- Randomized, global, registrational Phase 3 trial of monotherapy tovorafenib vs SoC chemotherapy
- Eligibility: Patients aged up 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 RAPNO-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 RAPNO-LGG 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.



DAY301

PTK7 Targeted Antibody Drug Conjugate (ADC)

# DAY301: Next Generation ADC Targeting PTK7

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## PTK7: Clinically-Validated ADC Target

Anti-tumor activity of anti-PTK7 ADC demonstrated in Phase 1b trial of Pfizer / Abbvie's cofetuzumab pelidotin<sup>1</sup>

## DAY301: Potential First-in-Class Asset

Novel ADC active in preclinical models, designed to maximize therapeutic window

## Substantial Development and Commercial Opportunities for DAY301

High PTK7 expression in multiple adult and pediatric tumor histologies

U.S. IND Cleared – Target First Patient Dosed in Q4 2024 / Q1 2025

# PTK7: A Clinically-Validated ADC Target

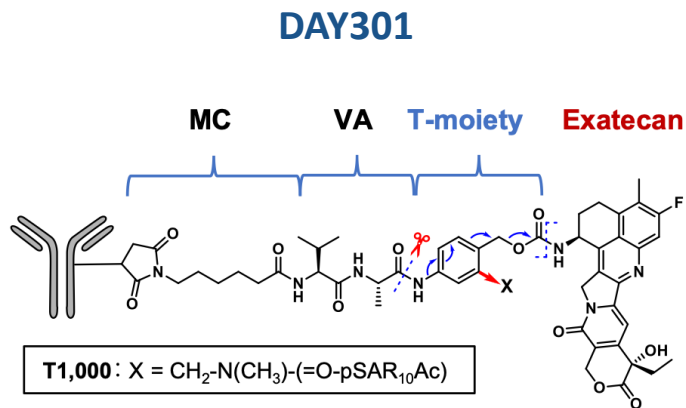
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## Potential opportunity for a next-generation PTK7 ADC with improved therapeutic index

- Clinical results for cofetuzumab pelidotin<sup>1</sup> demonstrated proof of concept for PTK7-targeted ADCs
- Cofetuzumab pelidotin activity seen in multiple tumor types:
  - Ovarian (Pt-resistant): ORR 27% (n=63)
  - TNBC: ORR 21% (n=29)
  - NSCLC: ORR 19% (n=31)
  - mDOR: 4.2-5.7m for Ovarian (Pt-resistant)/TNBC/NSCLC
  - mPFS: 1.5-2.9m for Ovarian (Pt-resistant)/TNBC/NSCLC
- Aur0101 program limited by toxicity, resulting in reduced dose intensity and duration
- A next generation product with optimized properties and a better therapeutic index may achieve greater clinical efficacy

# DAY301: Potential First-In-Class Asset

DAY301 has been designed to maximize therapeutic index and overcome limitations of prior programs

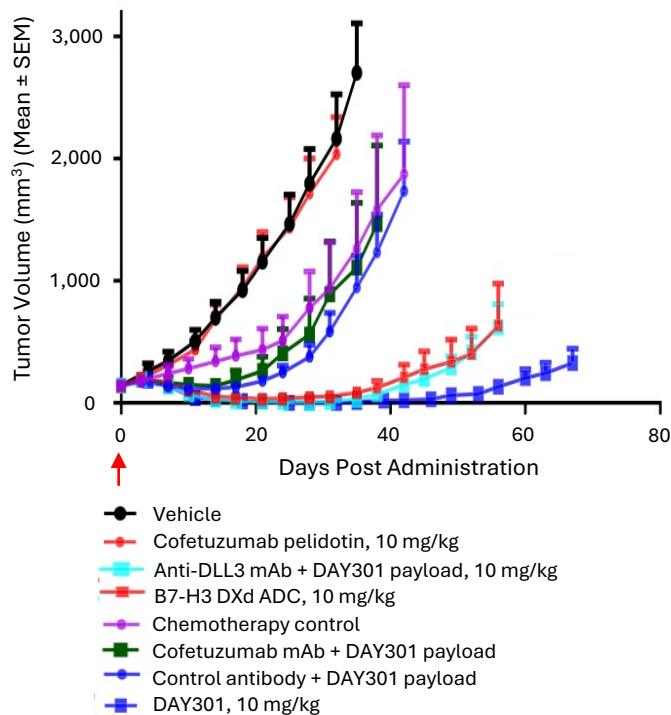


- Tumor regression at tolerable doses seen in multiple preclinical models
- Higher HNSTD in cyno toxicology studies; payload with known safety profile
- High cell permeability / bystander effect; low efflux (not a P-gp substrate)
- Novel, highly hydrophilic, cleavable linker
- Moderate-to-high affinity antibody with favorable stability and developability profile
- Drug-antibody-ratio (DAR) of 8, shown to be effective for other ADCs in solid tumors
- IP: Composition of Matter patent term expected 2044, once issued

