ERASCA

On a Journey to Erase Cancer

Erasca Corporate Presentation

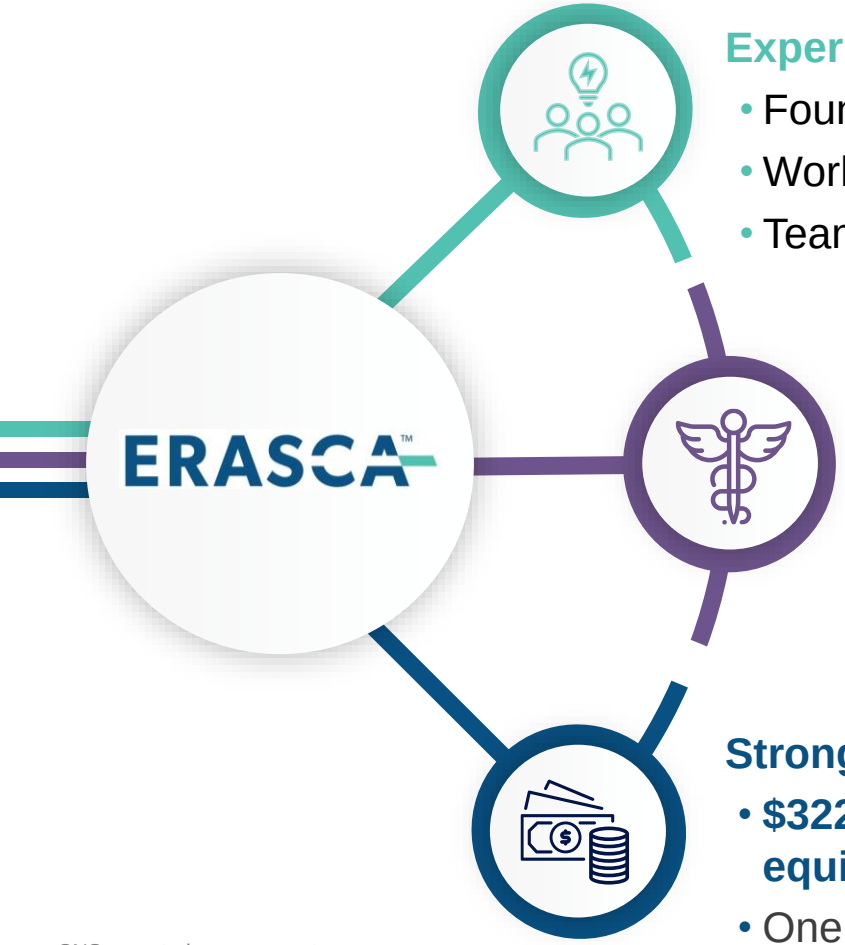
March 2024

Disclaimer: Forward Looking Statements & Market Data

We caution you that this presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding our future results of operations and financial position, business strategy, research and development plans, the anticipated timing (including the timing of initiation and the timing of data readouts), costs, design and conduct of our ongoing and planned preclinical studies and clinical trials for our product candidates, the potential benefits from our current or future arrangements with third parties, the timing and likelihood of success of our plans and objectives, the impact of the deprioritization of certain programs, and future results of anticipated product development efforts, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. The inclusion of forward-looking statements should not be regarded as a representation by us that any of our plans will be achieved. Actual results may differ from those set forth in this presentation due to the risks and uncertainties inherent in our business, including, without limitation: our approach to the discovery and development of product candidates based on our singular focus on shutting down the RAS/MAPK pathway, a novel and unproven approach; we only have three product candidates in clinical development and all of our other development efforts are in the preclinical or development stage; the analysis of pooled phase 1 and phase 2 naporafenib + trametinib data covers two clinical trials with different designs and inclusion criteria, which cannot be directly compared, and therefore may not be a reliable indicator of efficacy data; due to differences between trial designs and subject characteristics, comparing data across different trials may not be a reliable indicator of data; preliminary results of clinical trials are not necessarily indicative of final results and one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data and more patient data become available, including the risk that an uPR to treatment may not ultimately result in a cPR to treatment after follow-up evaluations; we have not completed any clinical trials of naporafenib and are reliant on data generated by Novartis in prior clinical trials conducted by it; our planned SEACRAFT trials may not support the registration of naporafenib; our assumptions around which programs may have a higher probability of success may not be accurate, and we may expend our limited resources to pursue a particular product candidate and/or indication and fail to capitalize on product candidates or indications with greater development or commercial potential; potential delays in the commencement, enrollment, and completion of clinical trials and preclinical studies; our dependence on third parties in connection with manufacturing, research, and preclinical and clinical testing; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval, and/or commercialization, or may result in recalls or product liability claims; unfavorable results from preclinical studies or clinical trials; results from preclinical studies or early clinical trials not necessarily being predictive of future results; the inability to realize any benefits from our current licenses, acquisitions, or collaborations, and any future licenses, acquisitions, or collaborations, and our ability to fulfill our obligations under such arrangements; our assumptions around which programs may have a higher probability of success may not be accurate, and we may expend our limited resources to pursue a particular product candidate and/or indication and fail to capitalize on product candidates or indications with greater development or commercial potential; regulatory developments in the United States and foreign countries; later developments with the FDA or European health authorities may be inconsistent with the feedback received to date regarding our development plans and trial designs; fast track designation or orphan drug designation may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval; our ability to fund our operating plans with our current cash, cash equivalents, and marketable securities into the second half of 2026; and other risks described in our prior filings with the Securities and Exchange Commission (SEC), including under the heading "Risk Factors" in our annual report on Form 10-K for the year ended December 31, 2023, and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and we undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. 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 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. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

Our name is our mission: to erase cancer

Vision to one day erase cancer[1] in at least 100,000 patients annually as a leading global oncology company



Experienced leadership team and SAB with track record of serial successes

- Founded by **Jonathan Lim, MD & Kevan Shokat, PhD** around disruptive idea to target RAS
- World class scientific advisory board of **leading pioneers** in RAS/MAPK pathway
- Team with deep experience in efficient planning and execution of **global clinical trials**

Industry leading portfolio focused on shutting down the RAS/MAPK pathway

- **Naporafenib pan-RAFi** with first-in-class (FIC) potential and Fast Track Designation for NRASm melanoma & FIC potential in RAS Q61X solid tumors
- **ERAS-007 ERKi** with best-in-class potential for BRAFm CRC
- **ERAS-801, CNS-penetrant EGFRi** with FIC potential for EGFR-driven rGBM

Strong financial position with high quality investor base and industry visibility

- **$322M in cash, cash equivalents, and marketable securities[2]**, plus **$45M oversubscribed equity financing** announced on 3/27/2024; anticipated cash runway into **H2 2026**
- One of **Fierce Biotech's 2021 "Fierce 15"** most promising biotechnology companies

CNS = central nervous system

[1] Number of patients alive and free of cancer or free from cancer progression 2 yrs after starting an Erasca regimen, as measured by disease-free survival (adjuvant setting) and progression-free survival (metastatic setting)

[2] Audited, as of December 31, 2023

ERASCA™

SAB includes world's leading experts in the RAS/MAPK pathway

Kevan Shokat, PhD

Erasca co-founder. World expert in RAS who pioneered development of approaches to inhibit KRAS G12C (RAS-GDP) and active states of RAS (RAS-GTP)

UCSF University of California San Francisco

Stephen Blacklow MD, PhD

World expert in SHP2 who helped pioneer development of the first SHP2 inhibitor with Novartis

HARVARD MEDICAL SCHOOL · Dana-Farber Cancer Institute

Ryan Corcoran, MD, PhD

World expert in ERK, having studied nearly every ERK inhibitor that has been or is being developed, as well as targeted therapies directed against KRAS, BRAF, and MEK mutations

HARVARD MEDICAL SCHOOL · MASSACHUSETTS GENERAL HOSPITAL CANCER CENTER

Pablo Rodriguez-Viciana, PhD

World expert in RAS/MAPK pathway with focus on the SHOC2 phosphatase complex as a unique regulatory node required for efficient pathway activation in the context of diseases such as cancer and RASopathies

UCL CANCER INSTITUTE UCL

Karen Cichowski, PhD

World expert in RAS/MAPK pathway signaling and identifying novel combination therapies to shut it down

HARVARD MEDICAL SCHOOL · BWH BRIGHAM AND WOMEN'S HOSPITAL

George Demetri, MD

World expert in targeted oncology therapies who pioneered the development of Gleevec®, which helped launched the precision oncology revolution

HARVARD MEDICAL SCHOOL · Dana-Farber Cancer Institute

Michael Varney, PhD

World expert in structure-based drug design; former head of research at Agouron and former head of Genentech's Research and Early Development (gRED)

Genentech

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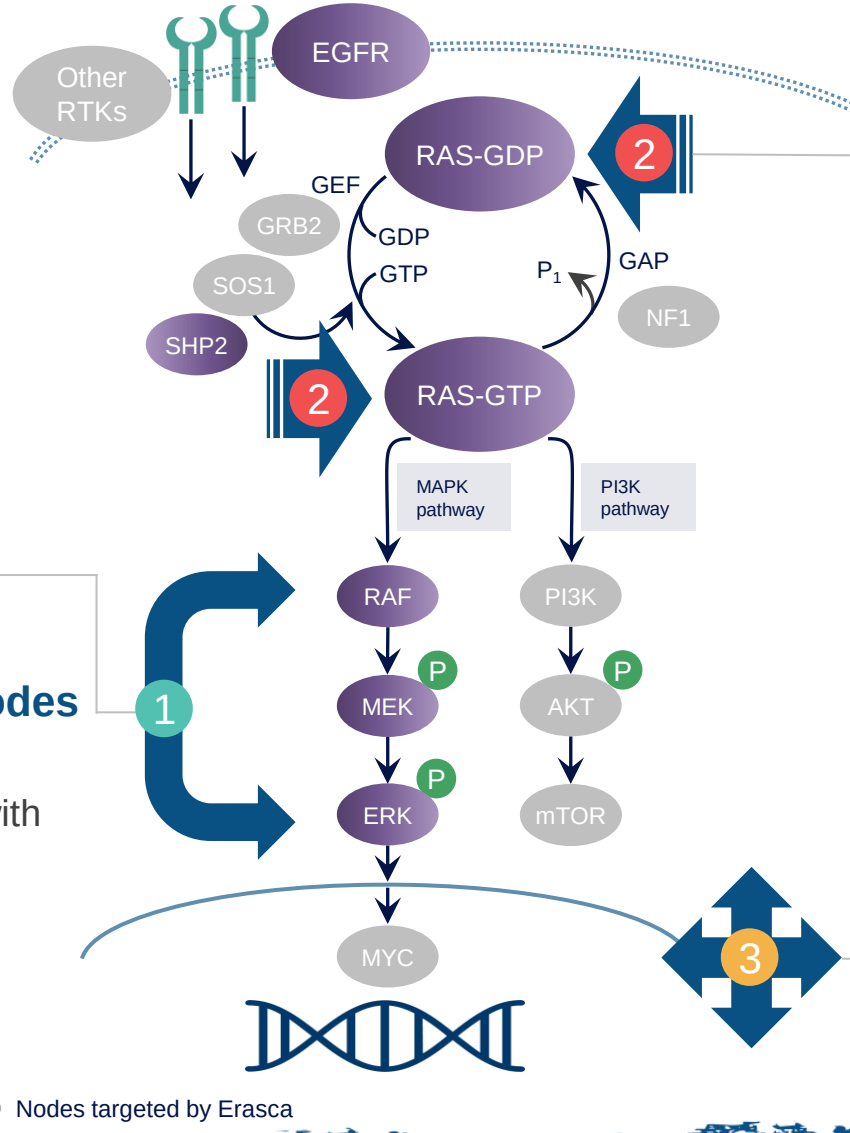
Our singular focus is on the RAS/MAPK pathway

Our Strategy

Comprehensively shut down the RAS/MAPK pathway



1 **Target upstream and downstream RAS/MAPK nodes**

with single agents and clamp oncogenic drivers (MAPKlamp) with combinations

2 **Target RAS directly**

with single agents and combinations with upstream, downstream, and escape route targeted therapies

3 **Target escape routes**

enabled by other proteins or pathways to further disrupt RAS/MAPK pathway signaling

Deep modality-agnostic RAS/MAPK pathway-focused pipeline

Program/ Company	Target	Modality	Indication	Discovery	IND-enabling	Phase 1	Phase 2	Phase 3	Worldwide Rights
Naporafenib	BRAF/CRAF		Pan-RAS Q61X tissue agnostic			SEACRAFT-1			ERASCA
			NRASm melanoma			SEACRAFT-2 (planned)			ERASCA
ERAS-007	ERK1/2		BRAF V600E CRC			HERKULES-3			ERASCA
ERAS-801	EGFR		EGFR-altered GBM			THUNDERBBOLT-1			ERASCA
ERAS-4	Pan-KRAS		KRASm solid tumors						ERASCA
ERAS-12	EGFR D2/D3		EGFR & RAS/MAPK altered tumors						ERASCA
Affini-T	KRAS G12V/D		KRASm solid tumors						affini

small molecule large molecule TCR T cell therapy ERASCA Ventures investment

Erasca's clinical development plan generates multiple ways to win for patients

Indication	RAS Q61X solid tumors	NRASm melanoma post-IO	BRAFm CRC EC-naïve	EGFR-altered rGBM
Benchmark	SOC is largely chemo	ORR 7% mDOR NA	ORR 20% mDOR 6.1 mos.	ORR 3-9% mDOR NA
Regimen tested	**naporafenib** + trametinib	**naporafenib** + trametinib	**ERAS-007** + encorafenib + cetuximab	**ERAS-801** monotherapy
Erasca trial(s)	SEACRAFT-1[1]	SEACRAFT-2[2]	HERKULES-3[3]	THUNDERBBOLT-1

Active CTCSAs

NOVARTIS
[1] May 2023: Trametinib (Mekinist®) for SEACRAFT-1
[2] Feb 2024: Trametinib (Mekinist®) for SEACRAFT-2

Lilly
[3] Mar. 2022: Cetuximab (Erbitux®) for HERKULES-3

Pfizer
[3] Sep. 2021: Encorafenib (Braftovi®) for HERKULES-3

Pierre Fabre
[3] Nov. 2022: Encorafenib (Braftovi®) for HERKULES-3

CTCSA: clinical trial collaboration and supply agreement
ORR: overall response rate; DOR: duration of response; GBM: glioblastoma

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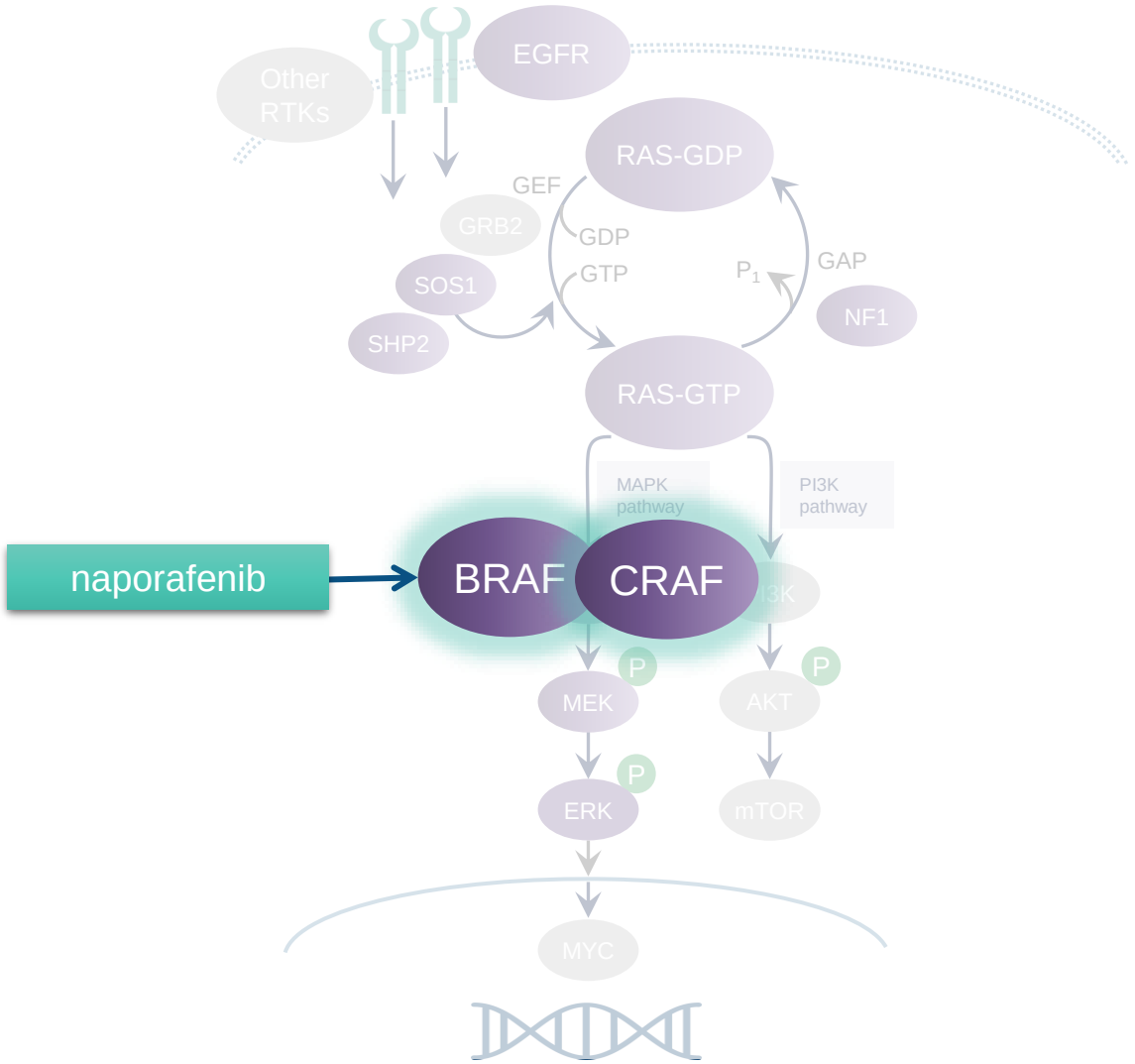
Erasca's naporafenib pan-RAFi could address unmet needs in patients with both NRASm melanoma and RAS Q61X solid tumors



