ERASCA

On a Journey to Erase Cancer

Erasca Corporate Presentation

January 2025

Eric N., naporafenib clinical trial participant and cancer survivor, and his wife Margaret

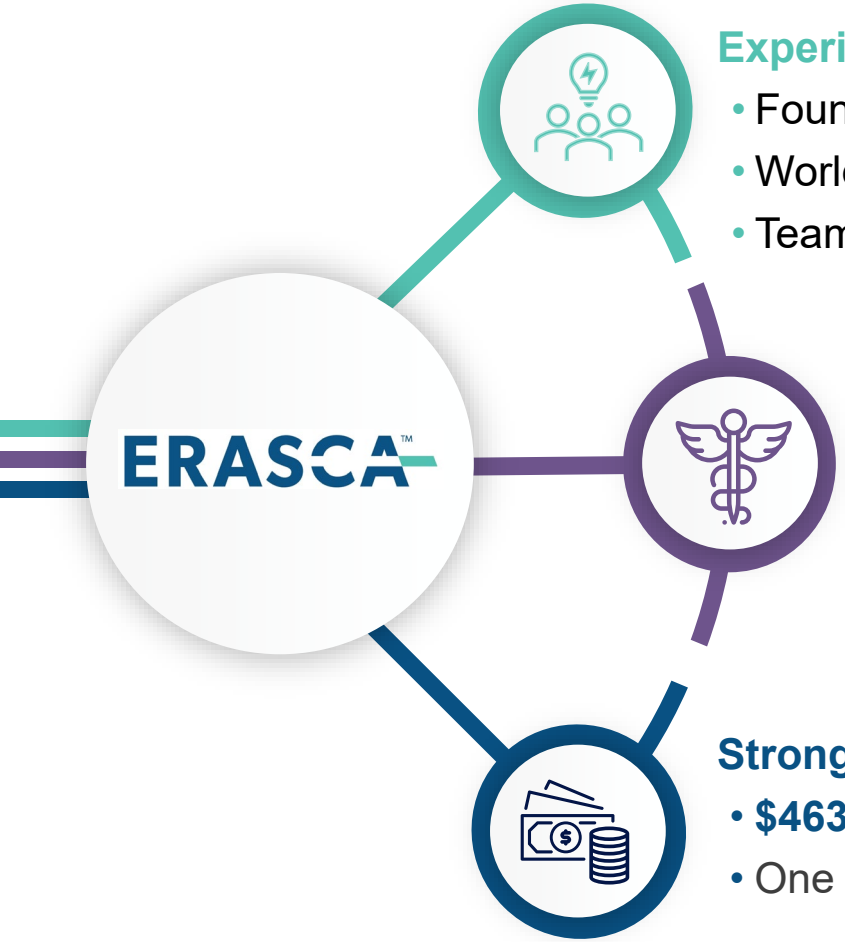
Disclaimer: Forward Looking Statements & Market Data

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 therapeutic benefits of our product candidates, our intellectual property protection, 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 one product candidate in clinical development and all of our other development efforts are in the preclinical stage; our assumptions about ERAS-0015's or ERAS-4001's development potential are based in large part on the preclinical data generated by the licensors and we may observe materially and adversely different results as we conduct our planned studies and trials; 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; the analysis of pooled Phase 1 and Phase 2 naporafenib plus 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 ORR, mPFS, or mOS 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; our SEACRAFT trials may not support the registration of naporafenib; later developments with the FDA or EU health authorities may be inconsistent with the feedback received to date regarding our development plans and trial designs; Fast Track 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; potential delays in the commencement, enrollment, data readout, 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; regulatory developments in the United States and foreign countries; our ability to obtain and maintain intellectual property protection for our product candidates and maintain our rights under intellectual property licenses; our ability to fund our operating plans with our current cash, cash equivalents, and marketable securities into the second half of 2027; 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.