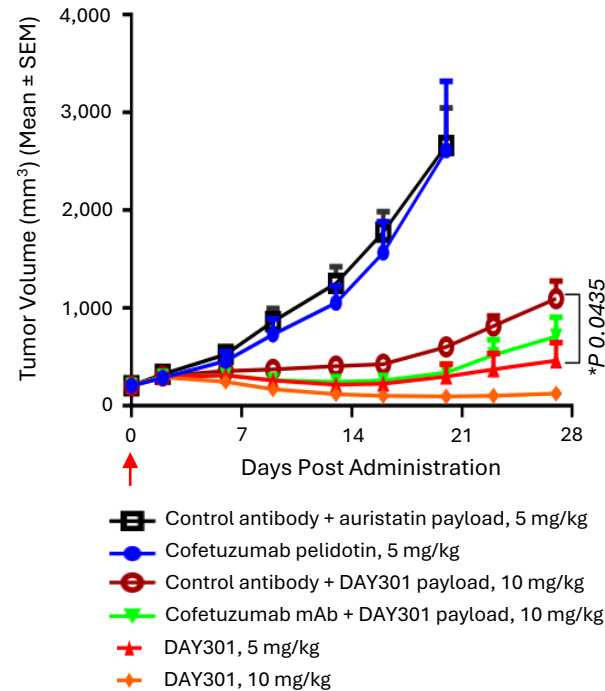
# DAY301: First-in-Class Potential

Improved tumor regression activity demonstrated for DAY301 vs. benchmarks in multiple preclinical models

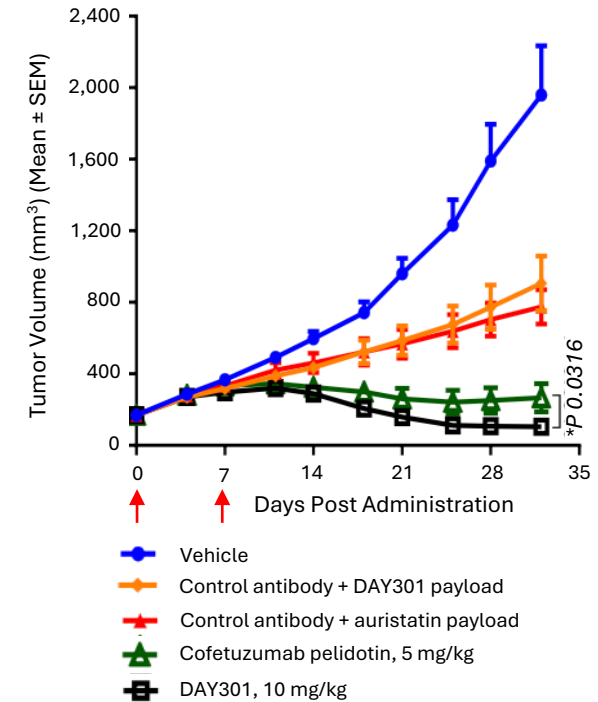
**PDX 362797 SCLC**  
H-score 210



**PDX 362310 TNBC**  
H-score 255



**PDX LD1-200615 HNSCC**  
H-score 120



↑ Indicates when drug was administered

# DAY301: Encouraging Development And Commercial Opportunities

Indication	PTK7 Expression ( $\geq 1+$ )	U.S. Patient Population Cases/Deaths	ORR at Relapse	Median OS at Relapse
Endometrial	100% <sup>2</sup>	67,880/13,250 <sup>3</sup>	39% <sup>7</sup>	9 months <sup>7</sup>
Esophageal SCC	76% <sup>1</sup>	22,370/16,130 <sup>3</sup>	5% <sup>4</sup>	3 months <sup>4</sup>
Gastric	35% <sup>2</sup>	26,890/10,880 <sup>3</sup>	12% <sup>14</sup>	6-14 months <sup>15</sup>
Head & Neck SCC	75% <sup>1</sup>	54,540/11,580 <sup>3</sup>	32% <sup>5</sup>	7.8 months <sup>5</sup>
NSCLC	50% <sup>2</sup>	199,393/106,310 <sup>3</sup>	45-60% <sup>8</sup>	7-12 months <sup>9</sup>
Ovarian (platinum resistant)	30% <sup>2</sup> (95%)*	19,710/13,270 <sup>3</sup>	20-35% <sup>3</sup>	17.2 months <sup>6</sup>
Small Cell Lung	50% <sup>2</sup>	35,187/18,760 <sup>3</sup>	10-40% <sup>10</sup>	9-12 months <sup>11</sup>
TNBC	70% <sup>2</sup>	46,608/12,675 <sup>3,16</sup>	5-35% <sup>12</sup>	28 months <sup>13</sup>
Potential pediatric indications include: neuroblastoma, rhabdomyosarcoma and osteosarcoma				