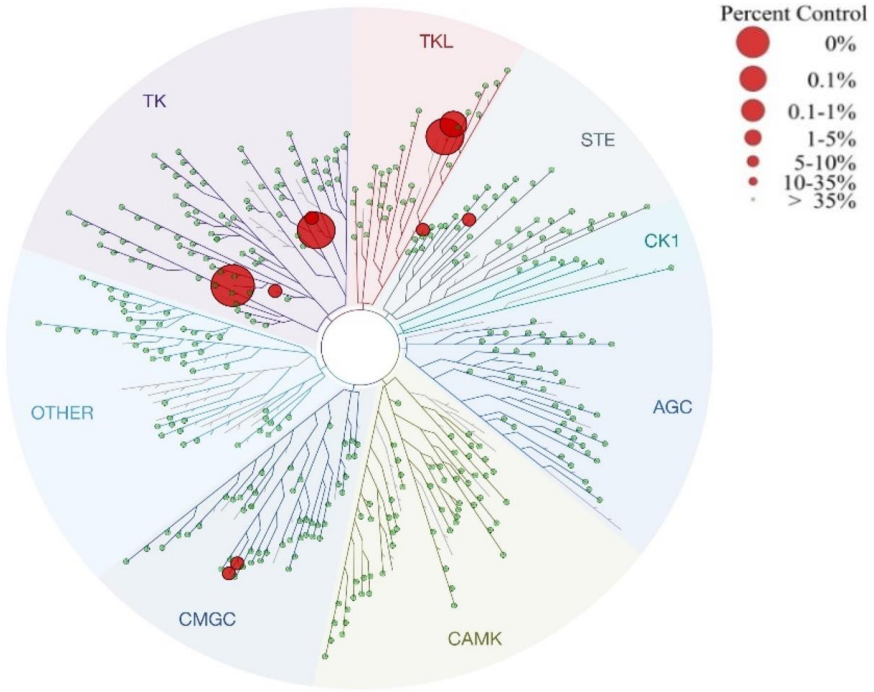
- Potently **inhibits CRAF and BRAF** and blocks downstream RAS/MAPK pathway signaling
- **Synergizes with trametinib** which targets MEK, the immediate downstream node of RAF
- Selectivity for BRAF and CRAF over ARAF is predicted to enable a **better therapeutic window**
- **Does not result in paradoxical BRAF activation**, a resistance mechanism observed with BRAF V600E inhibitors

Naporafenib is a potent and selective inhibitor of BRAF and CRAF with sub-nanomolar IC50 potency and most advanced pan-RAFi in development

Biochemical activity of naporafenib against RAF kinase family

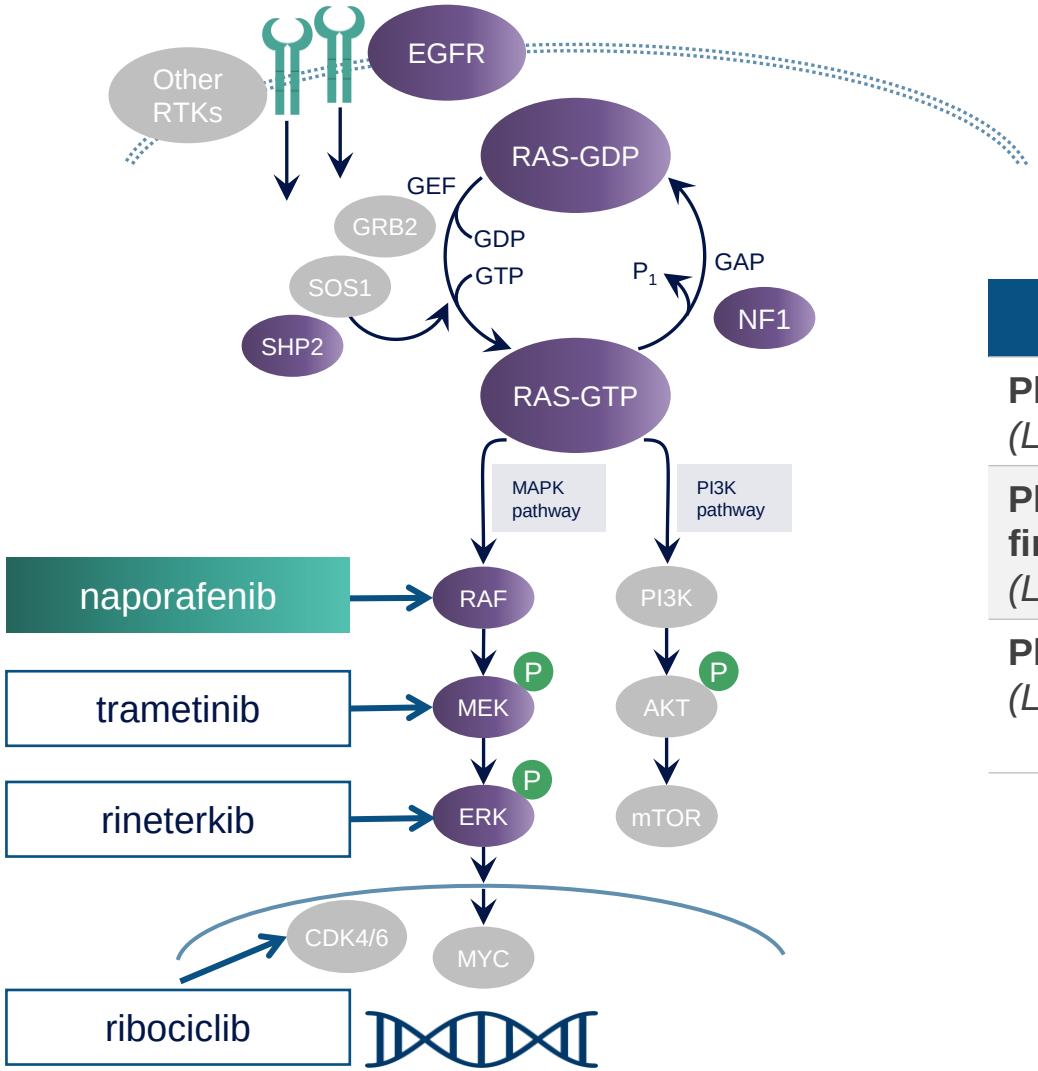
Assay	Value (nM)
Biochemical CRAF IC50 (IC_{50})	0.1
Biochemical BRAF IC50 (IC_{50})	0.2
Biochemical ARAF Inhibition (IC_{50})	6.4

Biochemical activity of naporafenib across 456 kinases (KINOMEscan)



Source: Monaco K-A, Delach S, et al. LXH254, a Potent and Selective ARAF-Sparing Inhibitor of BRAF and CRAF for the Treatment of MAPK-Driven Tumors. 2021. PMID: 33355204; Ramurthy S, Taft BR, et al. Design and Discovery of N-(3-(2-(2-Hydroxyethoxy)-6-Morpholinopyridin-4-Yl)-4-Methylphenyl)-2-(trifluoromethyl)isonicotinamide, a Selective, Efficacious, and Well-Tolerated RAF Inhibitor Targeting RAS Mutant Cancers: The Path to the Clinic. 2020. PMID: 31059256

Naporafenib has been dosed in more than 500 patients to date, establishing its safety, tolerability, and preliminary PoC in multiple indications



Study (Trial #)	Description	N
Ph 1 FIH study *(LXH254X2101)*	Naporafenib dose escalation in patients with RAS/MAPK-driven solid tumors	142
Ph 1b combo dose finding *(LXH254X2102)*	Dose-finding study (+ rineterkib, trametinib, or ribociclib) in patients with NRASm melanoma, KRASm or BRAFm NSCLC	241
Ph 2 combo study *(LXH254C12201)*	Evaluating efficacy (+ rineterkib, trametinib or ribociclib) in patients with NRASm or BRAF V600X melanoma	134

Total size of safety database > 500 patients
(includes monotherapy and combinations)

Source: Novartis Non-Confidential Materials; PoC = proof-of concept

Two-pronged naporafenib development approach addresses high unmet needs and multiple ways to benefit patients with RAS/MAPK-driven tumors

SEACRAFT-1: RAS Q61X Solid Tumors

- High unmet need and potential for tissue agnostic approach
- Phase 1b data for naporafenib + trametinib planned in Q2-Q4 2024

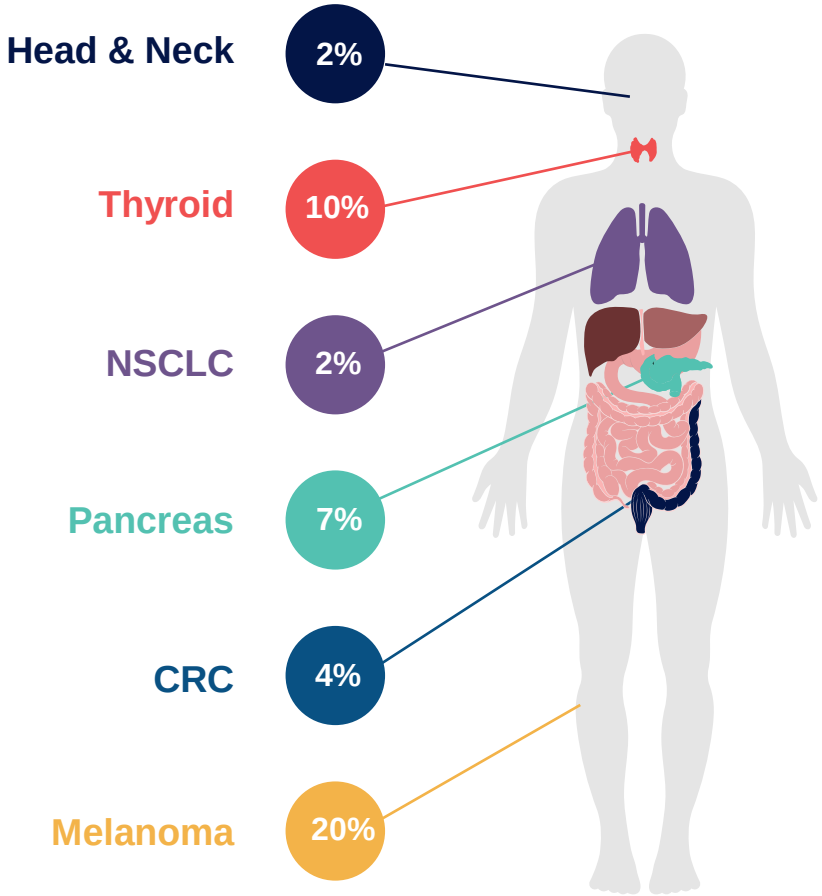
SEACRAFT-2: NRASm Melanoma

- Potential for full approval based on high unmet need and alignment on regulatory path
- Compelling Ph 1 and 2 POC data generated
- Phase 3 of naporafenib + trametinib planned to initiate in H1 2024

NRASm = NRAS mutated; POC = proof-of-concept

SEACRAFT-1: Naporafenib + trametinib has the potential to provide therapeutic benefit to patients with RAS Q61X solid tumors

Frequency of RAS Q61X across Solid Tumors



- RAS Q61X-driven tumors are promising targets for a selective pan-RAFi like naporafenib due to their **addiction to CRAF and BRAF**[1]
- RAS Q61X mutations are prevalent in tumor types with **high unmet need**
- RAS Q61X incidence in NSCLC and thyroid is **similar to the incidence of RET alterations** in those tumors[2]

1 Dorard C, et al. RAF proteins exert both specific and compensatory functions during tumour progression of NRAS-driven melanoma. Nat Comm, 2017. PMID: 28497782.
2 Lilly Product Website: https://www.retevmo.com

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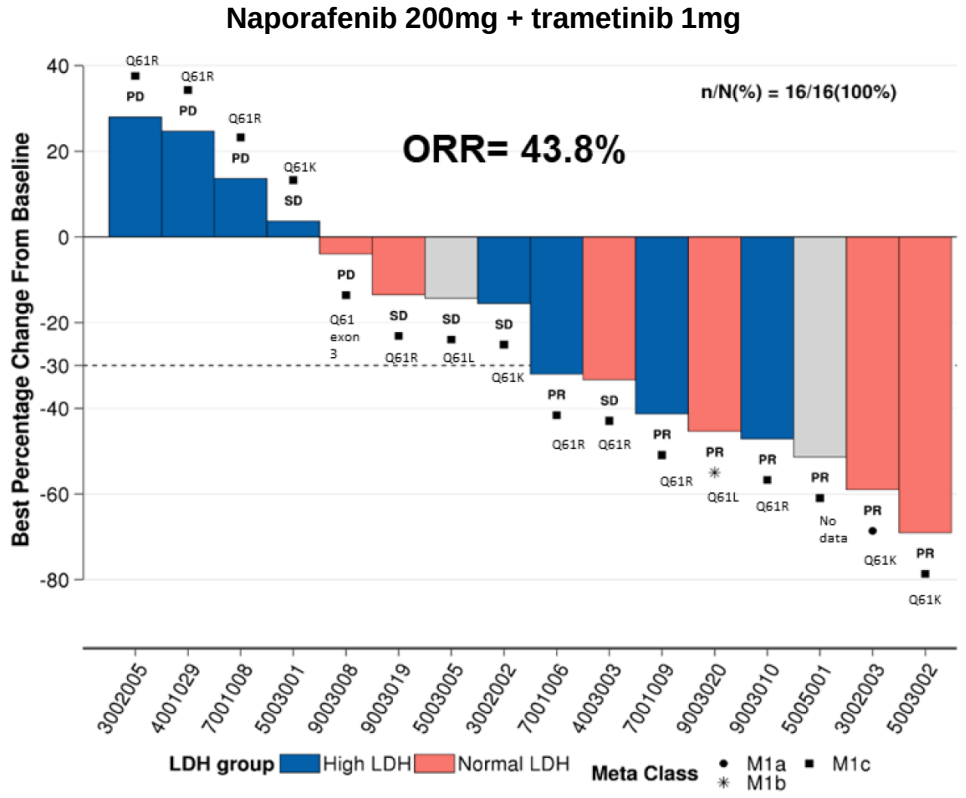
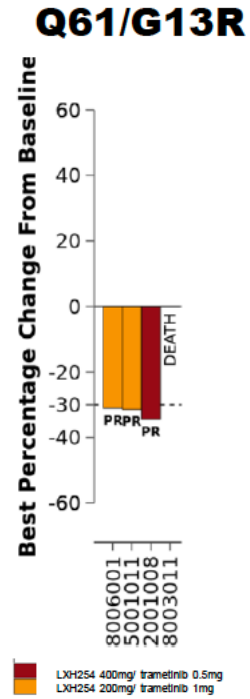
Preliminary clinical PoC in NRAS Q61X melanoma and KRAS Q61X NSCLC supports development in RAS Q61X tissue agnostic solid tumors (SEACRAFT-1)

NRASm Melanoma



- Strong antitumor activity, with confirmed ORR = 44%
- 15 out of 16 patients had confirmed codon Q61X melanoma (1 patient had no data)