ERASCA

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 development**

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

- **Naporafenib Pan-RAFi** with FIC potential and Fast Track Designation for NRASm melanoma + **other RAS/MAPK targeting agents**
- **ERAS-0015 Pan-RAS molecular glue** with BIC potential in RASm solid tumors
- **ERAS-4001 Pan-KRASi** with FIC potential in KRASm solid tumors

Strong financial position with high quality investor base and industry visibility

- **$463M in cash, cash equivalents, and marketable securities[2]**; cash runway into **H2 2027**
- One of **Fierce Biotech's 2021 "Fierce 15"** most promising biotechnology companies

[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] Unaudited, as of September 30, 2024
FIC: first-in-class; BIC: best-in-class; RASm: RAS mutated; KRASm: KRAS mutated

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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

Michael Varney, PhD

Erasca Chair of R&D. 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

René Bernards, PhD

World expert in functional cancer genetics and identifying new drug combinations based on genome-wide genetic approaches

Netherlands Cancer Institute Antoni van Leeuwenhoek

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

Karen Cichowski, PhD

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

Harvard Medical School · Brigham and Women's Hospital

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

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

Piro Lito, MD, PhD

World expert in KRAS-targeted therapeutics and precision oncology, with a focus on resistance mechanisms to RAS inhibitors

Memorial Sloan-Kettering Cancer Center — The Best Cancer Care. Anywhere.

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

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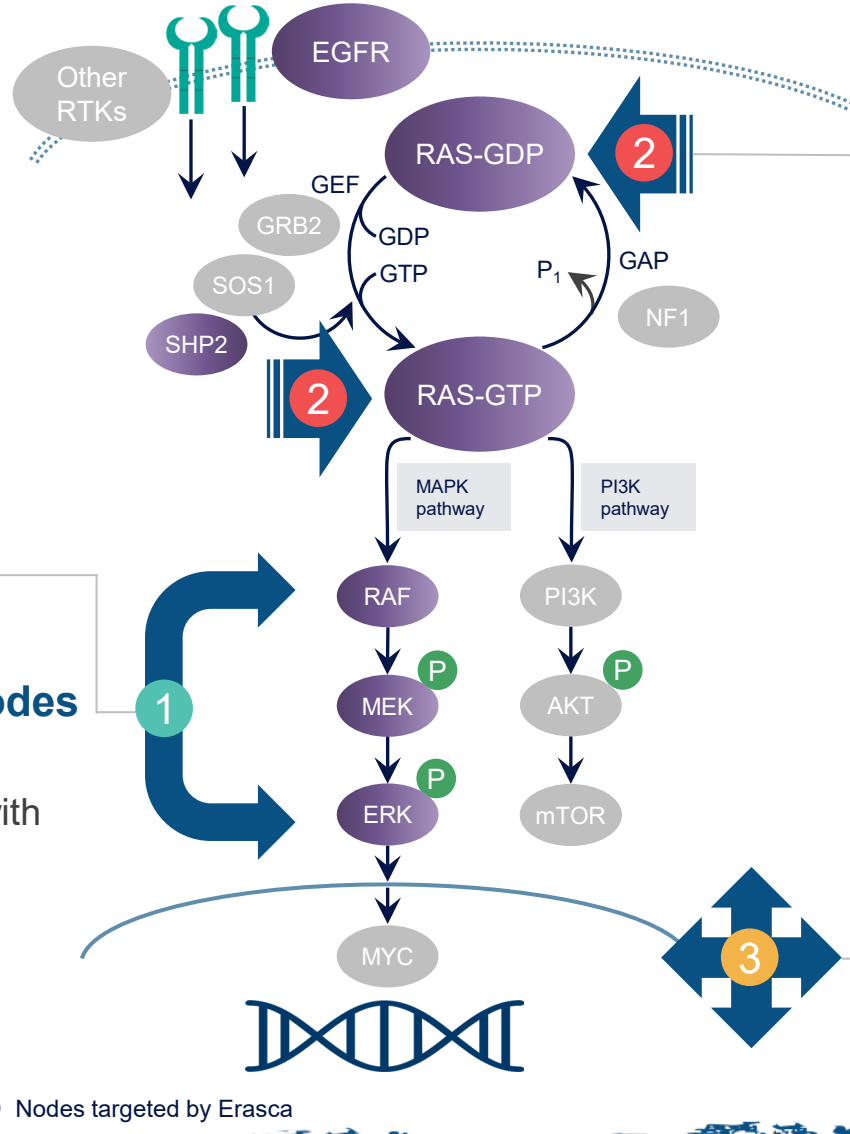
Our singular focus is on the RAS/MAPK pathway