# DAY301-001: Initial Phase 1a/b Clinical Trial Design

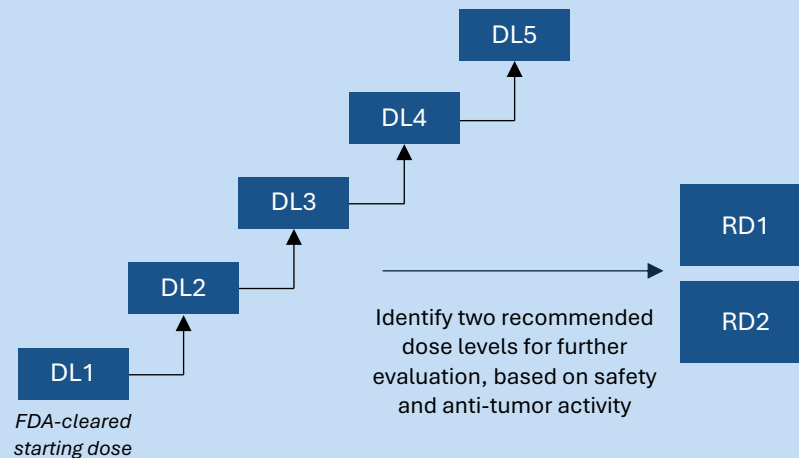
## Key Design Elements

- BOIN design for efficiency of dose escalation
- Backfill active dose levels to generate additional safety data
- Enroll tumor types with known high PTK7 expression
- Advance two recommended dose levels to Phase 1b
- Final dose optimization scheme and approval path pending discussions with FDA at end of dose escalation

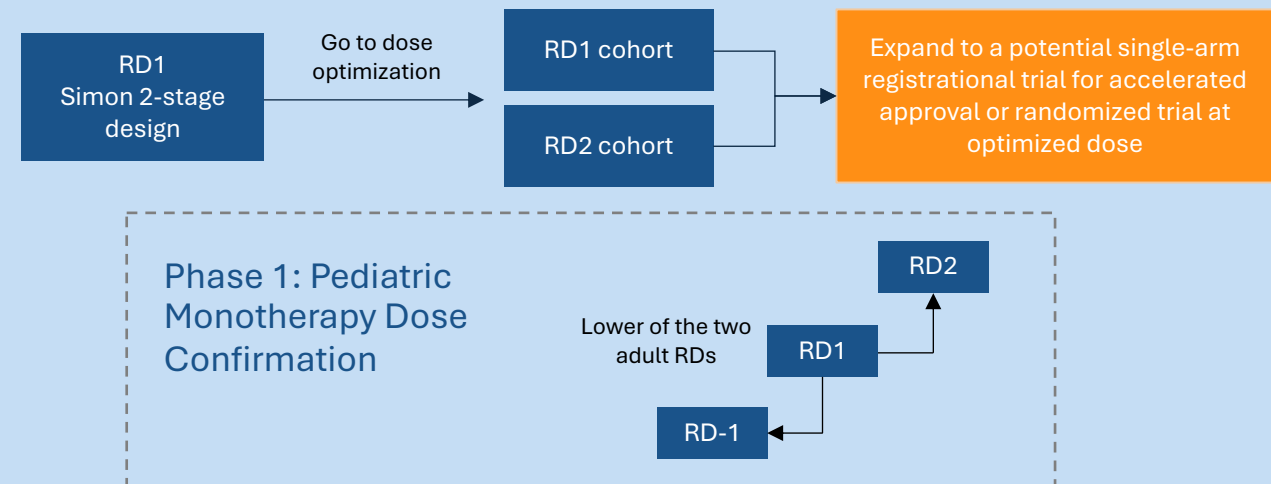
## Adult & Pediatric Development

- Potential adult indications include platinum resistant ovarian cancer, squamous NSCLC, esophageal SCC, HNSCC, endometrial, and/or SCLC
  - Patients to be selected based on PTK7 expression clinical trial assay
- Pediatric dose confirmation and efficacy assessment to begin near/at the end of adult dose escalation
  - Initial target indications include neuroblastoma, osteosarcoma, rhabdomyosarcoma

### Phase 1a: Monotherapy Dose Escalation



### Phase 1b: Monotherapy Dose Expansion and Optimization





# Summary



# Third Quarter 2024 Financial Results

Financial Summary (\$ in millions)	Three Months Ended 9/30/24	Three Months Ended 9/30/23	Nine Months Ended 9/30/24	Nine Months Ended 9/30/23
OJEMDA Net Revenue	20.1	--	28.3	--
License Revenue	73.7	--	73.7	--
<b>Total Revenue</b>	<b>\$93.8</b>	<b>\$--</b>	<b>\$101.1</b>	<b>\$--</b>
Cost of Product Revenue	1.6	--	2.3	--
Research and Development Expense <sup>1</sup>	33.6	33.2	165.9	93.2
Selling, General and Administrative Expense <sup>2</sup>	29.0	18.3	85.7	53.4
<b>Total Cost and Operating Expenses</b>	<b>\$64.1</b>	<b>\$51.4</b>	<b>\$253.9</b>	<b>\$146.5</b>
Non-operating Income <sup>3</sup>	6.5	5.3	122.8	12.1
Income Tax Benefit (Expense)	0.9	--	(0.7)	--
<b>Net Income (Loss)</b>	<b>\$37.0</b>	<b>(\$46.2)</b>	<b>(\$29.8)</b>	<b>(\$134.4)</b>

	9/30/24	9/30/23
Cash, cash equivalents and short-term investments	\$558.4	\$405.5

All financial information is unaudited. <sup>1</sup> Includes stock-based compensation expense of \$3.8 million and \$13.2 million for the three and nine months ended 9/30/24, and \$3.3 million and \$10.1 million for the three and nine months ended 9/30/23, respectively. <sup>2</sup> Includes stock-based compensation expense of \$7.8 million and \$24.0 million for the three and nine months ended 9/30/24, and \$6.3 million and \$18.4 million for the three and nine months ended 9/30/23, respectively. <sup>3</sup> Includes sale of Priority Review Voucher of \$108.0 million for the nine months ended 9/30/24.