KRASm NSCLC



Data cut-off date: 24 Nov 2021

- ORR in Q61/G13R mutated group (n=4) = 75%
- Confirmed/unconfirmed RECIST responses shown

Source: LXH254X2102 Ph 1b combination data from Novartis Non-Confidential Materials
PoC = proof-of-concept; ORR: overall response rate

SEACRAFT-2: Naporafenib + trametinib has the potential to be first-in-class targeted treatment for NRASm melanoma

Standard-of-Care

NRAS mutation related to aggressive disease traits

No targeted therapy approved for NRASm melanoma

Current treatment options post-IO are dismal (see figure)

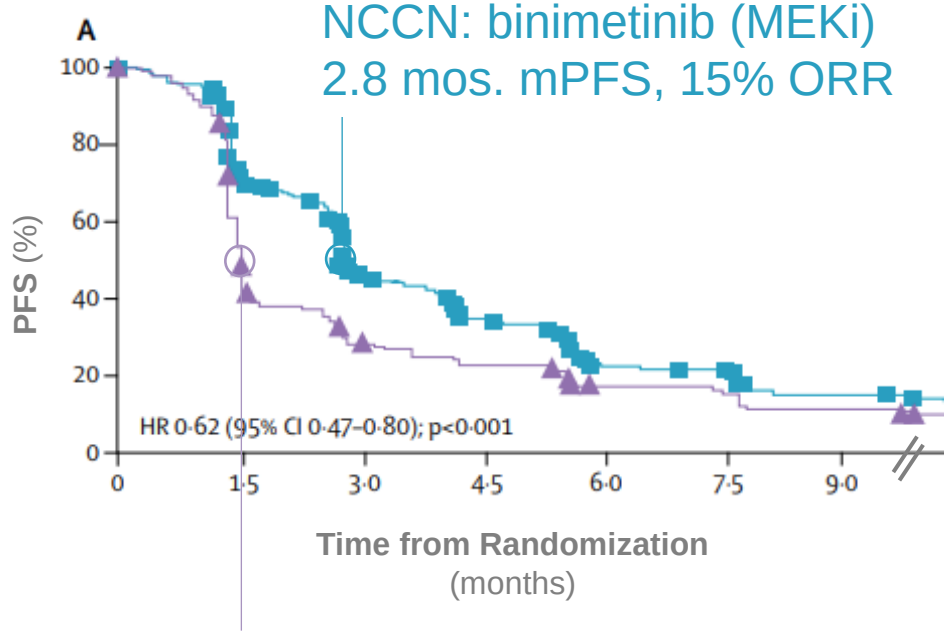
Naporafenib (pan-RAFi)

Successfully completed US, EU and UK EOP2 process for Phase 3 design

Napo + tram demonstrated compelling efficacy across Phase 1 and 2 studies (mPFS ~5 months)

FDA Fast Track Designation

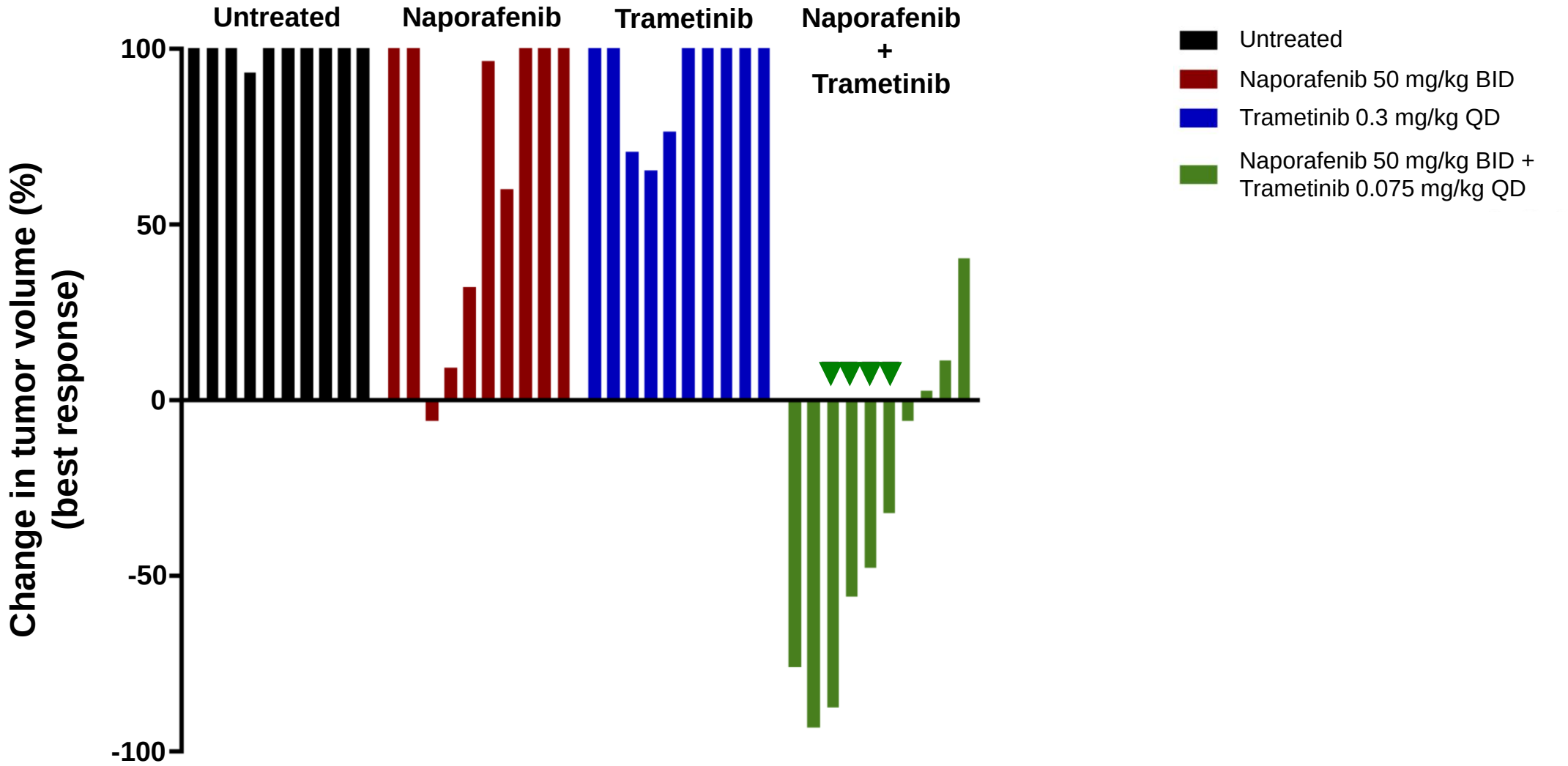
Potential to be first-to-market in NRASm melanoma



Adapted from Dummer et al. (Lancet Oncol (2017) 18:435-445)
Note: Benchmarks are most relevant for SC-2 mPFS, although study was conducted in a 1/2L setting

1 SEER Database (US) and ECIS Database (EU); AACR Genie
IO: immuno-oncology treatment; ORR: overall response rate; mPFS: median progression free survival; NCCN: National Comprehensive Cancer Network; SOC: standard of care; EOP2: end-of-Phase 2

In vivo efficacy of naporafenib and trametinib administered across 10 NRASm melanoma PDX models shows strong synergy of combination vs. either monotherapy

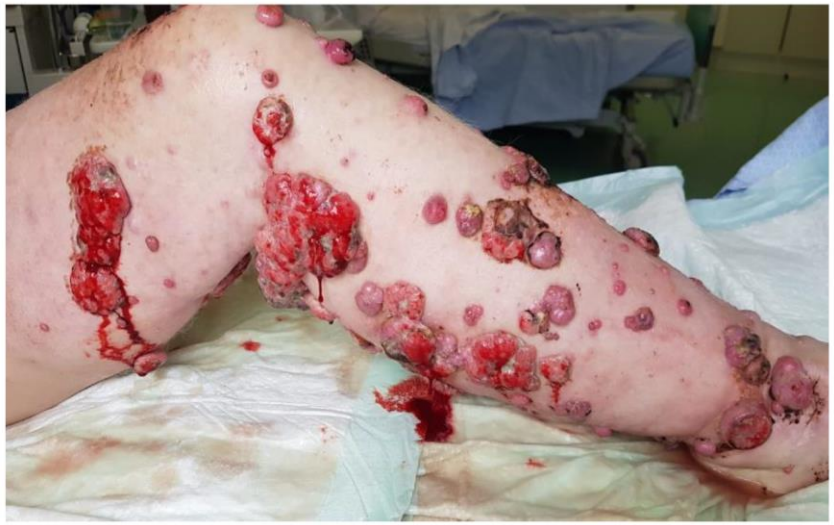


PDX = patient derived xenograft; mg = milligram; kg = kilogram; BID = twice a day; QD = once daily
Arrowheads represent models that were treated with a reduced dose of trametinib of 0.0375 mg/kg QD

NRASm melanoma case study: partial response with naporafenib + trametinib

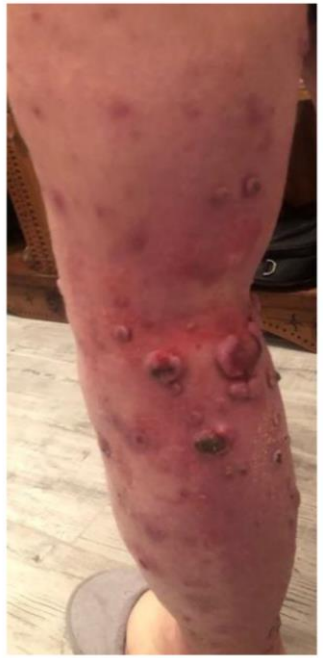
Pre-treatment

C1D1

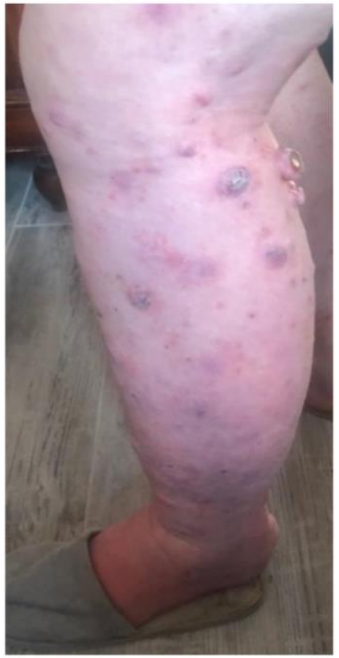


On treatment

C3D1



C6D1



Source: Novartis Non-Confidential Materials

Compelling, reproducible clinical efficacy across studies and doses shows potential to win on both SEACRAFT-2 primary endpoints (1/2)

	MEKi		SOC	Pooled Ph 1 and Ph 2[4]	
	Binimetinib[1]	Trametinib[2]	Chemo[3]	Naporafenib + Trametinib	
	45mg	2mg	1g/m² IV	200mg+1mg	400mg+0.5mg
	N=269	N=33	N=133	N=39	N=32
ORR n (%)	41 (15%)	5 (15%)	9 (7%)	12 (31%)	7 (22%)
DCR n (%)	157 (58%)	N/A	33 (25%)	28 (72%)	21 (66%)
mDOR months	6.9	*~6.9**	NE	7.4	10.2
mPFS months	2.8	*~2.8**	1.5	**5.1**	**4.9**

*Assumes trametinib efficacy is similar to published binimetinib efficacy results

US FDA Fast Track Designation: Dec 2023

- Compelling efficacy for both doses evaluated to date
- High unmet medical need for NRASm melanoma patients post-IO

PFS for napo + tram across doses exceeds PFS for approved SOC and single agent MEKi's

1 Dummer et al 2017; binimetinib is administered BID
2 Pooled analysis from the following publications: Falchook et al, 2012; Pigne et al, 2023; Salzmann et al, 2022; trametinib is administered QD
3 Dacarbazine is the approved chemotherapy in this indication
4 Ph 1 = CLXH254X2102 with DCO 4 Aug 2022; Ph 2 = CLXH254C12201 with DCO 30 Dec 2022
PFS includes both responders and non-responders
SOC: standard of care; N/A: not available; NE: not estimable; DCO: data cutoff; DCR: disease control rate; mDOR: median duration of response; ORR: objective response rate; mPFS: median progression free survival
The pooled phase 1 and phase 2 napo + tram data covers two clinical trials with different designs and inclusion criteria, which cannot be directly compared, and therefore may not be a reliable indicator of efficacy data
Due to differences between trial designs and subject characteristics, comparing data across different trials may not be a reliable indicator of data

PFS is an important metric, but OS is widely considered the gold standard in oncology trials

- Represents **length of time** patient is living after start of therapy
- **Reliable and precise measure** of efficacy among clinical trial endpoints
- Provides evidence of a drug's value in **prolonging a cancer patient's life**

> *"**OS is the ultimate endpoint**, … (after that) preventing the disease from progressing, is my second most important metric. "*
>
> - Medical Oncologist, Academic Hospital

PFS: progression-free survival; OS: overall survival

Compelling, reproducible clinical efficacy across studies and doses shows potential to win on both SEACRAFT-2 primary endpoints (2/2)

	MEKi		SOC	Pooled Ph 1 and Ph 2[4]	
	Binimetinib[1]	Trametinib[2]	Chemo[3]	Naporafenib + Trametinib	
	45mg	2mg	1g/m^2 IV	200mg+1mg	400mg+0.5mg
	N=269	N=33	N=133	N=39	N=32
mPFS months	2.8	*~2.8**	1.5	**5.1**	**4.9**
mOS months	~10-11 months (Benchmark #1: *NEMO Study*)			**~13 months**	**~14 months**
	~7 months *(Benchmark #2: Chart Review)*				
	~7 months *(Benchmark #3: C12201 BRAFm Patients[5])*				

Benchmarks most like SEACRAFT-2 patient population

Potential win on both SEACRAFT-2 primary endpoints (PFS and OS)

1 Dummer et al 2017; binimetinib is administered BID
2 Pooled analysis from the following publications: Falchook et al, 2012; Pigne et al, 2023; Salzmann et al, 2022; trametinib is administered QD
3 Dacarbazine is the approved chemotherapy in this indication
4 Ph 1 = CLXH254X2102 with DCO 4 Aug 2022; Ph 2 = CLXH254C12201 with DCO 30 Dec 2022
5 BRAF/MEK inhibitor-resistant BRAFm melanoma patients in Novartis's Phase 2 trial
SOC: standard of care; mPFS: median progression free survival; mOS: median overall survival
The pooled phase 1 and phase 2 napo + tram data covers two clinical trials with different designs and inclusion criteria, which cannot be directly compared, and therefore may not be a reliable indicator of efficacy data
Due to differences between trial designs and subject characteristics, comparing data across different trials may not be a reliable indicator of data