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

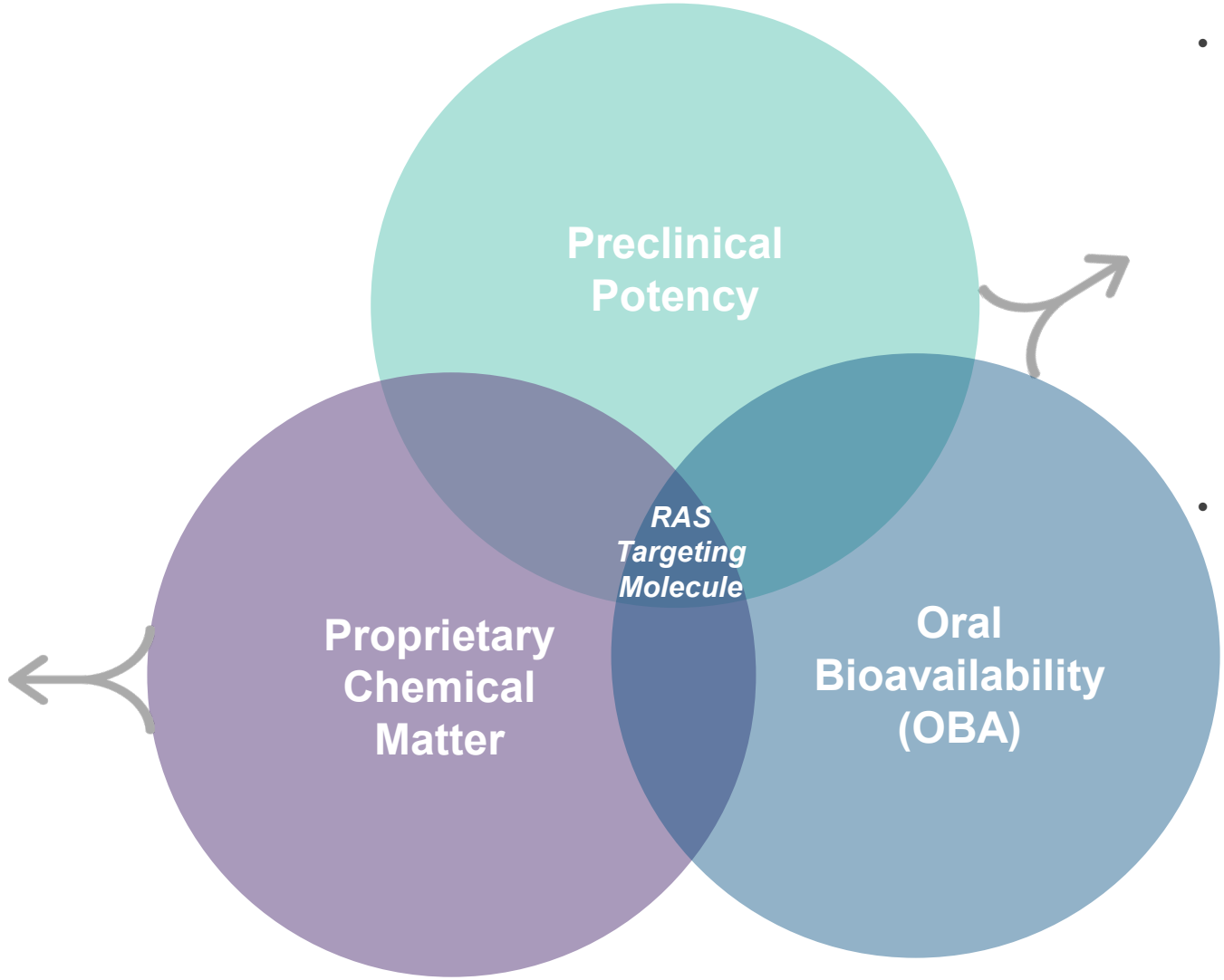
Program	Target	Modality	Indication	Discovery	IND-enabling	Phase 1	Phase 2	Phase 3	Worldwide Rights
Naporafenib	BRAF/CRAF		NRASm melanoma	SEACRAFT-2					ERASCA
			RAS/MAPK solid tumors	SEACRAFT-1					ERASCA
ERAS-0015	RAS		RASm solid tumors	AURORAS-1 (planned)					ERASCA, JOYO PHARMA[1]
ERAS-4001	KRAS		KRASm solid tumors	BOREALIS-1 (planned)					ERASCA
ERAS-12	EGFR D2/D3		EGFR & RAS/MAPK solid tumors						ERASCA