# Priorities as a Commercial-Stage Company

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## 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
- Develop DAY301, ADC targeting PTK7 in pediatric and adult solid tumors
- Advance early stage VRK1 program to clinical development

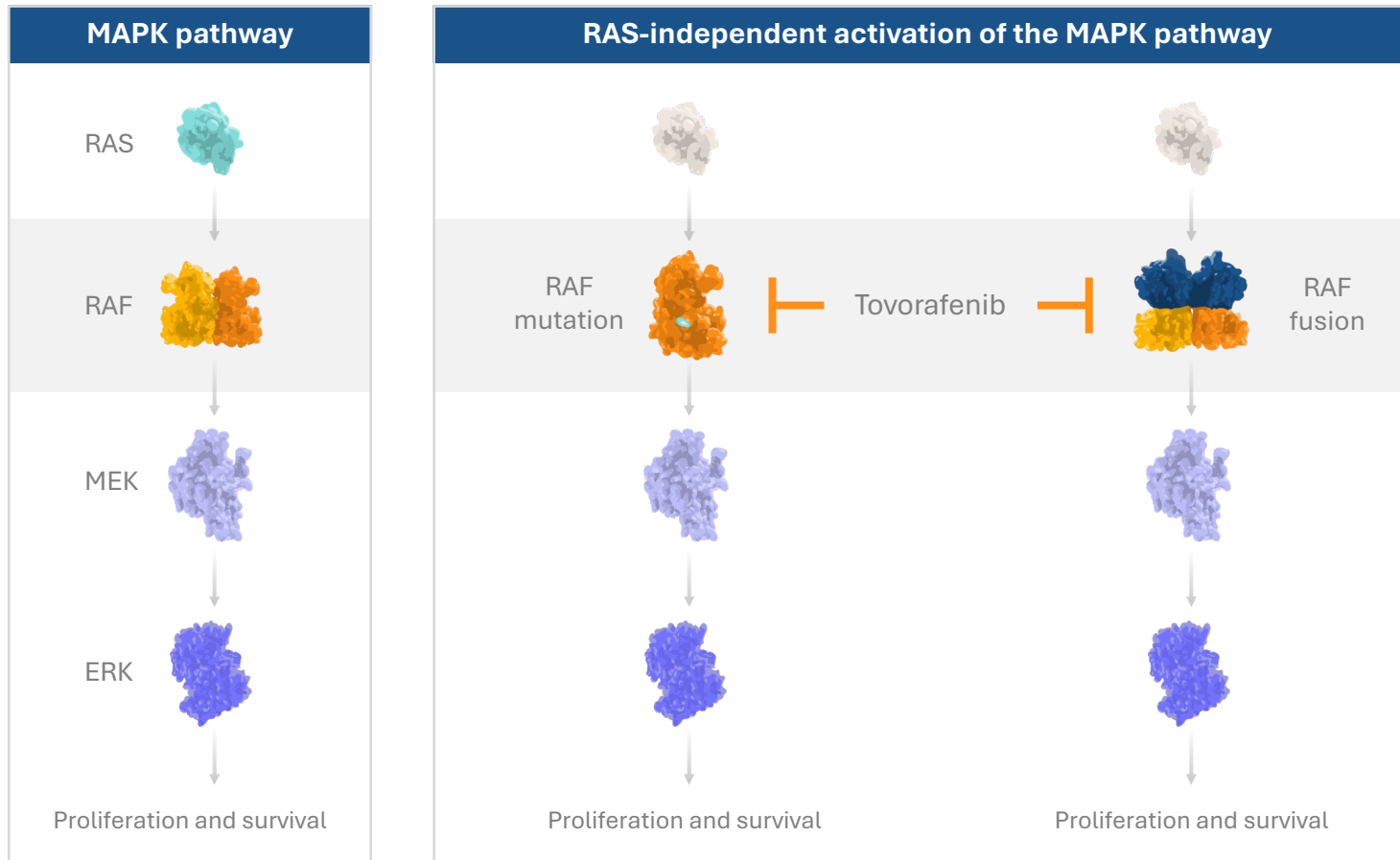
## Expand Pipeline

- 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

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



## Trial Design

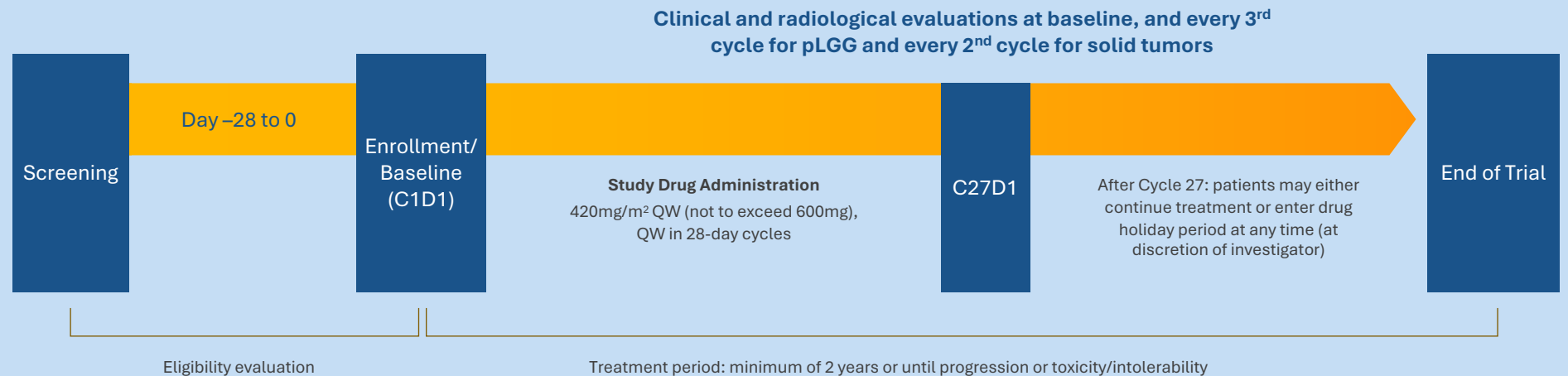
- Three arm, open-label, global registrational phase 2 trial
- **Pivotal Arm 1 (recurrent/progressive pLGG, n=77): harboring a KIAA1549-BRAF fusion or BRAF V600E mutation**
- Arm 2 (expanded access recurrent/progressive LGG, n=60): harboring an activating RAF alteration
- Arm 3 (extracranial solid tumors):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

## Endpoints (Pivotal Arm 1)

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





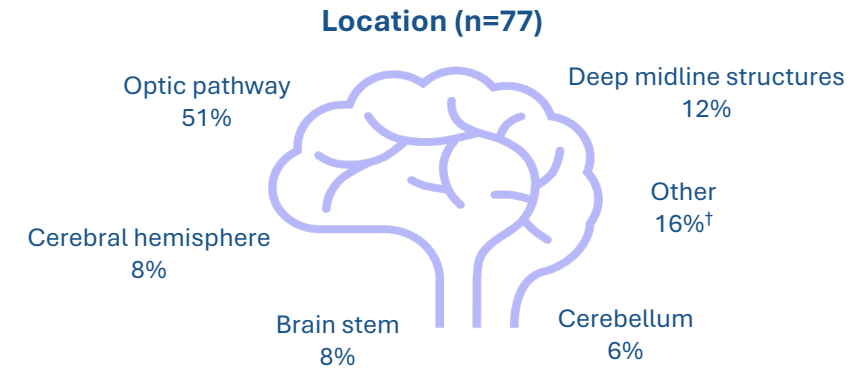
# Data from Pivotal Phase 2 FIREFLY-1 Trial