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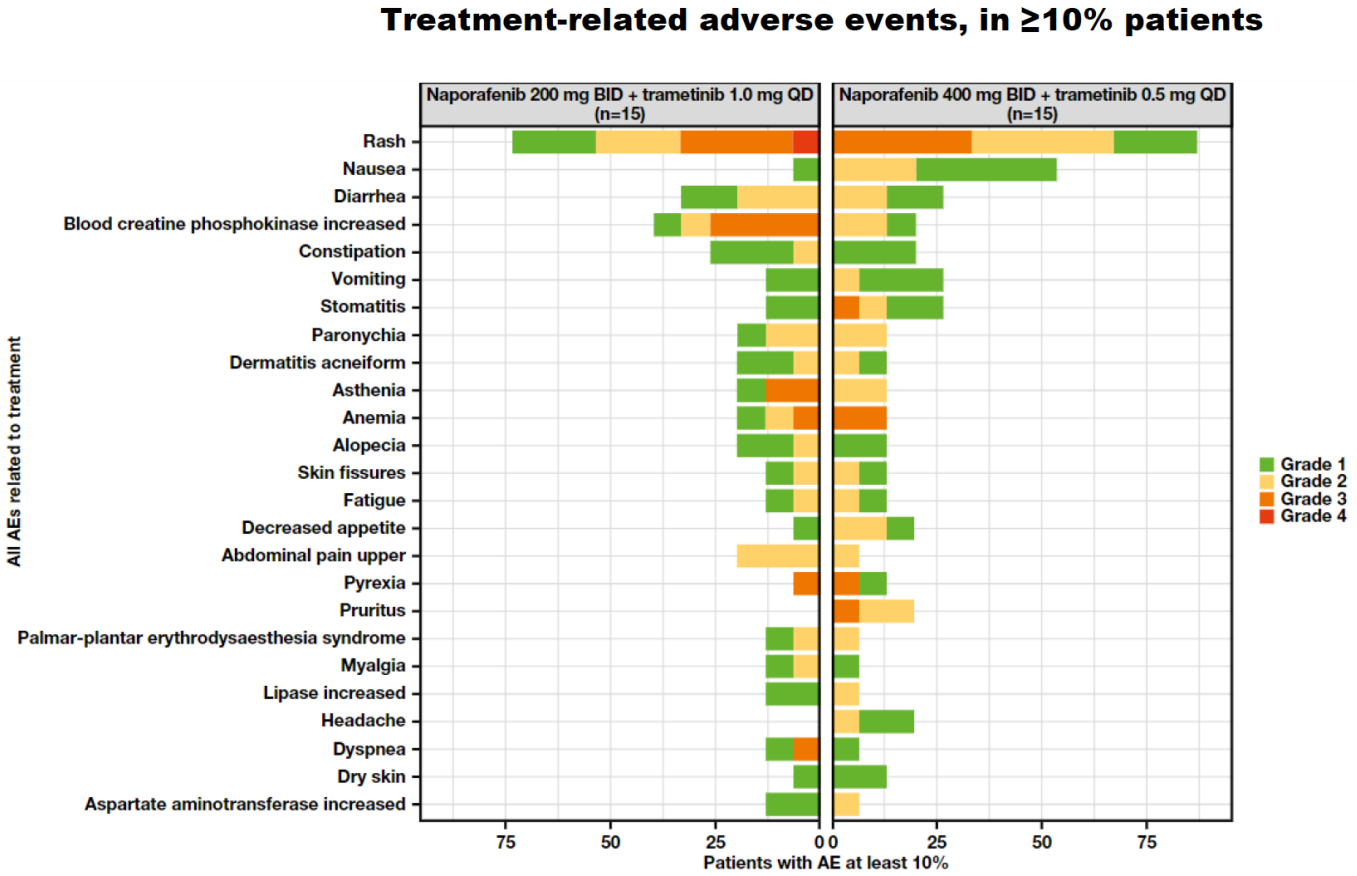
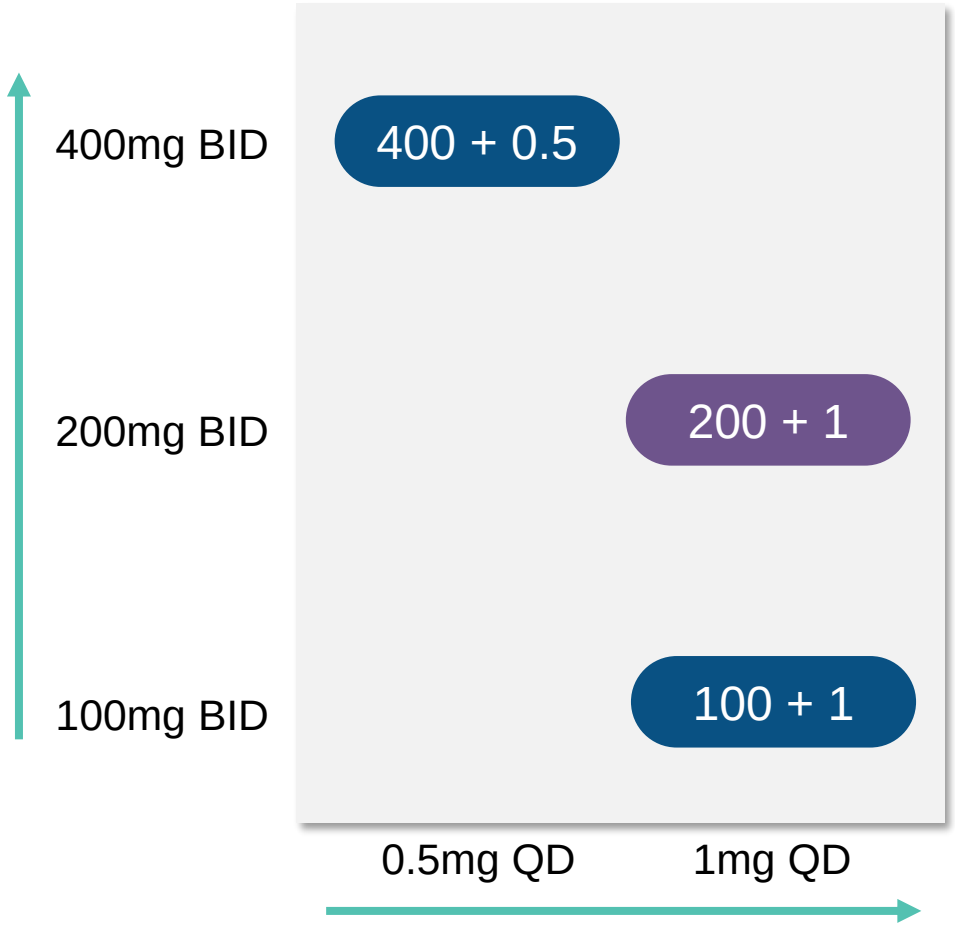
Naporafenib + trametinib demonstrated a favorable, manageable AE profile



- AE profile consistent with expected toxicities associated with RAF and MEK inhibition
  - 400+0.5 dose safe and tolerable
  - 200+1 dose safe but less tolerable without mandatory primary rash prophylaxis
- Primary prophylaxis of rash being implemented in both SC-1 and SC-2 provides opportunity to further improve safety and tolerability

AE: adverse event; BID: twice daily; QD: once daily; SC: SEACRAFT
Phase 1 data in NRASm melanoma from De Braud et al AACR 2022

Dose optimization designed to enhance combination benefit/risk profile to increase probability of regulatory success in light of Project Optimus



Data from **SEACRAFT-1** and **SEACRAFT-2** complement each other, allowing us to efficiently test the full effective dose range of naporafenib + trametinib within the two trials to optimize the benefit/risk profile in both indications of interest

SEACRAFT-1 dose

SEACRAFT-2 dose

* As part of the naporafenib + trametinib combination
BID: twice a day; QD: once a day

Pivotal Phase 3 and Phase 1b trial designs capitalize on promising efficacy signals and potentially support successful registration in multiple indications

SEACRAFT-1: RAS Q61X Solid Tumors (Single-arm Phase 1b)

Solid Tumors
Post-available therapy
RAS Q61X
(NRAS, HRAS, KRAS)

naporafenib + trametinib
(200mg + 1mg)

Study Endpoints

ORR (primary), DOR

N~30 – 100

Phase 1b designed to pivot to tissue specific or tissue agnostic Accelerated Approval path

SEACRAFT-2: NRASm Melanoma (Two-stage Phase 3)

Stage 1: Dose Optimization

Metastatic Melanoma
Post-ICI
NRASm
(Q61X and non-Q61X)

R

naporafenib + trametinib
(400mg + 0.5mg)

naporafenib + trametinib
(100mg + 1mg)

trametinib (2mg)

N~60 – 120

Stage 2: Regulatory Approval

Metastatic Melanoma
Post-ICI
NRASm
(Q61X and non-Q61X)

R

naporafenib + trametinib
(Dose selected in Stage 1*)

physician's choice
(trametinib, DTIC, TMZ)

Study Endpoints

PFS, OS (dual primary)
ORR, DOR (secondary)

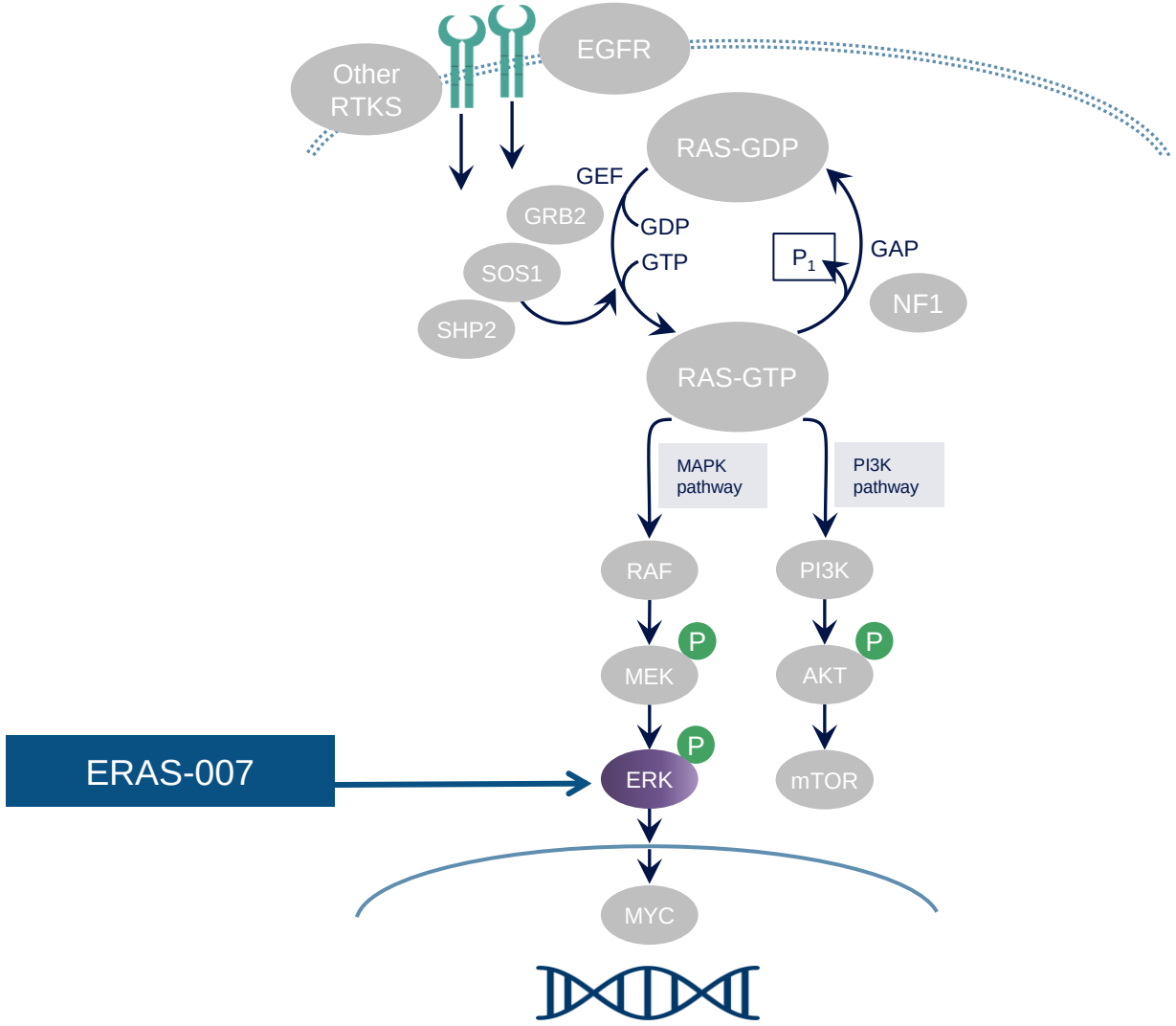
N~350

Positive PFS acceptable for potential initial approval

* Dose selection informed by data on 400+0.5 and 100+1 from SEACRAFT-2 Stage 1 as well as 200+1 from SEACRAFT-1
Note: Naporafenib dosed on a BID schedule; trametinib dosed on a QD schedule; crossover not allowed for SEACRAFT-2
ORR: overall response rate; DOR: duration of response; ICI: immune-checkpoint inhibitor; DTIC: dacarbazine; TMZ; temozolomide; PFS: progression-free survival; OS: overall survival

ERASCA

ERAS-007 ERKi could address unmet needs in ~45k patients annually in the US and Europe



Tumor Type	Addressable Patient Pop.
BRAF V600E CRC	45,000

We believe ERAS-007 is the most potent ERK inhibitor in development, with a uniquely longer target residence time

ERAS-007 was designed to be a **potent**, **selective,** reversible, oral inhibitor of ERK1/2

Assay Type	Assay	ERAS-007 IC50 (nM)
Biochemical	ERK1	2
	ERK2	2
Cell-based mechanistic (HT-29)	pRSK	7

ERAS-007 had longer target residence time vs. other ERKi's, which may allow for longer intervals between doses in patients

Compound	k_{off} (s^{-1})	Residence Time (min)
ERAS-007	**0.30×10^{-4}**	**550**
Ulixertinib	10.1×10^{-4}	16
Ravoxertinib	13.9×10^{-4}	12

HERKULES-3: ERAS-007 + EC is a potential best-in-class treatment for patients with BRAF V600E CRC

Incidence

~45,000 patients[1] diagnosed with BRAF V600E CRC in the US and Europe annually

Standard-of-Care

Encorafenib + cetuximab (EC) has improved SOC for patients but prognosis is still poor

Durability is largely limited by treatment resistance

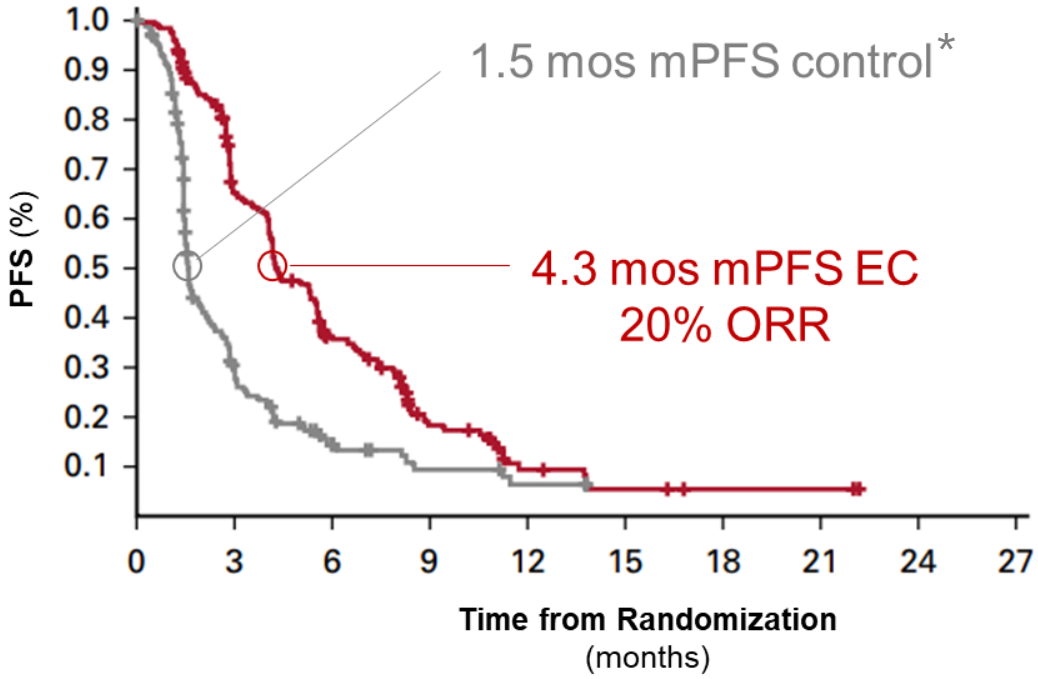
Triplet of binimetinib (MEKi) + EC only marginally improved clinical efficacy

ERAS-007 (ERKi)

Inhibiting the terminal RAS/MAPK pathway node has potential to shut down oncogenic signaling and prevent reactivation

Early signals of clinical efficacy in EC-naïve BRAFm CRC

Clinical data reinforce ability to safely combine ERAS-007 with multiple agents



Adapted from Tabanero et al. (JCO (2021) 4: 273-284)
*Control arm: investigators' choice of either cetuximab + irinotecan or cetuximab + FOLFIRI

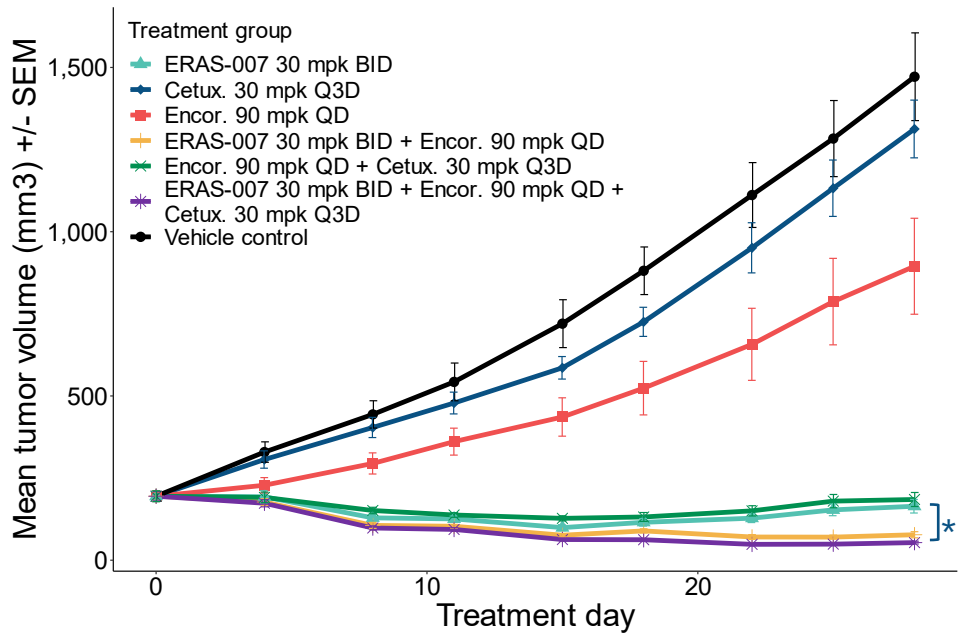
1 SEER Database (US) and ECIS Database (EU); AACR Genie
ORR: overall response rate; mPFS: median progression free survival