small molecule small molecule molecular glue large molecule

Note: Pipeline also includes ERAS-801 brain-penetrant EGFR inhibitor for EGFR-altered GBM (for which we are concluding a Phase 1 trial and exploring advancement, including via partnership and/or investigator-sponsored trials), ERAS-007 ERK1/2 inhibitor, and ERAS-601 SHP2 inhibitor. ERAS-007 and ERAS-601 are being assessed in preclinical studies as potential combination partners with other programs in our pipeline for RAS/MAPK pathway inhibition. Via Erasca Ventures, we made an equity investment into Affini-T Therapeutics, which is developing TCR T-cell therapies against KRAS G12V, KRAS G12D, and KRAS G12C.

[1] Licensor Joyo Pharmatech, Ltd., retains rights to People's Republic of China, Hong Kong and Macau, subject to Erasca's option to convert our territory to worldwide

Ideal RAS targeting molecules integrate three key attributes



- Bolsters ability to **maximize clinical and commercial value** in highly competitive market

- May enable **lower clinically active dose** which could translate to:
  - Lower risk of solubility-limited absorption and exposure plateau observed with another pan-RAS MG in development
  - Better GI tolerability profile due to lower drug load
  - Improved therapeutic window for any potential off-target toxicities
- KRAS G12Ci class has demonstrated how higher potency can translate into **improved clinical activity**

MG = molecular glue

ERAS-0015 and ERAS-4001 exhibit competitive profiles that exceed our TPP

	Preclinical Potency[1]	OBA[2]	IP[3]
ERAS-0015 Pan-RAS Molecular Glue	• In vitro: **0.2 – 13.8 nM IC50** in KRAS G12D/V/C/X, G13D, WT; activity in H/NRAS WT • In vivo: Tumor regression in KRAS G12D/V/R CDX models at low doses between **0.3 – 5 mpk PO QD**	• **38 – 48%** in small animal species • **17 – 22%** in large animal species	• IP exclusivity expected through **2043** • No patentability roadblocks identified to date
ERAS-4001 Pan-KRAS Inhibitor	• In vitro: **0.7 – 10.8 nM IC50** in KRAS G12D/V/C and KRAS WT; **5.8 – 56 nM IC50** in KRAS G12X and G13D; no activity in H/NRAS • In vivo: Tumor regression in KRAS G12D/V CDX models at doses between **30 - 300 mpk PO BID**	• **Up to 27%** in small animal species • **16%** in large animal species	• IP exclusivity expected through **2043** • No patentability roadblocks identified to date

Potential BIC **Pan-RAS MG** for RASm solid tumors, which showed ~5x – 10x greater potency and favorable ADME properties and PK performance in animal species (vs. current Pan-RAS MG in development)

Potential FIC/BIC **Pan-KRAS** or **"KRAS-selective" SMi** that spared H/NRAS WT, predicted to provide a wider therapeutic window (vs. Pan-RAS MG) for KRASm solid tumors and address KRASwt activation to prevent resistance (vs. mutant-selective inhibitors)

Pan-KRAS SMi + **Pan-RAS MG** "RASKlamp" combo could uniquely shut down MAPK signaling in KRASm solid tumors

TPP: target product profile; OBA: oral bioavailability; IP: intellectual property; FIC: first-in-class; BIC: best-in-class; WT: wildtype; SMi: small molecule inhibitor; MG: molecular glue; [1] in vitro potency assessed by CTG 2D and 3D-cell proliferation assay IC50s; [2] OBA assessed by %F; [3] IP includes composition of matter, methods of use, and methods of making licensed compounds; date is absent any patent term adjustments or extensions

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ERAS-0015 and ERAS-4001 exhibit competitive profiles that exceed our TPP