June 5, 2023 data cutoff

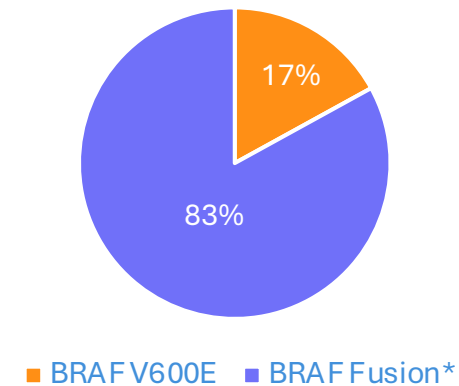


# FIREFLY-1 Baseline Patient Characteristics

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



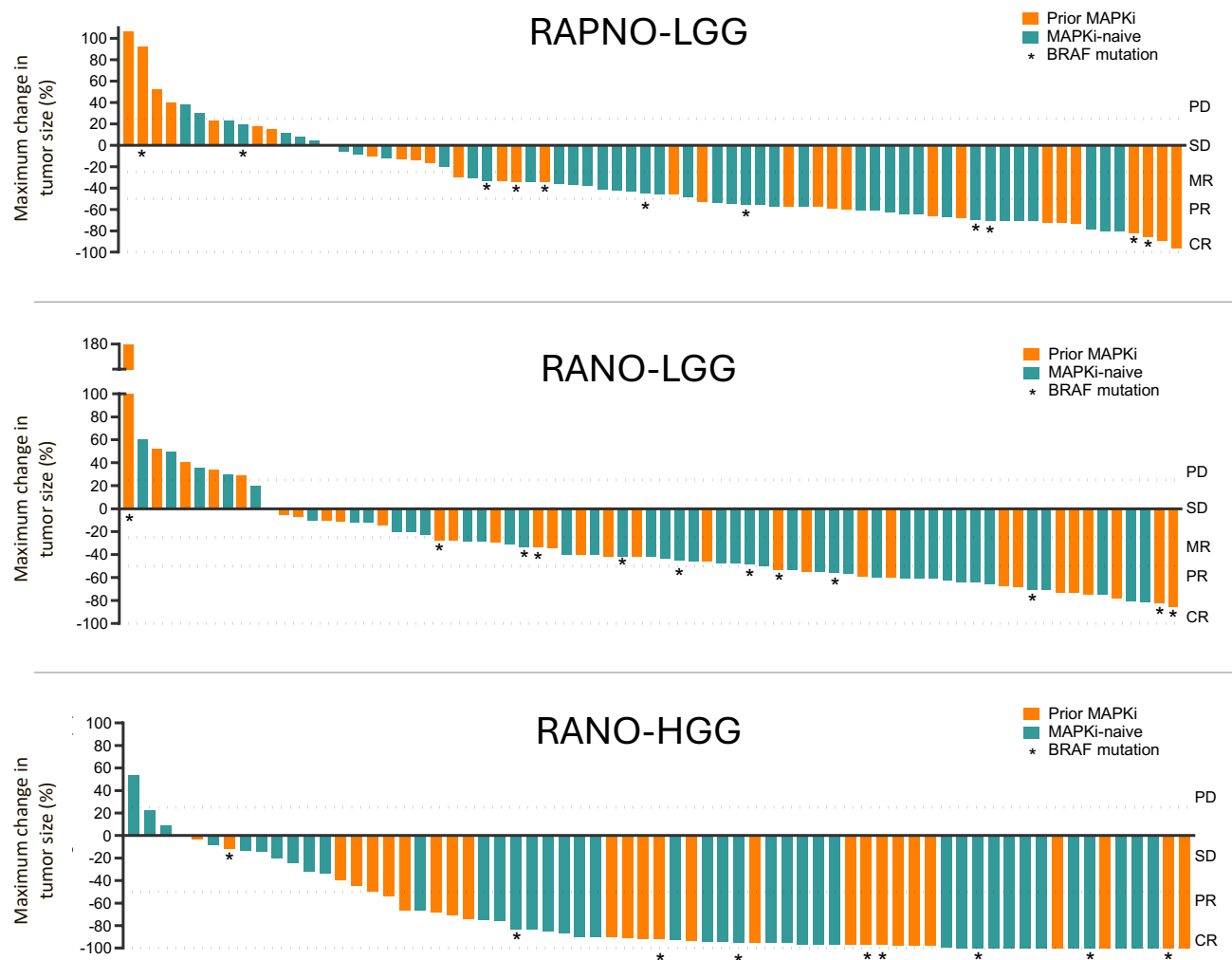