ERAS-007 + EC in BRAFm CRC:

Robust in vivo combination activity in BRAF V600E CRC

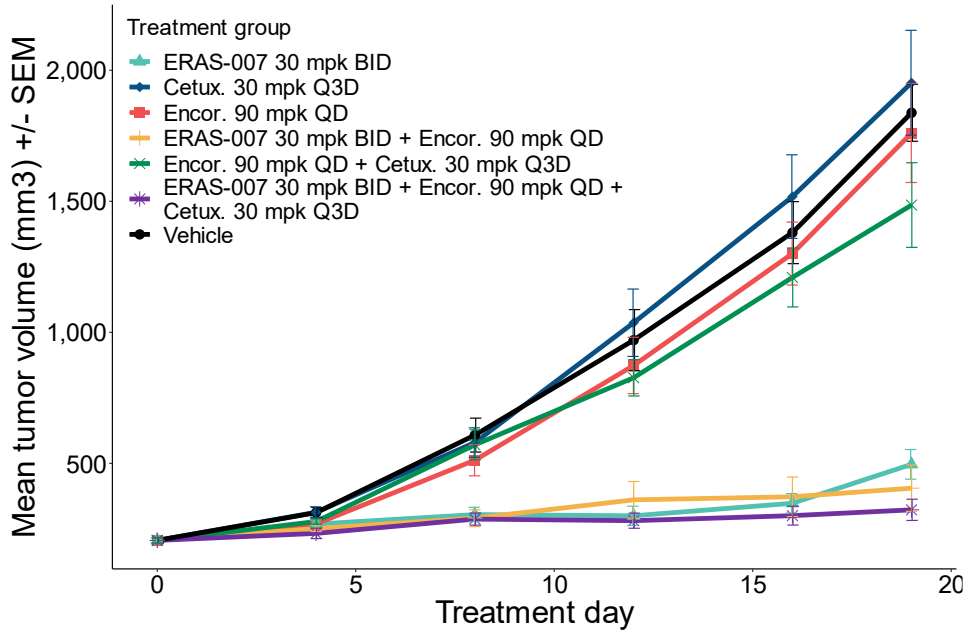
TGI in WiDr (BRAF V600E CRC)

EC-sensitive CDX Model



TGI in RKO (BRAF V600E CRC)

EC-resistant CDX Model

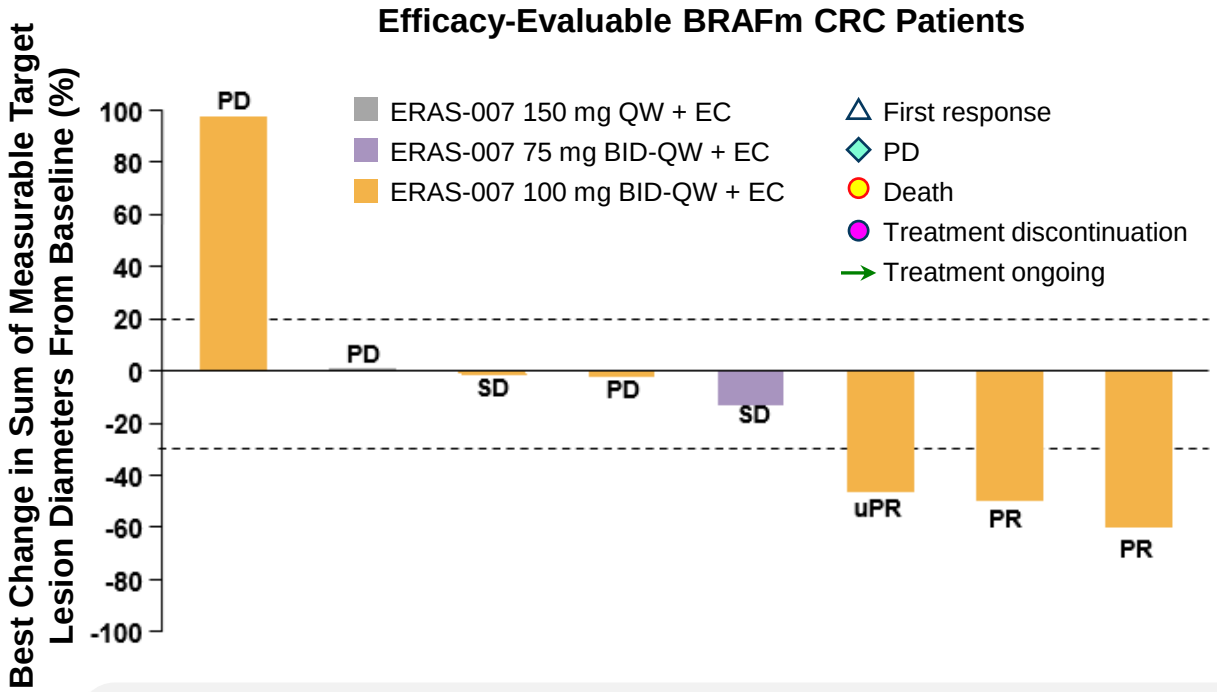


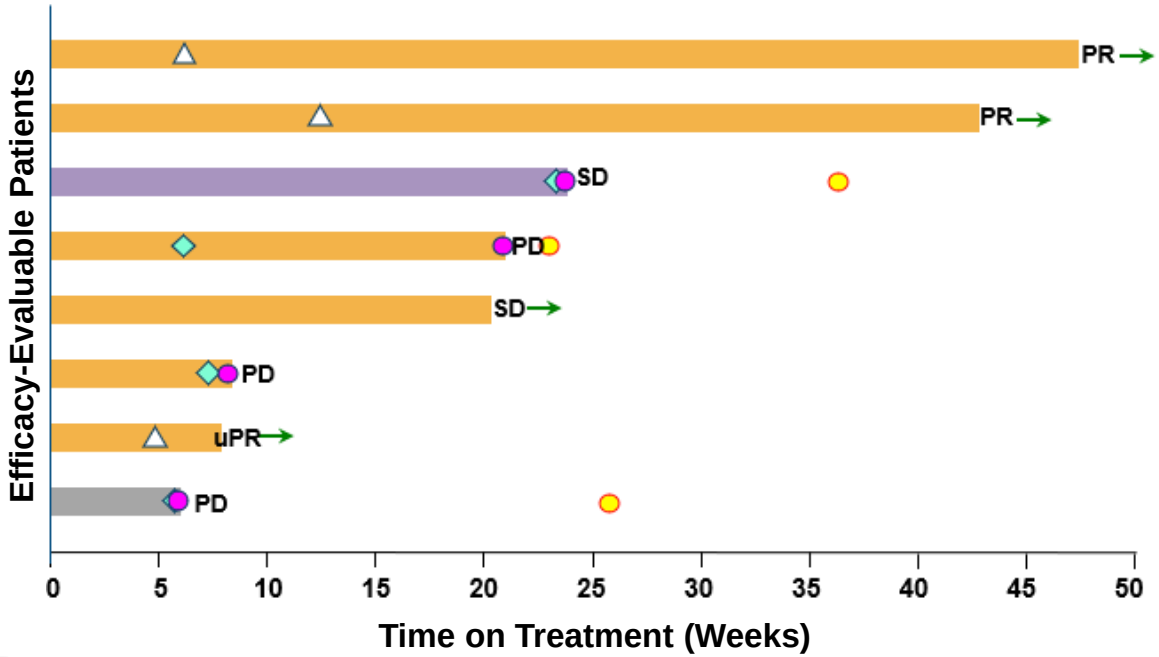
- ERAS-007 60 mpk QD dose showed similar activity to 30 mpk BID, either as a mono or combo Tx with encor. +/- cetux.
- ERAS-007 combinations were generally well tolerated across the tested models as demonstrated by the minimal percentage body weight changes observed.

*p-value < 0.01

TGI = tumor growth inhibition; Cetux. = cetuximab; Encor. = encorafenib; EC = encorafenib plus cetuximab (BEACON regimen); mpk = milligrams per kilogram; BID = twice a day; Q3D = once every 3 days; QD = once daily

Meaningful activity in EC-naïve BRAFm CRC supports initial focus on and dose expansion of this patient segment





In **EC-naïve BRAFm CRC** patients <u>at the highest dose tested</u> (100 mg BID-QW):

- 50% (3/6) response rate (2 confirmed PR, 1 uPR[1])
- 67% (4/6) disease control rate[2]
- Both confirmed responders were still on treatment as of the data cutoff date with duration of exposure >40 weeks
  - BEACON mDOE 19 weeks[3]

In **EC-naïve BRAFm CRC** patients <u>across all dose levels</u>:

- 38% (3/8) response rate
- 63% (5/8) disease control rate

Data cutoff as of 21MAY2023
Response on the bar represents the best overall response based on investigator assessments.

1 Per site communication, the patient with uPR was still in response at the subsequent scan (26MAY2023), which was conducted 25 days after the first post-baseline scan

2 Disease control rate (DCR) = CR + PR + SD; uPR is included

3 Median duration of exposure (mDOE) as reported in Kopetz et al. NEJM 2019

EC: encorafenib + cetuximab; PD: progressive disease; CR: complete response; PR: confirmed partial response; uPR: unconfirmed partial response; SD: stable disease; mDOE: median duration of exposure

ERAS-007 QW: ERAS-007 oral once a week / ERAS-007 BID-QW: ERAS-007 oral twice a day on a single day each week

ERAS-007 + EC was generally well tolerated with primarily Grade 1 or 2 TRAEs observed

Treatment-related* Adverse Events Reported in ≥ 20% of All Patients

(arranged by descending frequency in the ALL Any Grade column)

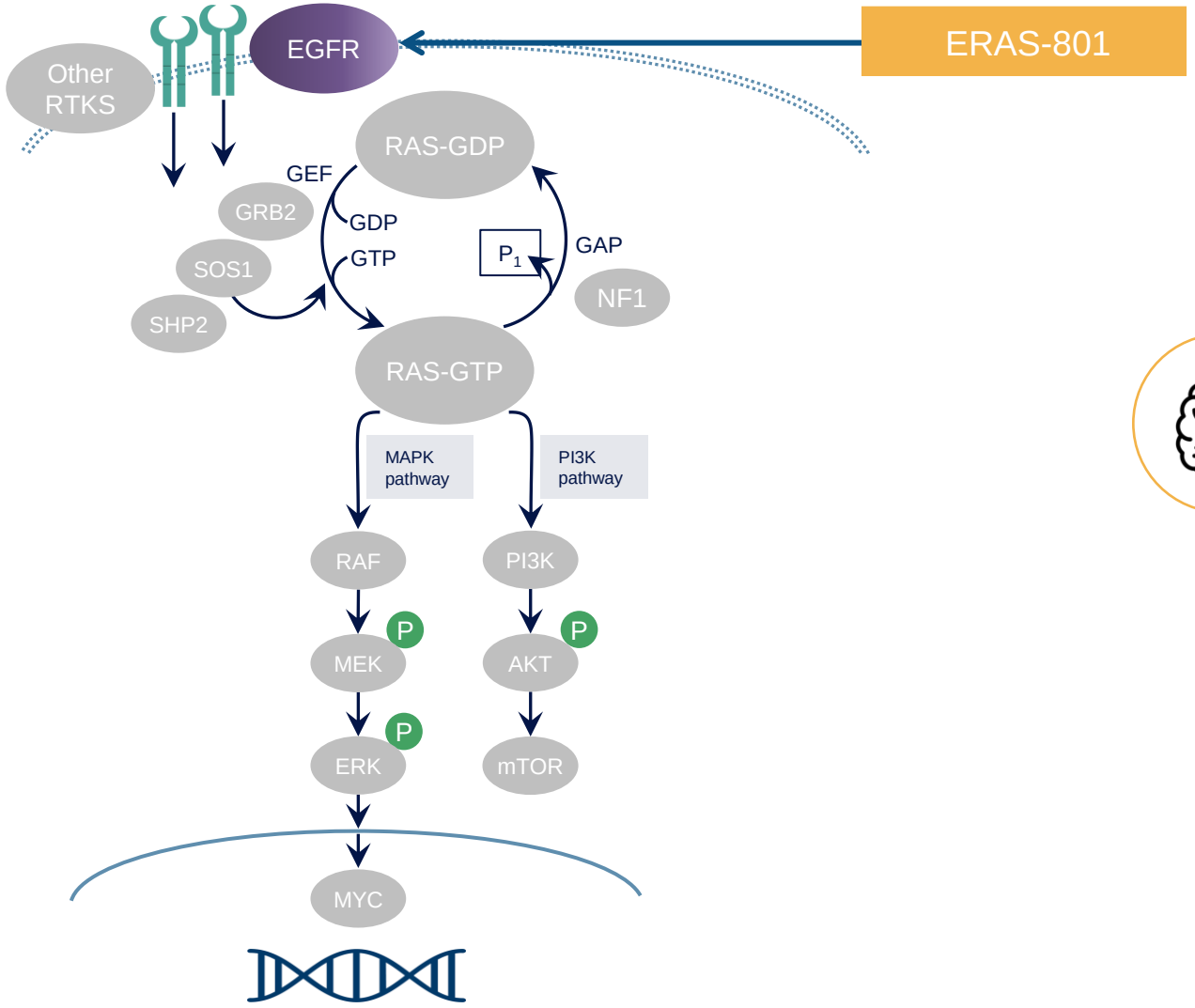
ERAS-007 Dose + EC[a]	150 mg QW[b] (n = 2)		75 mg BID-QW[c] (n = 6)		100 mg BID-QW[c] (n = 12)		ALL (n = 20)	
Preferred Term	Any Grade n (%)	Grade ≥ 3 n (%)	Any Grade n (%)	Grade ≥ 3 n (%)	Any Grade n (%)	Grade ≥ 3 n (%)	Any Grade n (%)	Grade ≥ 3 n (%)
Fatigue	1 (50)	1 (50)	3 (50)	0	3 (25)	0	7 (35)	1 (5)
Diarrhea	0	0	2 (33)	0	4 (33)	0	6 (30)	0
Headache	0	0	3 (50)	0	3 (25)	1 (8)	6 (30)	1 (5)
Anaemia	1 (50)	0	2 (33)	1 (17)	2 (17)	1 (8)	5 (25)	2 (10)
Nausea	0	0	3 (50)	0	2 (17)	0	5 (25)	0
Subretinal fluid	0	0	1 (17)	0	3 (25)	0	4 (20)	0
Vomiting	1 (50)	0	2 (33)	0	1 (8)	0	4 (20)	0

- No Grade 4 or 5 TRAEs were observed
- ERAS-007 100 mg BID-QW dose is being expanded in combination with approved doses of EC to assess signals of efficacy in patients with EC-naïve BRAF V600E mCRC