ERAS-0015
Pan-RAS
Molecular Glue

Potential best-in-class Pan-RAS molecular glue

- ~5x – 10x greater potency vs. pan-RAS MG in development
- Favorable ADME properties and PK performance in animals vs. pan-RAS MG in development
- Designed to address RASwt activation to prevent resistance vs. mutant-selective inhibitors

ERAS-4001
Pan-KRAS
Inhibitor

Potential first-in-class and best-in-class KRAS inhibitor

- Designed to spare H/NRAS WT
- Wider therapeutic window predicted vs. pan-RAS MG for KRASm solid tumors
- Designed to address KRASwt activation to prevent resistance vs. mutant-selective inhibitors

TPP = target product profile; MG: molecular glue; ADME: absorption, distribution, metabolism, and excretion; PK: pharmacokinetic; WT: wild type; KRASm: KRAS mutant

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ERAS-0015's higher CYPA binding affinity may be a differentiator from RMC-6236, demonstrating potential best-in-class profile

Assay	ERAS-0015 (nM)	RMC-6236 (nM)	Binding affinity difference: ERAS-0015/ RMC-6236
SPR K_D	4.5	92	**21x**
ITC K_D	5.3	44.1	**8x**

8-21x higher binding affinity to cyclophilin A (CYPA) may enable more potent RAS inhibition

SPR: surface plasmon resonance; K_D: equilibrium dissociation constant; ITC: isothermal titration calorimetry

ERAS-0015 demonstrated significantly more potent inhibition of cell growth across KRAS mutant cell lines vs. RMC-6236

Mutation	Tumor type	Cell line	ERAS-0015 cell growth inhibition (nM)	RMC-6236 cell growth inhibition (nM)	ERAS-0015:RMC-6236 Fold Potency
KRAS G12C	NSCLC	H358 (adagrasib-resistant)	0.8	3.6	**4.5x**
	NSCLC	LU99	1.4	5.4	**3.9x**
KRAS G12D	NSCLC	A-427	13.3	59.2	**4.5x**
	CRC	SW620	0.2	1.3	**6.5x**
	CRC	GP2d	0.9	4.6	**5.1x**
	PDAC	AsPc-1	2.0	26.7	**13.4x**
	PDAC	HPAC	4.8	15.5	**3.2x**
	PDAC	PK-59	10.7	10.7	**1x**
	PDAC	KP-4	5.0	19.7	**3.9x**
	PDAC	Panc 04.03	5.7	26.4	**4.6x**
KRAS G12V	Lung Cancer	NCI-H727	0.4	1.7	**4.3x**
	Lung Cancer	NCI-H441	1.4	16.7	**11.9x**
	CRC	SW480	0.8	6.8	**8.5x**
	PDAC	CAPAN-1	2.5	7.1	**2.8x**
	Ovarian leiomyosarcoma	RKN	0.7	1.6	**2.3x**
KRAS G12R	PDAC	PSN-1	5.3	17.1	**3.2x**
KRAS G12S	NSCLC	A-549	4.1	38.3	**9.3x**
KRAS Q61R	PDAC	Panc 02.13	7.4	44.3	**6x**
KRAS G13D	CRC	LoVo	2.8	1.5	**0.5x**
	CRC	HCT-116	5.5	26.2	**4.8x**
KRAS WT Amplified	Gastric	MKN-1	13.8	55.8	**4x**
EGFR L858R / T790M	NSCLC	H1975	6.5	11.4	**1.8x**
MET amplified	NSCLC	EBC-1	4.4	16.9	**3.8x**
BRAF V600E	Melanoma	A375	>6,000	>6,000	**N/A**

Sub-nM to nM potency against multiple KRAS wildtype, KRAS mutant, and RTK altered cell lines