**BRAF alteration (n=77)**



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.



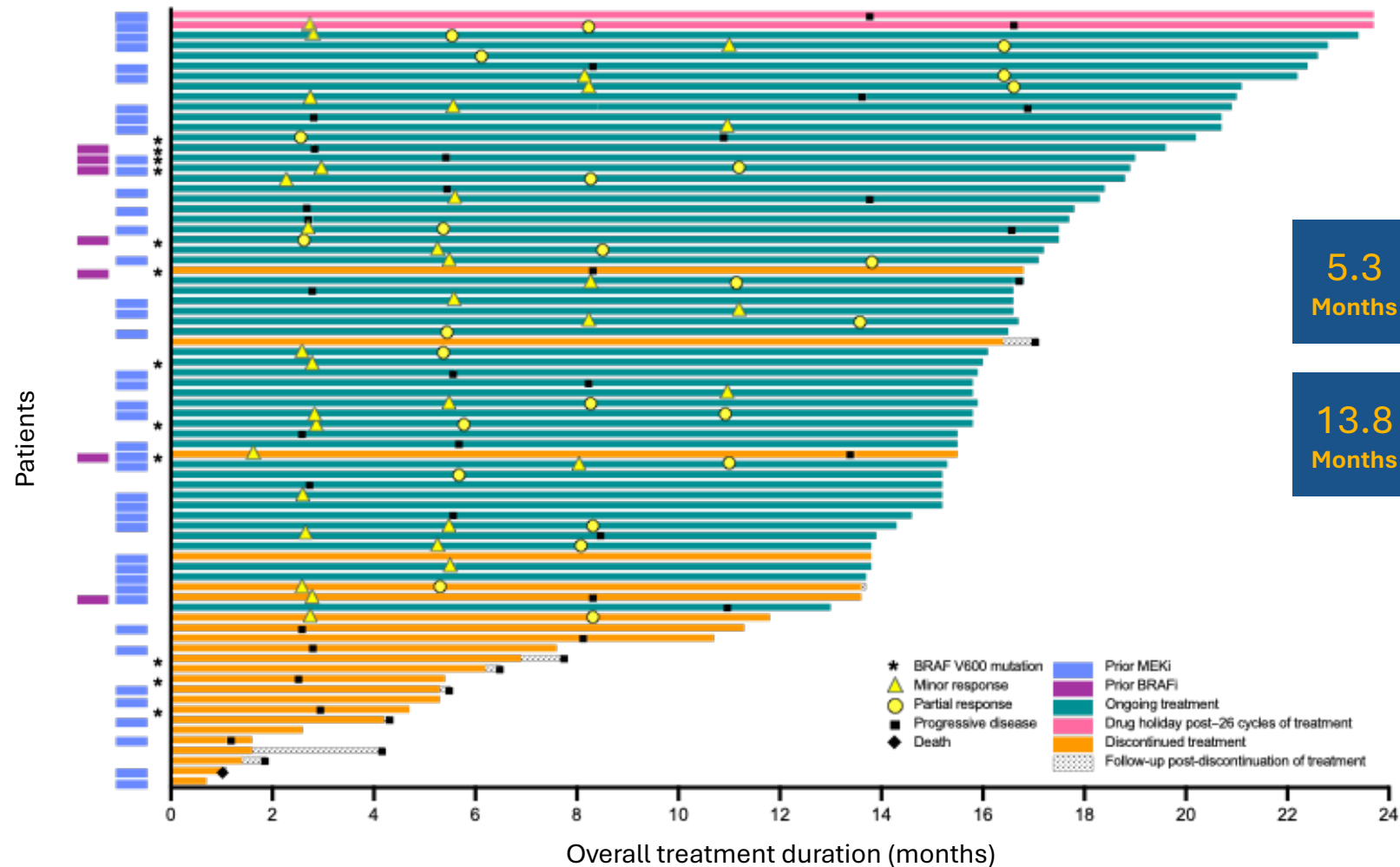
# Tumor Response To Tovorafenib Using RAPNO-LGG, RANO-LGG and RANO-HGG