Data cutoff 23MAR2023 / * Related to ERAS-007

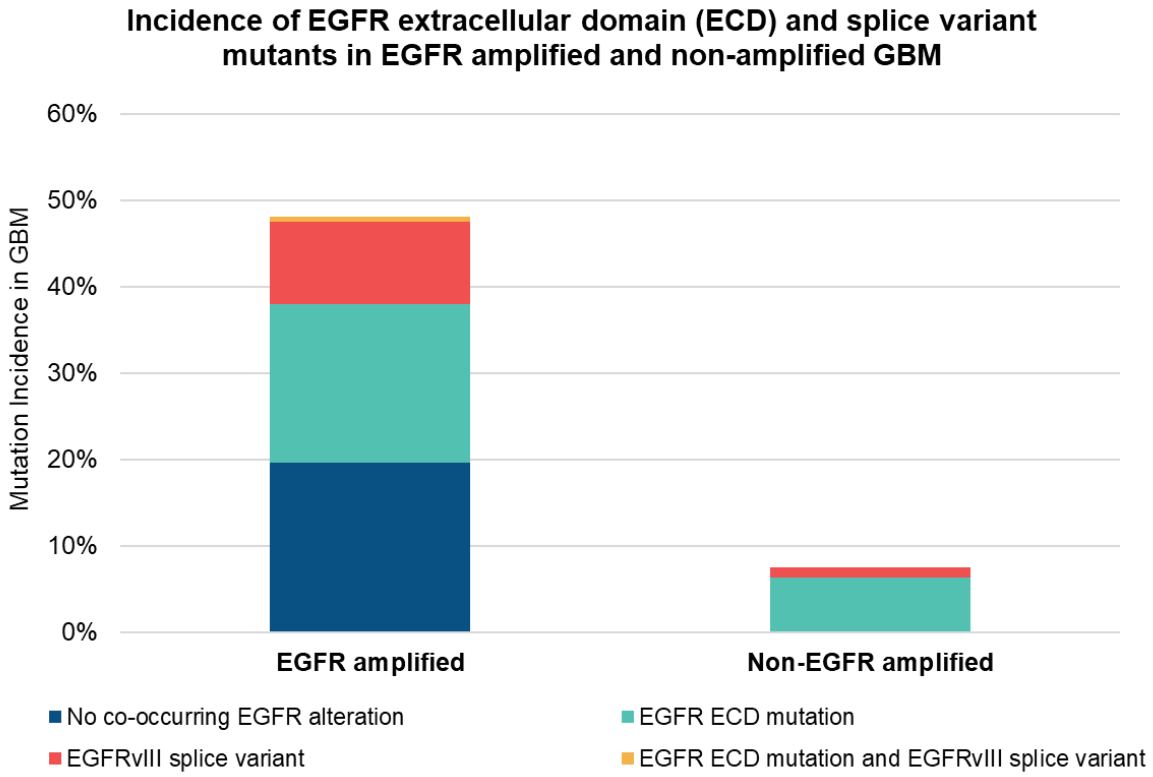
[a]EC: encorafenib 300 mg oral daily + cetuximab 500 mg/m^2 intravenous infusion once every 2 weeks [b]ERAS-007 QW: ERAS-007 oral once a week. [c]ERAS-007 BID-QW: ERAS-007 oral twice a day on a single day each week

ERAS-801 EGFRi could address high unmet need in 37k patients in US and EU



Tumor Type	Addressable Patient Pop.
Glioblastoma multiforme	37,000

Poor activity of legacy EGFRi in GBM due to minimal activity against GBM-specific EGFR alterations and poor CNS penetration

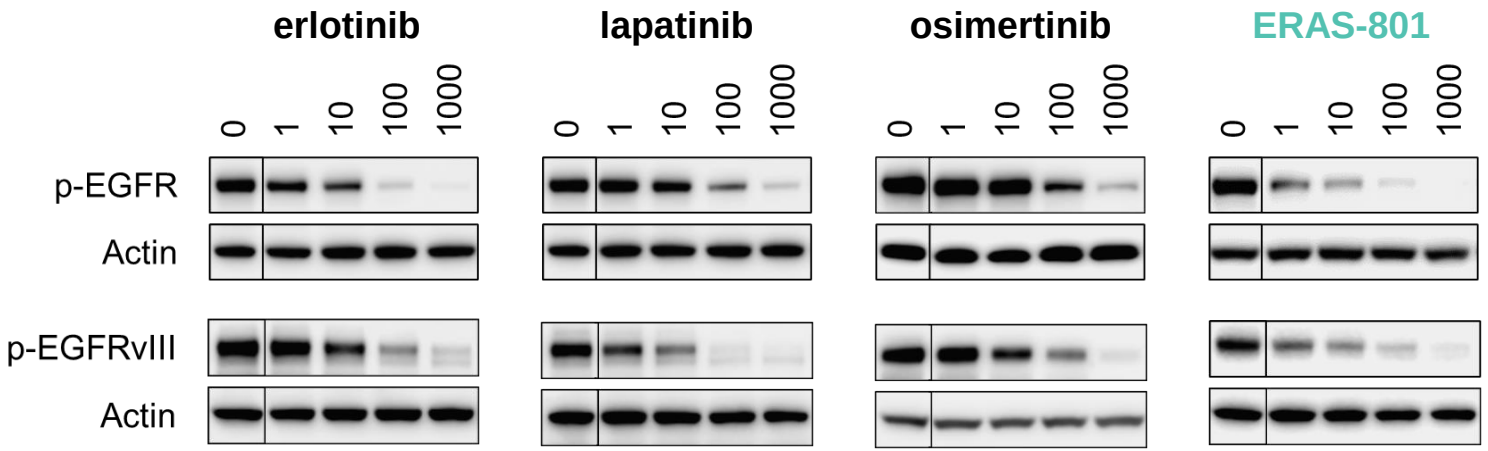


Therapy (brain penetration %)	Clinical Trial Results*: NSCLC/BrCa	Clinical Trial Results: GBM
Erlotinib (8%)	Recurrent NSCLC: Improved PFS and OS vs. chemo (Ph 3)	Failed (Ph 2)
Lapatinib (0.1%)	Recurrent HER2 BrCa: Improved PFS vs. chemo (Ph 3)	Failed (Ph 2)
Gefitinib (1.1%)	1L NSCLC: Improved PFS and OS vs. chemo (Ph 3)	Failed (Ph 2)
Afatinib (0.7%)	1L NSCLC: Improved PFS vs. chemo (Ph 3)	Failed (Ph 2)

*For illustrative purposes only and not a head-to-head comparison. Differences exist between trial designs and subject characteristics and caution should be exercised when comparing data across studies.

TCGA *Cell*, 2013
GBM: glioblastoma; CNS: central nervous system; PFS: progression free survival; OS: overall survival

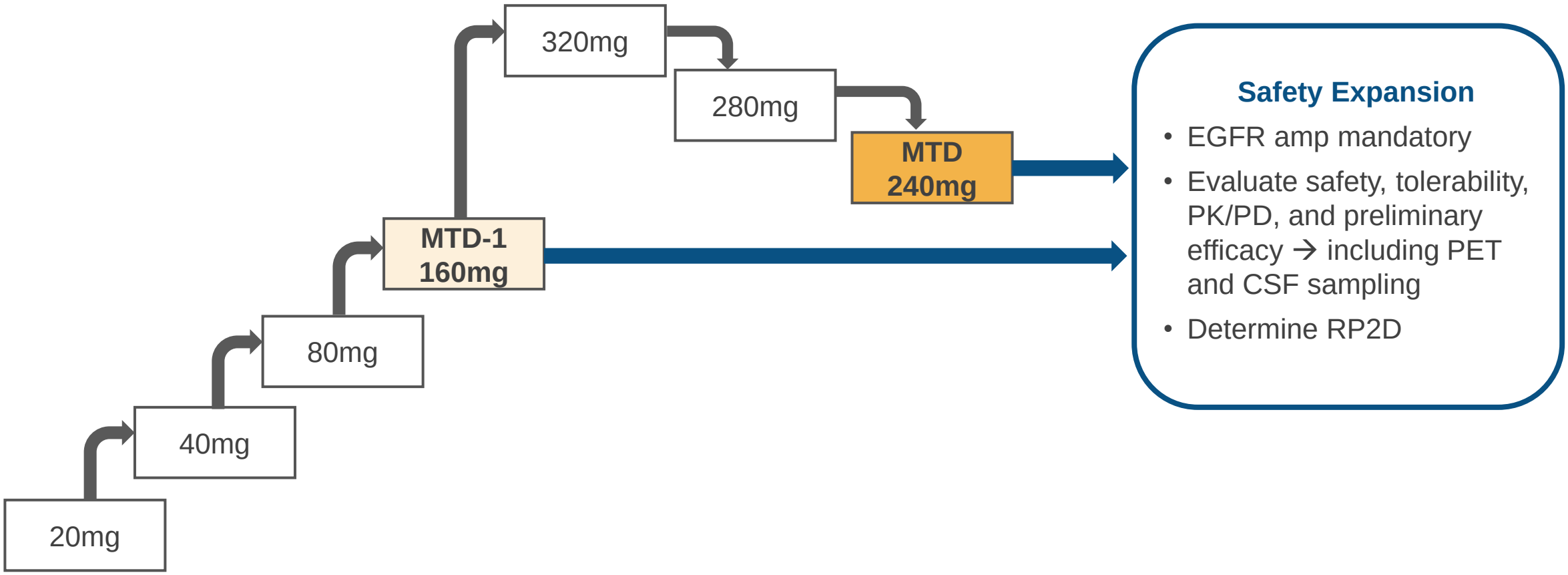
ERAS-801, a potent EGFRvIII/wt inhibitor with a $K_{p,uu}$ over 4-fold higher than approved EGFR inhibitors, was specifically designed to inhibit EGFR in GBM



Compound	Company	K_p, brain (mouse)	$K_{p,uu}$, brain (mouse)[1]
ERAS-801	**Erasca[2]**	**8.2**	**1.3**
osimertinib	AstraZeneca	0.99	0.29
afatinib	Boehringer Ingelheim	0.25	0.05
erlotinib	Genentech	0.06	0.13
gefitinib	AstraZeneca	0.36	0.10
dacomitinib	Pfizer	0.61	0.49

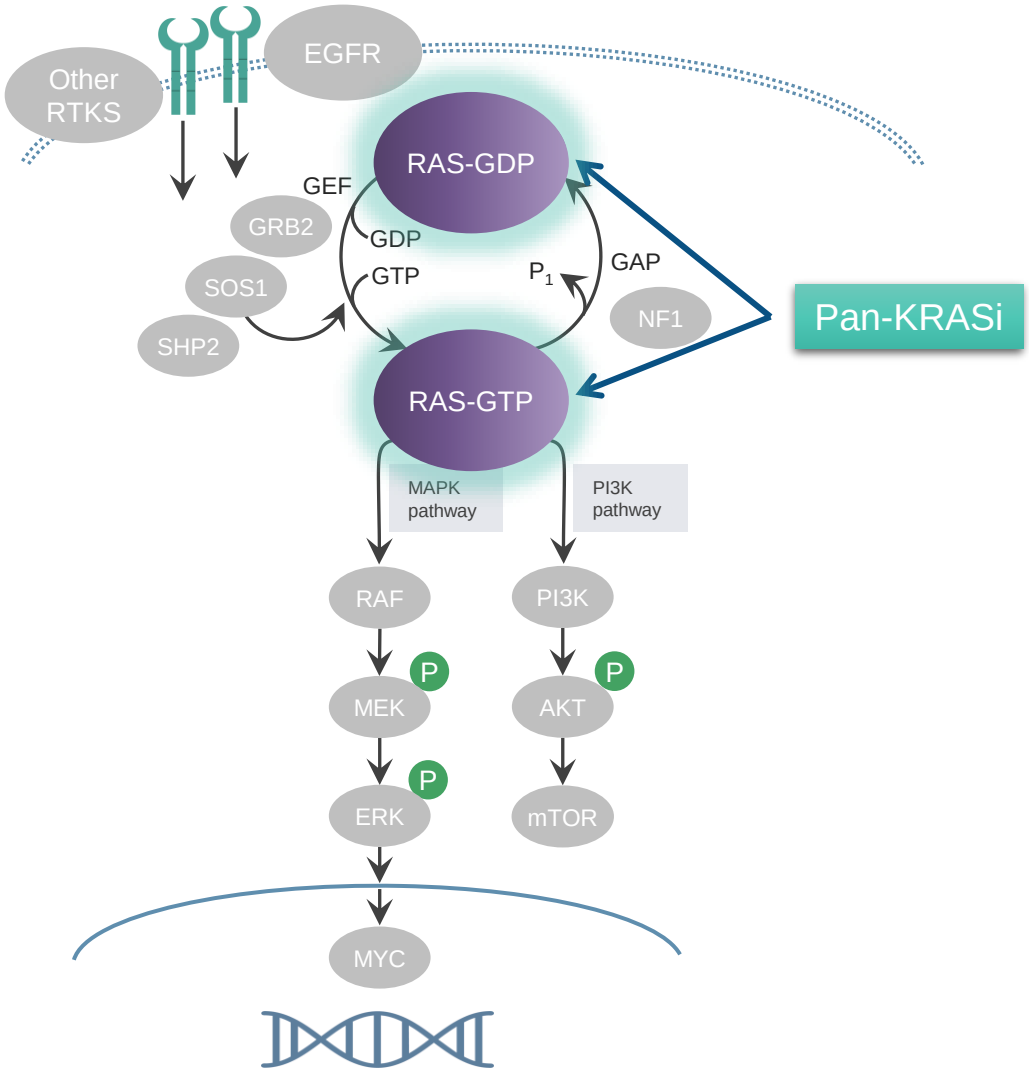
1 $K_{p,uu}$ is a measure of the ratio of unbound brain concentration to unbound plasma concentration
2 Updated PK data generated by Erasca
Kim M, et al. Brain Distribution of a Panel of Epidermal Growth Factor Receptor Inhibitors Using Cassette Dosing in Wild-Type and Abcb1/Abcg2-Deficient Mice. Drug Metab. Dispos., 2019. PMID: 30705084

THUNDERBBOLT-1: Dose escalation cohorts



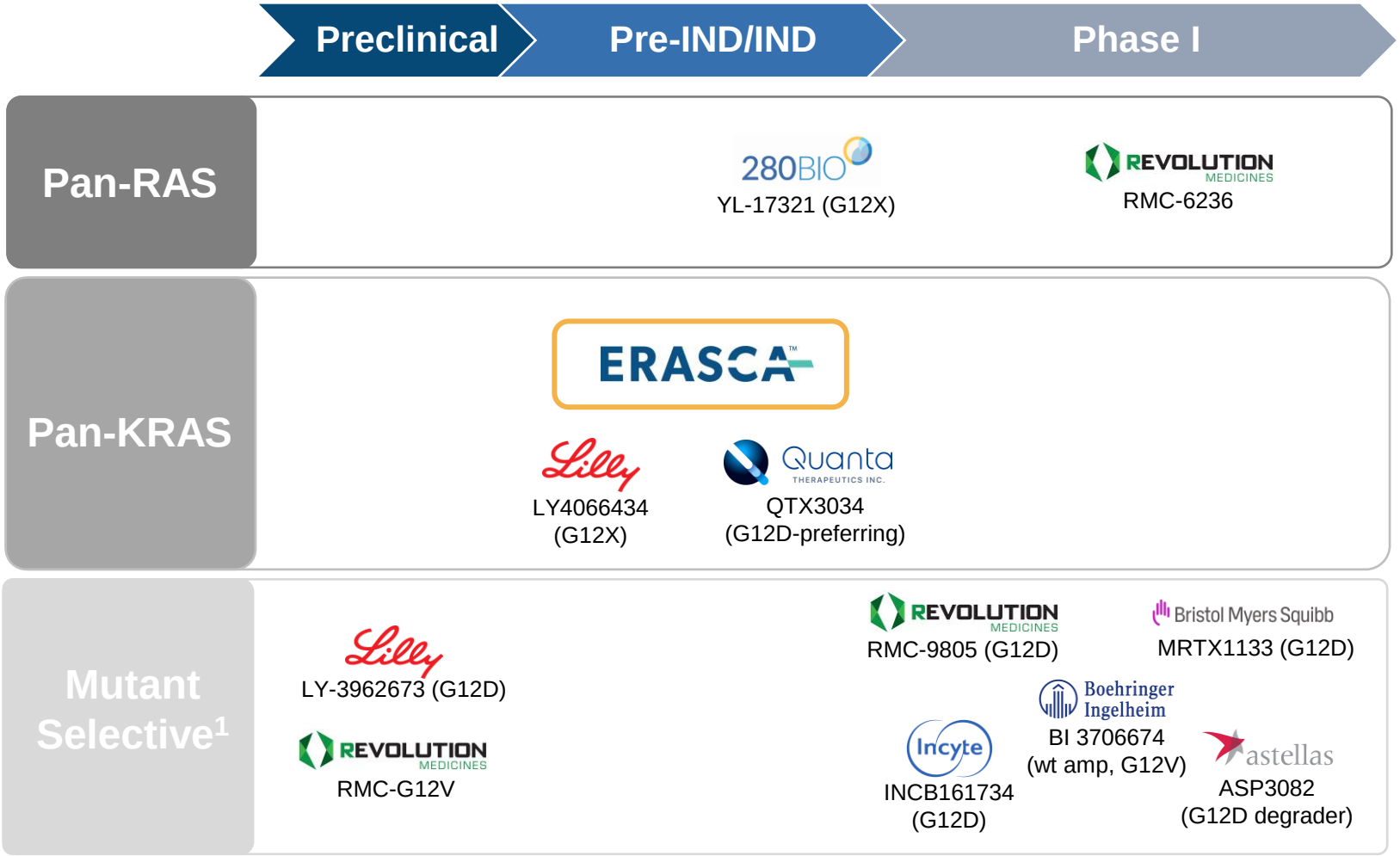
Clinicaltrials.gov: NCT05222802
Note: ERAS-801 dosed QD
MTD: maximum tolerated dose; MTD-1 (aka, MTD-minus-1): one dose level below MTD; QD: once daily; amp: amplified; RP2D: recommended Phase 2 dose