RTK: receptor tyrosine kinase

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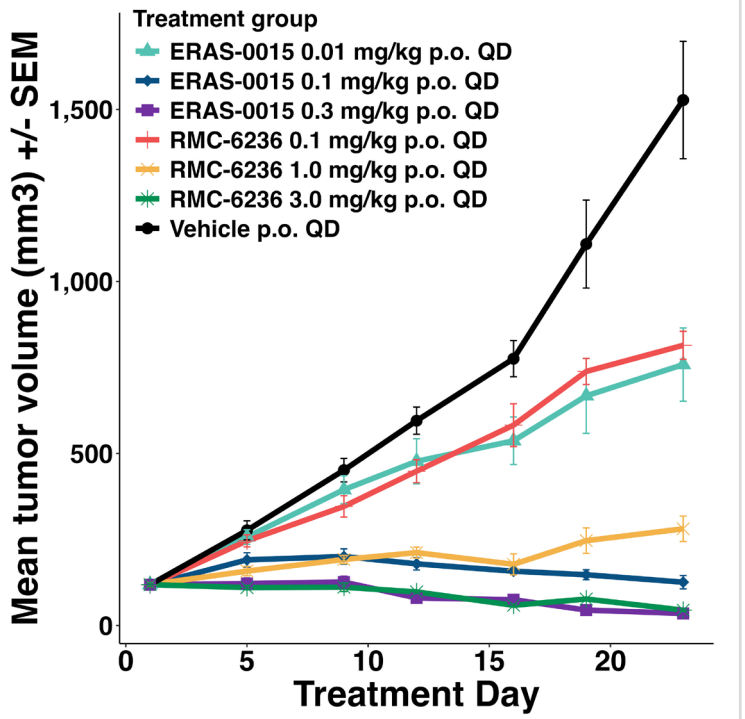
ERAS-0015: Showed 10x higher potency than RMC-6236, achieving tumor regression in a KRAS G12D PDAC CDX model

TGI in KRAS G12D PK-59



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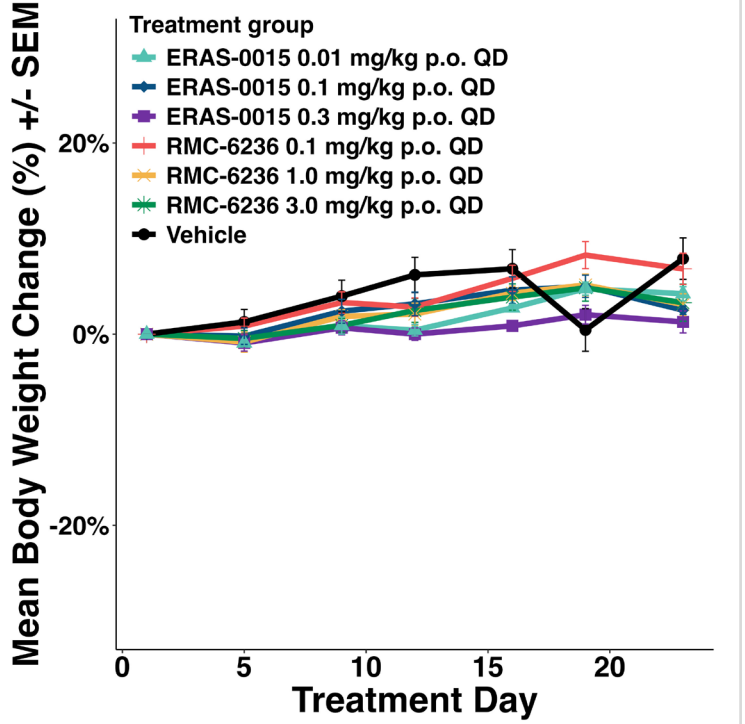