Response (IRC)	RAPNO-LGG n=76	RANO-LGG N=76	RANO-HGG N=69
<b>ORR,* n (%)</b>	<b>39 (51)</b>	<b>40 (53)</b>	<b>46 (67)</b>
95% CI	40-63	41-64	54-78
<b>CBR,* n (%)</b>			
SD of any length of time	62 (82)	63 (83)	64 (93)
SD ≥12 months	43 (57)	46 (61)	54 (78)
<b>BOR,* n (%)</b>			
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)
<b>Median DOR, months</b>	<b>13.8</b>	<b>14.4</b>	<b>16.6</b>
95% CI	11.3-NR	11.0-NR	11.6-NR
<b>Median TTR, months</b>	<b>5.3</b>	<b>5.5</b>	<b>3.0</b>
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.

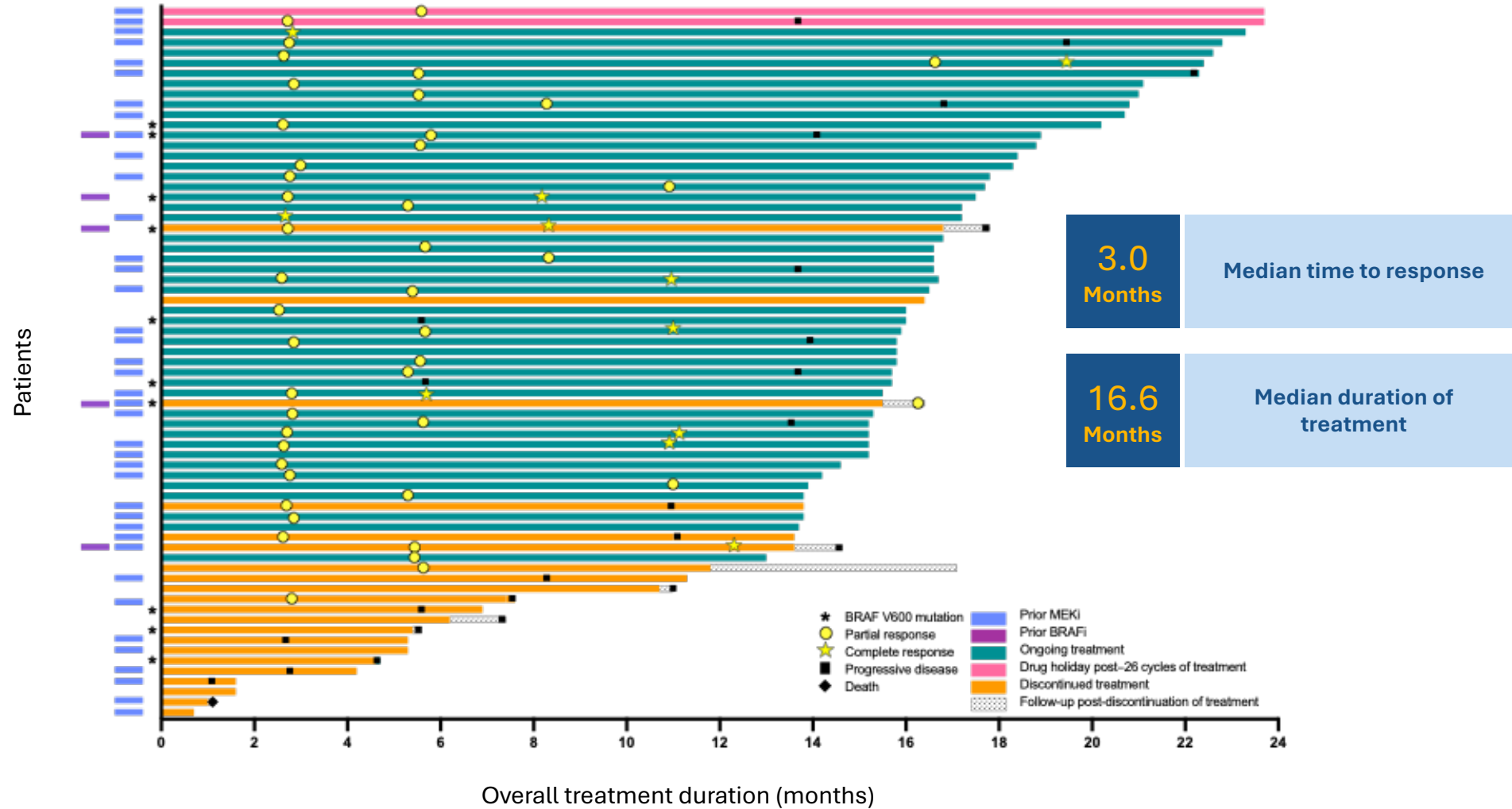
# Duration Of Tovorafenib Therapy For All Patients With RAPNO-LGG Evaluable Lesions