Erasca is exploring internal and external opportunities to develop a potent, KRAS-selective and orally bioavailable pan-KRAS inhibitor



- Approach inhibits KRAS by **targeting the S-IIP**
- Promising approach is designed to **target all G12X mutations**, such as G12D and G12V, **as well as G13X**
- Pan-KRAS drugs could provide **deep and durable target inhibition** with low risk of HRAS/NRAS wildtype mediated toxicity
- Pan-KRAS drugs have the **potential to address a broad patient population** including patients where:
  - Mutant-selective KRAS drugs are unavailable
  - Both **mutant and wildtype forms** of KRAS can **contribute to oncogenic signaling**
- Selectivity for KRAS over HRAS/NRAS is desired for **improved tolerability** relative to pan-RAS approach

RAS targeting landscape drives importance of identifying development candidates with first-in-class or best-in-class potential



Comments on Class

- ⊕ Encouraging preliminary clinical data
- ⊖ Tolerability, combinability may be challenging

- ⊕ Opportunity for greater therapeutic window by specifically targeting KRAS
- ⊕ More straightforward mechanism via KRAS Switch II pocket binding mode
- ⊖ Translation to clinical efficacy TBD

- ⊕ Potential for greater potency against specific mutation of interest
- ⊖ Oral bioavailability and stability have proven challenging for G12Di
- ⊖ Susceptible to resistance mediated by wildtype RAS of the same isoform

Note: Select coopetitors shown; list is not intended to be exhaustive

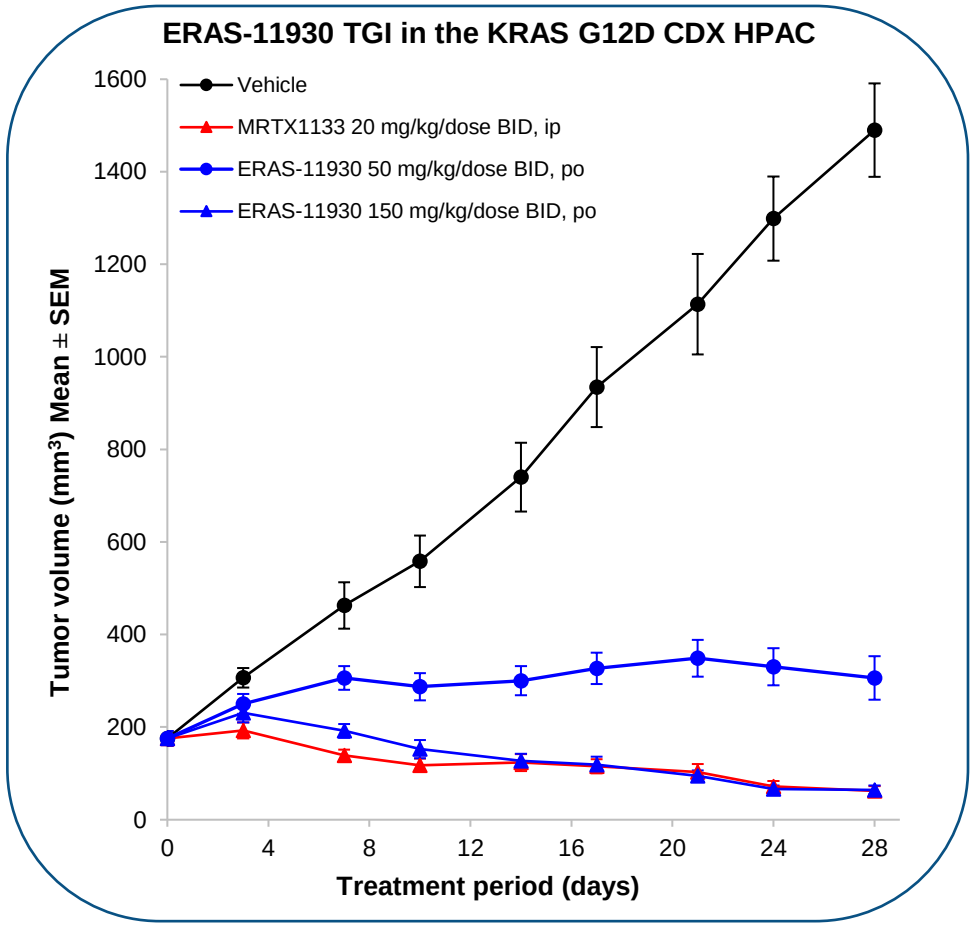
[1] Mutant selective beyond KRAS G12C inhibitors

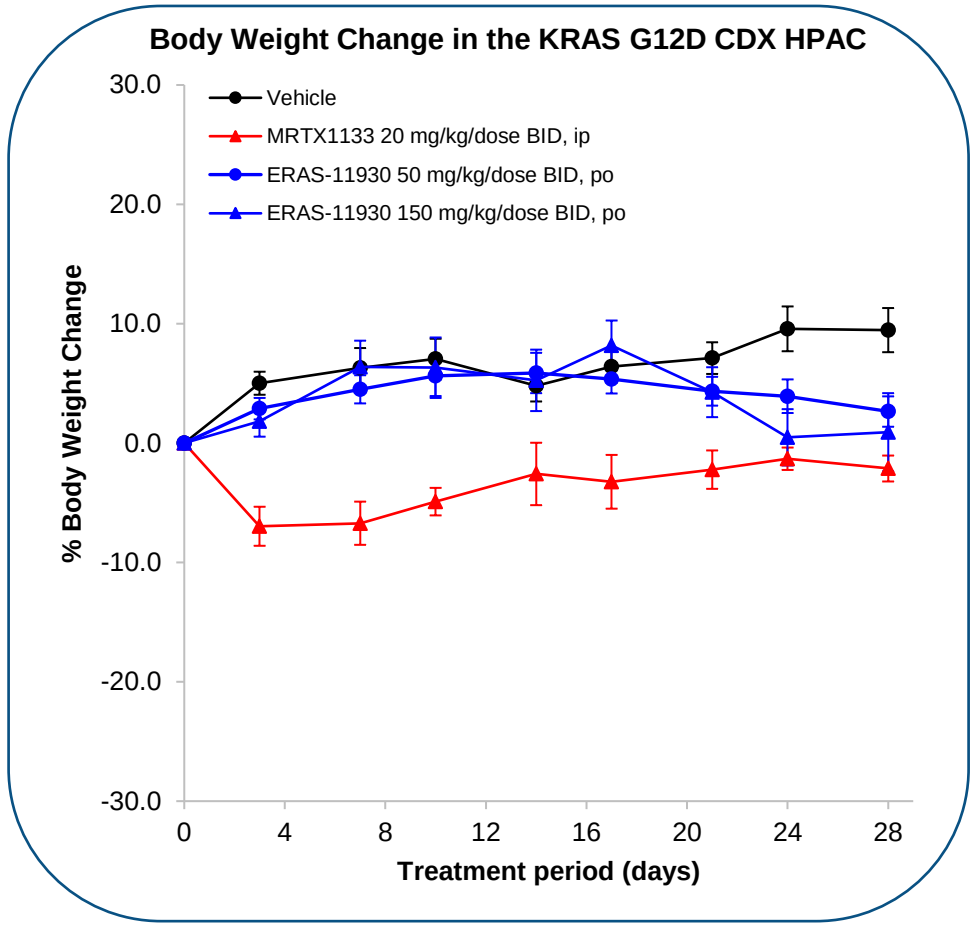
Erasca's internal pan-KRASi's showed promising in vitro potency and in vivo PK

Assay		Erasca's Internal pan-KRAS Compounds				Coopetitors' Compounds		
		ERAS-12943	ERAS-12879	ERAS-12056	ERAS-11930	MRTX1133	RMC-6236	Loxo LY-4066434
Inhibitor Class		S-IIP targeting	S-IIP targeting	S-IIP targeting	**S-IIP targeting**	S-IIP targeting	Molecular Glue (Ras and Cyclophilin A)	S-IIP targeting
Target(s)		Pan-KRAS	Pan-KRAS	Pan-KRAS	**Pan-KRAS**	KRAS G12D Selective	Pan-RAS	Pan-KRAS
KRAS G12D Kd by SPR (nM)		0.0080	0.019	0.24	**0.012**	~0.0002	Not relevant for S-IIP inhibitor comparisons	0.44
KRAS WT Kd by SPR (nM)		0.062	0.39	0.35	**0.19**	0.31	Not relevant for S-IIP inhibitor comparisons	0.26
KRAS G12D AsPC-1	4/24-hour pERK IC_{50} (nM)	1.5 / 3.6	5.4 / 6.5	6.7 / 48	**4 / 20**	6	0.4-3*	13
	5-day 3D CTG IC_{50} (nM)	1.9	5.4	17.7	**8.2**	20	1-27*	29
KRAS G12V SW620	4-hour pERK IC_{50} (nM)	Queued	2.3	8.0	**2.4**	ND	0.4-3*	8.5
	5-day 3D CTG IC_{50} (nM)	Queued	29	24.2	**20**	ND	1-27*	30
% F (PO dose)		14 (40 mg/kg)	32 (50 mg/kg)	12 (50 mg/kg)	**13.5 (50 mg/kg)**	0.2 (10 mg/kg)	24-33 (10 mg/kg)	43 (30 mg/kg)
PK Species		mouse	mouse	mouse	**mouse**	rat	mouse	mouse

* range in G12X cell line panel

Erasca's pan-KRASi showed promising in vivo activity in KRAS G12D PDAC CDX model





- MRTX1133 sets a high bar since it is the most potent S-IIP binding, G12D selective clinical compound we have observed
- ERAS-11930 showed dose dependent TGI, achieving tumor regression at the orally administered 150 mg/kg BID dose
- ERAS-11930 achieved comparable tumor regression relative to MRTX1133 at its MTD dose (20 mg/kg BID, IP)
- Mouse mortality observed when MRTX1133 was administered at higher doses (e.g., 30 mg/kg BID, IP)

Anticipated key milestones and clinical trial readouts

Program *Mechanism*	**Trial Name** *Indication* *(Combo partner if applicable)*	**Anticipated Milestone**
Naporafenib *Pan-RAF inhibitor*	**SEACRAFT-1** *RAS Q61X Solid Tumors* *(+ trametinib)*	• **Q2 2024 – Q4 2024:** Ph 1b combination data[1]
	SEACRAFT-2 *NRASm Melanoma* *(+ trametinib)*	• **H1 2024:** Ph 3 pivotal trial initiation • **2025:** Ph 3 stage 1 randomized dose optimization data[1]
ERAS-007 *ERK1/2 inhibitor*	**HERKULES-3** *EC-naïve BRAFm CRC* *(+ encorafenib and cetuximab)*	• **H1 2024:** Ph 1b combination data[1]
ERAS-801 *CNS-penetrant EGFR inhibitor*	**THUNDERBBOLT-1** *Glioblastoma*	• **2024:** Ph 1 monotherapy data[1]

[1] Data to include safety, pharmacokinetics (PK), and efficacy at relevant dose(s) in relevant population(s) of interest

Compelling investment thesis

EXPERIENCED TEAM WITH TRACK RECORD OF SERIAL SUCCESSES

Seasoned drug developers who have advanced multiple programs from discovery to IND to global approvals

WORLD-CLASS SCIENTIFIC ADVISORY BOARD

Includes leading pioneers in: KRAS (Shokat, UCSF), SHP2 (Blacklow, HMS), ERK (Corcoran, MGH), RAS/MAPK pathway (Rodriguez-Viciana, UCL; Cichowski, HMS), precision oncology (Demetri, DFCI), and biopharma (Varney, Genentech)

BROAD PORTFOLIO TO ERASE CANCER

We have built one of the deepest pipelines in the industry to comprehensively shut down the RAS/MAPK pathway, with the potential to address unmet needs in over 5 million patients globally

THREE CLINICAL-STAGE COMPOUNDS

Differentiated profiles including naporafenib, a Phase 3-ready pan-RAF inhibitor for NRASm melanoma and Q61X tissue agnostic solid tumors, ERAS-007 ERK inhibitor, and ERAS-801, a CNS-penetrant EGFR inhibitor for GBM

MULTIPLE POTENTIAL NEAR-TERM AND LONG-TERM VALUE DRIVERS

Focused clinical development plan with multiple clinical readouts in 2024 and beyond and a strong research engine to drive first-in-class or best-in-class compounds into the clinic

ERASCA

ERASCA

Thank You!

~5.4m lives at stake annually worldwide with RAS/MAPK pathway alterations; 70+% of unmet needs are “blue oceans” with no approved targeted therapies

New cases estimated worldwide per annum (thousands; numbers may not add up due to rounding)

Alterations	GBM	HNSCC	NSCLC	CRC	Melanoma	PDAC	Other solid tumors	US	EU	ROW	Global
EGFR*	125	513	184	338	-	-	-	74	209	876	1,159
NF1	25	58	98	34	33	1.9	434	75	158	451	684
KRAS G12C	-	2.8	240	57	-	5.1	45	36	82	232	349
KRAS G12D	0.2	4.7	68	238	0.5	178	201	65	171	455	691
N/H/KRAS Q61X	0.4	23	35	80	69	32	155	51	105	239	394
Other K/N/HRAS	0.6	40	168	457	6	211	344	114	297	817	1,228
BRAF V600E/K	2.0	1.9	23	180	93	1.4	158	63	127	271	461
BRAF Class 2/3	0.5	4.7	29	24	7.9	0.5	86	17	38	98	153
Other BRAF	-	-	3.9	-	1.9	0.3	0.5	0.7	1.0	4.9	6.6
MEK	0.2	1.9	12	8.8	4.6	0.2	22	5.2	11	33	50
Co-occurring activating MAPK pathway alterations**	1.4	10	62	59	37	7.1	84	32	68	160	261
US	12	29	93	114	77	51	153	533			
EU	34	76	194	398	116	124	324		1,267		
Rest of World	109	555	635	964	60	264	1,053			3,636	
Global	155	660	923	1,476	253	438	1,530				5,436

Blue ocean opportunities Red ocean opportunities

* Post-Osimertinib resistant population shown for EGFRm NSCLC except for SCLC transformation

** Co-occurring activating MAPK pathway alterations exclude EGFR overexpression

Source: SEER database (2020), ECIS database (2020), GLOBOCAN database (2020), The AACR Project GENIE Consortium version 8.1 (2020), TCGA Research Network: https://www.cancer.gov/tcga, Tyner JW et al. (2018) PMID: 30333627, Brenner CW et al (2013) PMID: 24120142, Chen J et al. (2020) PMID: 32015526, and Ostrom QT, et al. (2020) PMID: 33123732

ERASCA

Naporafenib: Potential first-in-class pan-RAF inhibitor

PRECLINICAL

DCC-3084
IND-enabling

IRICoR-Ipsen
Licensed from IRICoR

CUL-BRAF
Degrader

CLINICAL

ERASCA
naporafenib (Ph 3 ready)
+ trametinib: Ph 1 and 2 ORR 33% in NRASm melanoma

belvarafenib (Ph 1b[1])
+ cobimetinib: ORR 26% (5/19) in NRASm melanoma

tovorafenib (Ph 1b[2])
+ pimasertib (investigational MEKi): in progress

BDTX-4933
Ph 1 in KRASm NSCLC

exarafenib (Ph 1[3])
+ binimetinib: ORR 29% (2/7 efficacy evaluable)

lifirafenib (Ph 1b)
+ mirdametinib (investigational MEKi): ORR 23% (14/62)

brimarafenib (Ph 1)
+ mirdametinib (investigational MEKi): in progress

plixorafenib (Ph 2)
dimer breaker
+ cobicistat: in progress

JZP815 (Ph 1)
Monotherapy evaluation in progress

Most advanced pan-RAF inhibitor

- Dosed in more patients (500+) than any other pan-RAF inhibitor in development
- Potential to be first-to-market and raise SOC in prioritized indications

PoC established

- Evaluating naporafenib in indications where it has already shown promising PoC – namely, NRASm melanoma and RAS Q61X solid tumors