TGI Summary

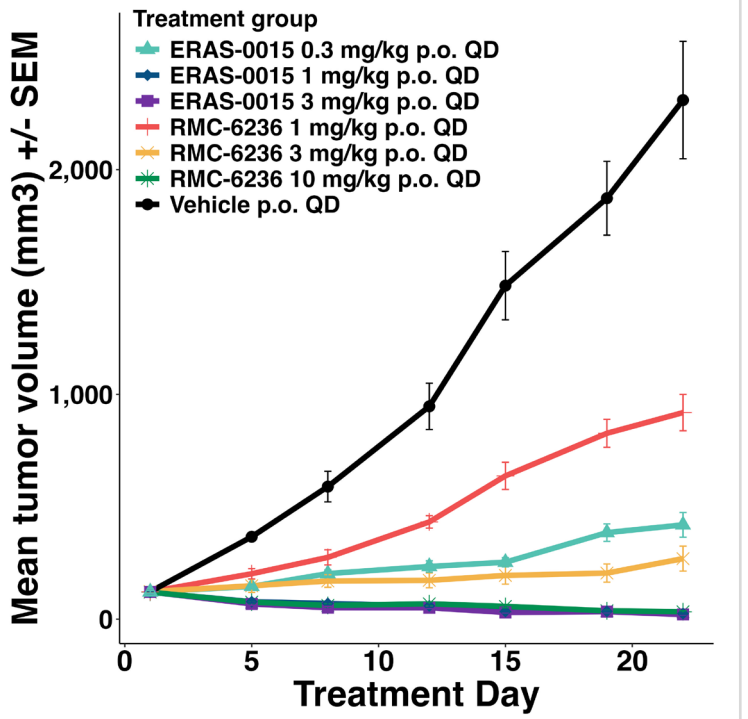
Therapy	Dose	TGI on Day 23
ERAS-0015	0.01 mg/kg	55%
	0.1 mg/kg	99%
	0.3 mg/kg	106%
RMC-6236	0.1 mg/kg	51%
	1.0 mg/kg	89%
	3.0 mg/kg	105%

- ERAS-0015 achieved comparable tumor regression to RMC-6236 in this model at 1/10th of the dose at 0.3 mg/kg p.o. QD
- No dose reductions or holidays and no body weight loss for all doses of ERAS-0015

p.o.: orally administered; QD: once daily; CDX: cell line-derived xenograft; TGI: tumor growth inhibition

ERAS-0015: Showed 10x higher potency than RMC-6236, achieving tumor regression in an insensitive KRAS G12V NSCLC CDX model

TGI in KRAS G12V NCI-H727



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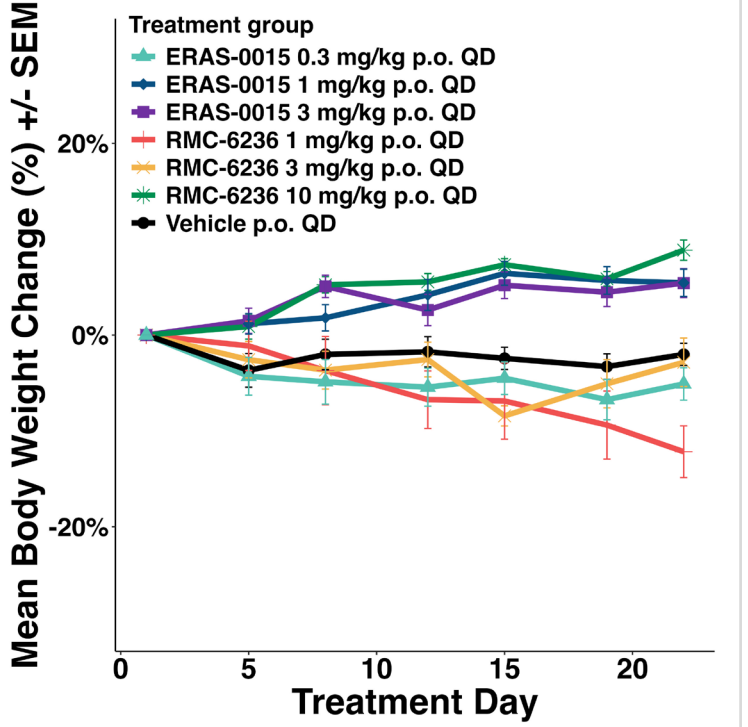