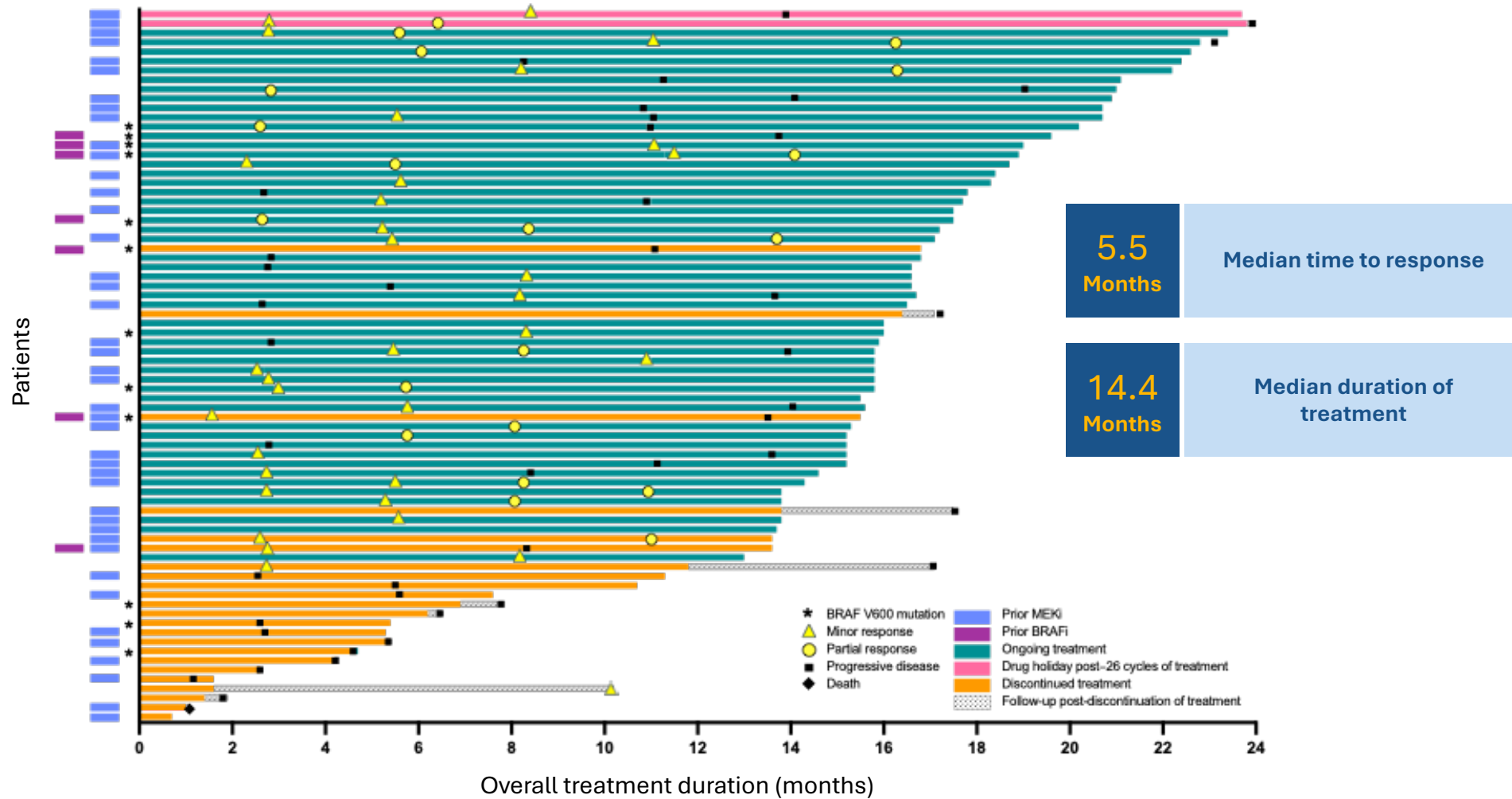
**5.3 Months**  
Median time to response

**13.8 Months**  
Median duration of treatment

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



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



# 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 <sup>2</sup>		RANO-LGG <sup>3,4</sup>		RANO-HGG <sup>1</sup>	
	n		n		n	
<b>ORR,* n (%)</b>	<b>76</b>	<b>39 (51)</b>	<b>76</b>	<b>40 (53)</b>	<b>69</b>	<b>46 (67)</b>
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)
<b>CBR,* n (%) (SD of any length of time)</b>	<b>76</b>	<b>62 (82)</b>	<b>76</b>	<b>63 (83)</b>	<b>69</b>	<b>64 (93)</b>
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)
<b>CBR,* n (%) (SD ≥12 months)</b>	<b>76</b>	<b>43 (57)</b>	<b>76</b>	<b>46 (61)</b>	<b>69</b>	<b>54 (78)</b>
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)
<b>Median DOR, months (95% CI)**</b>	<b>39</b>	<b>13.8 (11.3-NR)</b>	<b>40</b>	<b>14.4 (11.0-NR)</b>	<b>46</b>	<b>16.6 (11.6-NR)</b>
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)



# 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