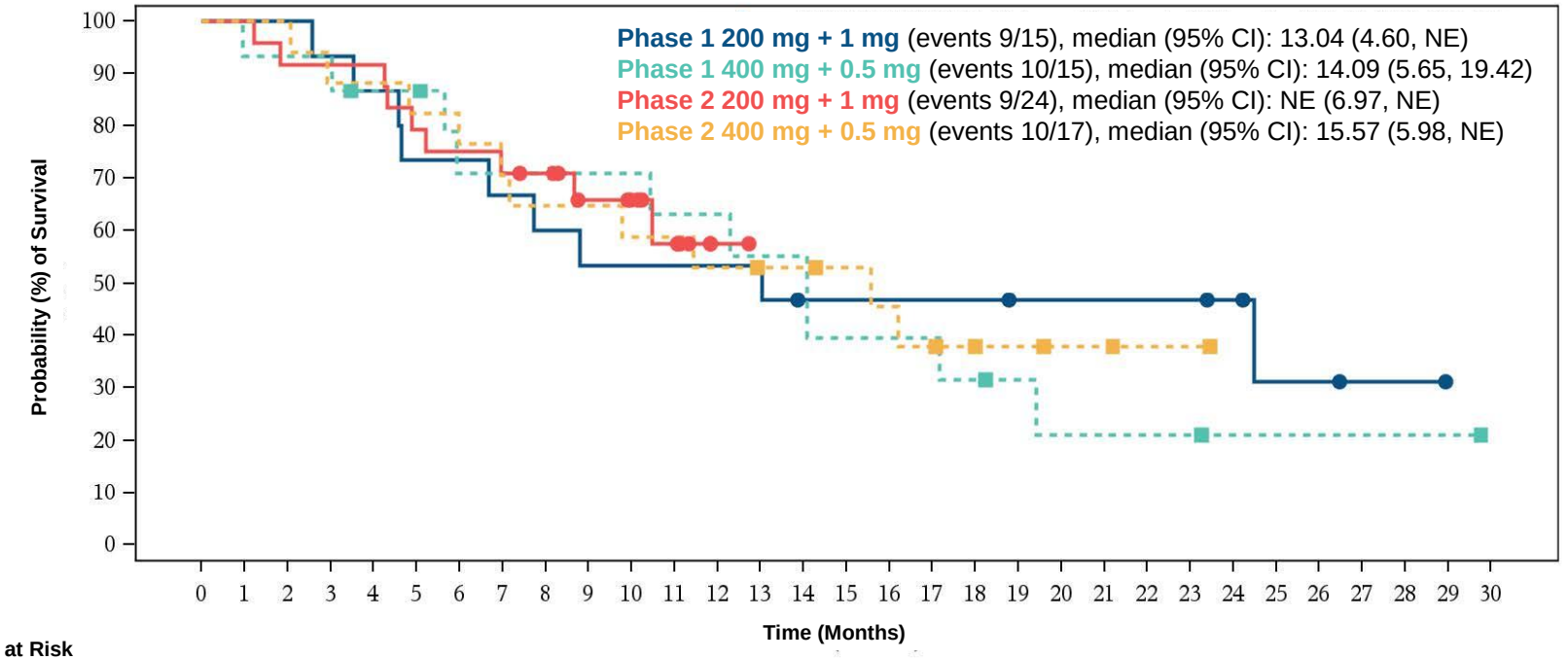
Strong complementarity with Erasca pipeline

- Highly complementary, if not synergistic, with the rest of Erasca's RAS/MAPK pathway-targeting pipeline

[1] Belvarafenib is also being evaluated for the treatment of BRAF Class II mutant or fusion-positive tumors and BRAF Class III mutant positive tumors in a Ph 2 platform trial
[2] NDA has been accepted for tovorafenib in its lead indication, frontline pLGG (pediatric low-grade glioma)
[3] Exarafenib in Ph 1b for monotherapy indication in BRAF-driven tumors

ORR: overall response rate; SOC: standard of care; PoC: proof-of-concept

Napo + tram OS data showed high consistency across studies and doses



# Patients at Risk																													
Phase 1 200 mg + 1 mg	15	15	15	14	13	11	11	10	9	8	8	8	8	8	6	6	6	6	6	5	5	5	5	5	4	2	2	1	1	0	0
Phase 1 400 mg + 0.5 mg	15	14	14	14	12	12	9	9	9	9	9	8	8	7	7	5	5	5	4	3	2	2	2	2	1	1	1	1	1	1	0
Phase 2 200 mg + 1 mg	24	24	22	22	22	19	18	17	16	12	10	7	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Phase 2 400 mg + 0.5 mg	17	17	17	15	15	14	13	12	11	11	10	10	9	8	8	7	6	5	4	3	2	2	1	1	0	0	0	0	0	0	0

NRASm
mOS: ~13-15 months
(across doses and studies)

Reproducibility of these results across studies and doses increases our confidence in the mOS observations

mOS: median overall survival
Differences exist between trial designs and subject characteristics and caution should be exercised when comparing data across trials.

ERAS-007: Potential best-in-class ERK1/2 inhibitor in a field marked by attrition

TERMINATED

GDC-004

Tolerability issues

KO-947

Placed on partial clinical hold; IV administered

CC-90003

MTD "did not offer sufficiently encouraging profile to proceed"

CLINICAL

ulixertinib (Ph 2)

Being evaluated in monotx and +HCQ; CoM through 2025

ERAS-007 (Ph 2)

+ EC: 50% (3/6) RR in EC-naïve CRC; expansion ongoing

ASTX029 (Ph 2)

Monotx dose level identified in FIH study

temuterkib (Ph 1)

Reported monotherapy ORR of 0% (n=51)

JSI-1187 (Ph 1)

+ dabrafenib: dose escalation for BRAF V600E/K solid tumors

ATG-017 (Ph 1)

First data readout and RP2D were expected Q1/Q2 2023

MK-8353 (Ph 1)

ORR 20% (3/15 efficacy evaluable); not listed in pipeline

rineterkib (Ph 1)

Reported monotx ORR of 2% (n=65); not listed on pipeline

Hit-and-run profile optimizing efficacy, tolerability

- Highest potency and longest target residence time of known ERKi's enable ERAS-007 to be dosed intermittently instead of daily like other clinical ERKi's

Safety and tolerability established

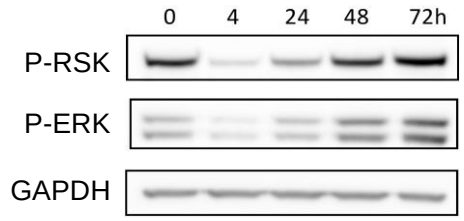
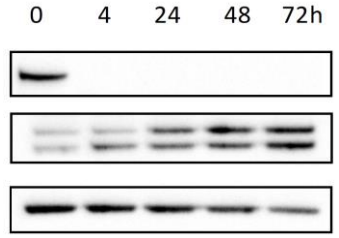
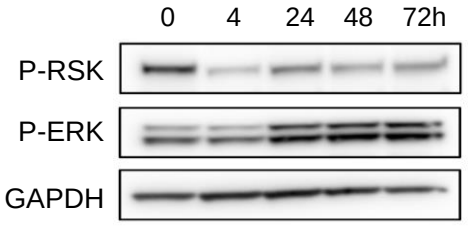
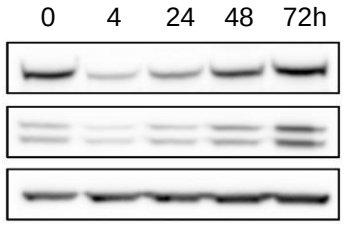
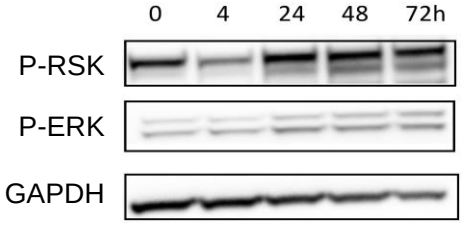
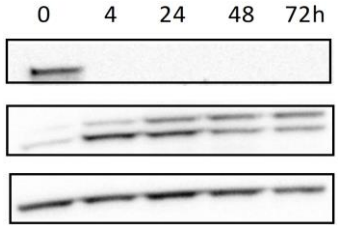
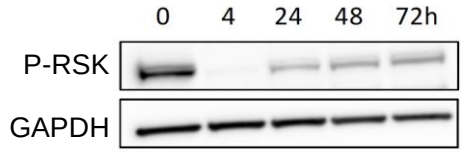
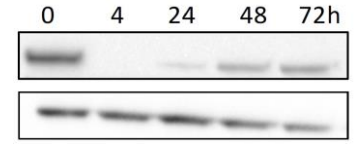
- Comparable if not better tolerability than other clinical ERKi's particularly as it relates to rash
- Intermittent dosing regimen has the potential to further optimize clinical utility

Encouraging signs of efficacy

- Monotherapy responses observed in FIH and HERKULES-1 trials
- Meaningful initial activity observed in patients with EC-naïve BRAFm CRC treated with ERAS-007 + EC

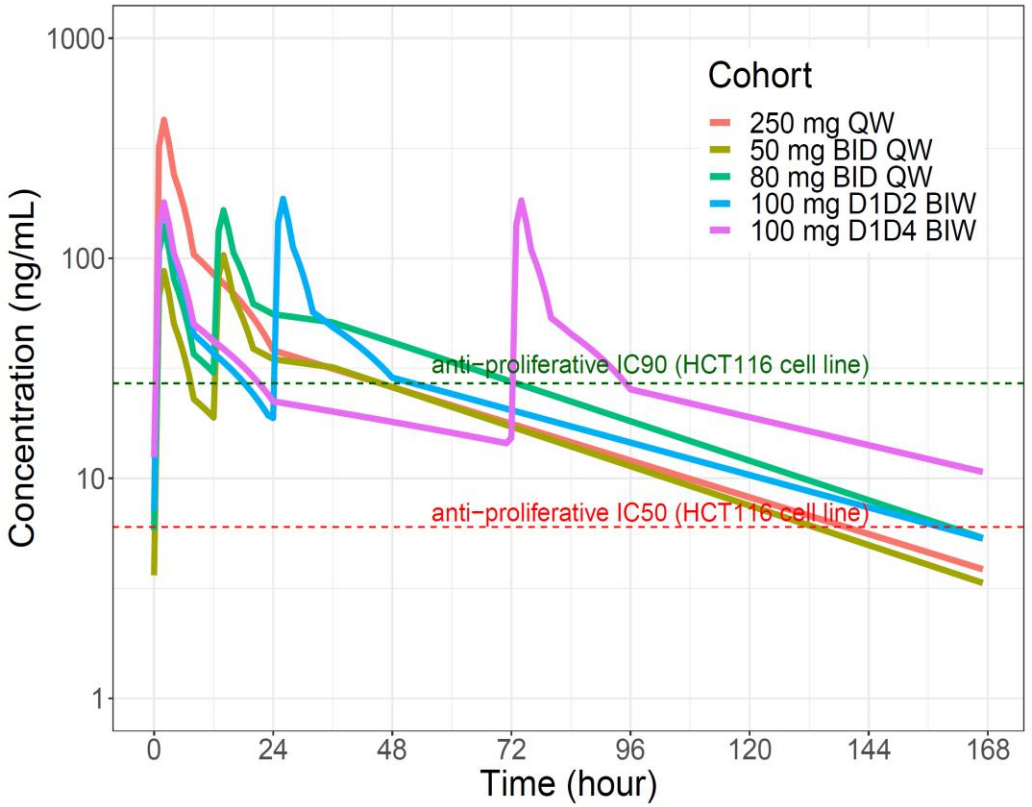
MTD: maximum tolerated dose; monotx: monotherapy; HCQ: hydroxychloroquine; CoM: composition of matter patent; ORR: overall response rate; RR: response rate; EC: encorafenib + cetuximab; RP2D: recommended Phase 2 dose; FIH: First-in-Human

ERAS-007 blocked the MAPK feedback reactivation observed with MEK or other ERK plus BRAF inhibitor combinations

BRAF V600E CRC Cell Lines	MEKi combination	ERKi combinations		
	Binimetinib 1 µM + Encorafenib 0.1 µM	ERAS-007 0.1 µM + Encorafenib 0.1 µM	LY3214996 1 µM + Encorafenib 0.1 µM	Ravoxertinib 1 µM + Encorafenib 0.1 µM
RKO				
HT29				
MAPK Feedback	REACTIVATION	NO REACTIVATION	REACTIVATION	REACTIVATION

Source: Unpublished data

Phase 1 PK data showed QW is preferable to QD dosing; Simulations suggest BID-QW dosing may improve PK/PD profiles and combinability even more

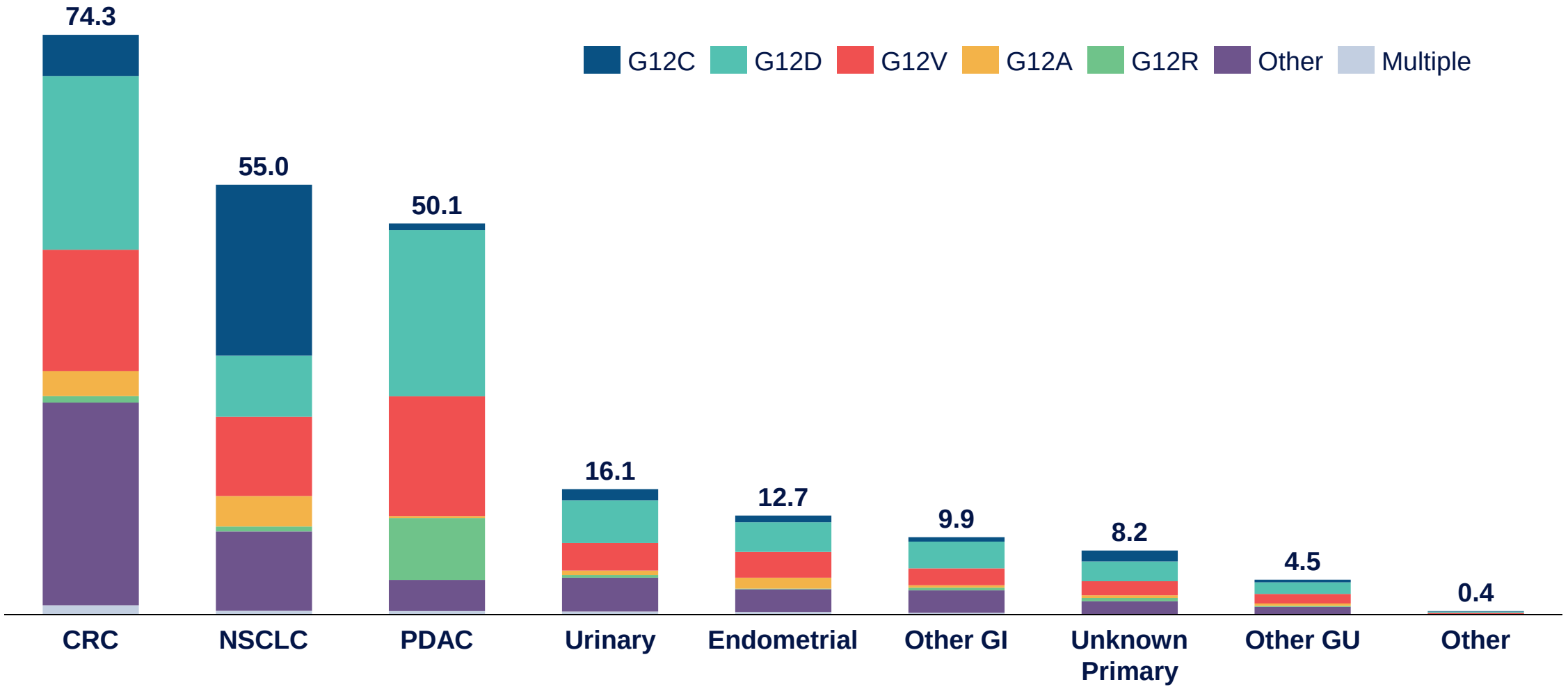


Dosing Regimen	C_{max}, ng/mL	C_{min}, ng/mL	T>IC90	T<IC50
250 mg QW	425	3	~2/7	~1/7
50 mg BID-QW	103	3	~2/7	~1/7
80 mg BID-QW	165	5	~3/7	~0.5/7
100 mg D1D2 BIW	186	5	~2/7	~0.5/7
100 mg D1D4 BIW	183	11	~2/7	0

GOAL is to maximize the time above IC90 to improve cancer cell killing, while maintaining C_{min} near or below IC50 to give normal cells a treatment break (i.e., extend time below IC50)

~230k patients are diagnosed annually in the US with solid tumors harboring KRAS mutations

Estimated number of patients affected by KRAS mutant tumors in the US (thousands)



Adapted from Lee J., Sivakumar S., Schrock A., et al. "Comprehensive pan-cancer genomic landscape of KRAS altered cancers and real-world outcomes in solid tumors." NPJ Precision Oncology, 2022. PMID: 36494601.

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