TGI Summary

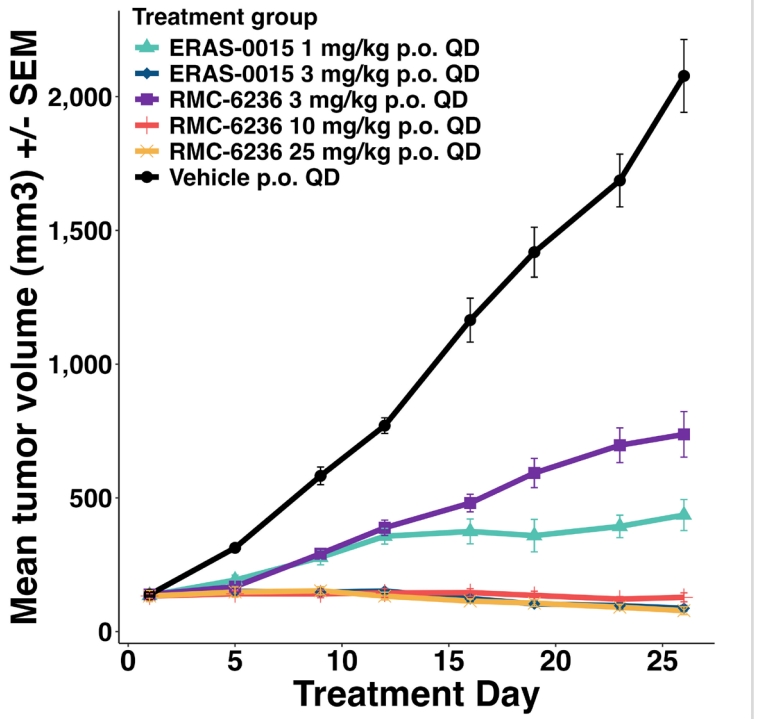
Therapy	Dose	TGI on Day 22
ERAS-0015	0.3 mg/kg	86%
	1 mg/kg	104%
	3 mg/kg	105%
RMC-6236	1 mg/kg	64%
	3 mg/kg	83%
	10 mg/kg	104%

- ERAS-0015 achieved comparable tumor regression to RMC-6236 in this model at 1/10th the dose at 1 mg/kg p.o. QD
- ERAS-0015 was well tolerated at all doses

p.o.: orally administered; QD: once daily; CDX: cell line-derived xenograft; TGI: tumor growth inhibition

ERAS-0015: Showed ~8x higher potency than RMC-6236, achieving tumor regression in a KRAS G12V CRC CDX model

TGI in KRAS G12V SW620



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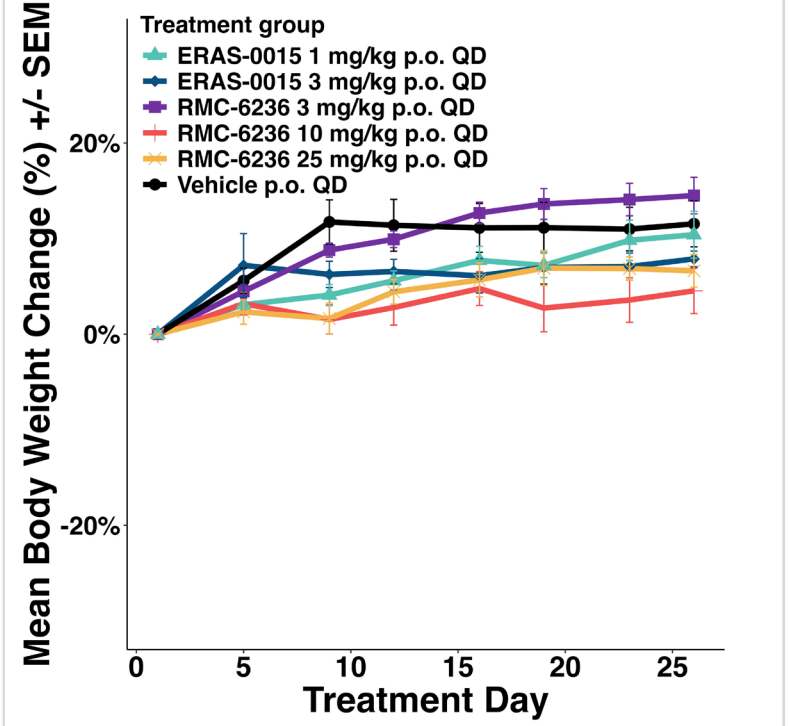

TGI Summary

Therapy	Dose	TGI on Day 26
ERAS-0015	1 mg/kg	85%
	3 mg/kg	102%
RMC-6236	3 mg/kg	69%
	10 mg/kg	100%
	25 mg/kg	103%

- ERAS-0015 achieved comparable tumor regression to RMC-6236 in this model at ~1/8th the dose at 3 mg/kg p.o. QD
- No dose reductions, holidays, or body weight loss

p.o.: orally administered; QD: once daily; CDX: cell line-derived xenograft; TGI: tumor growth inhibition

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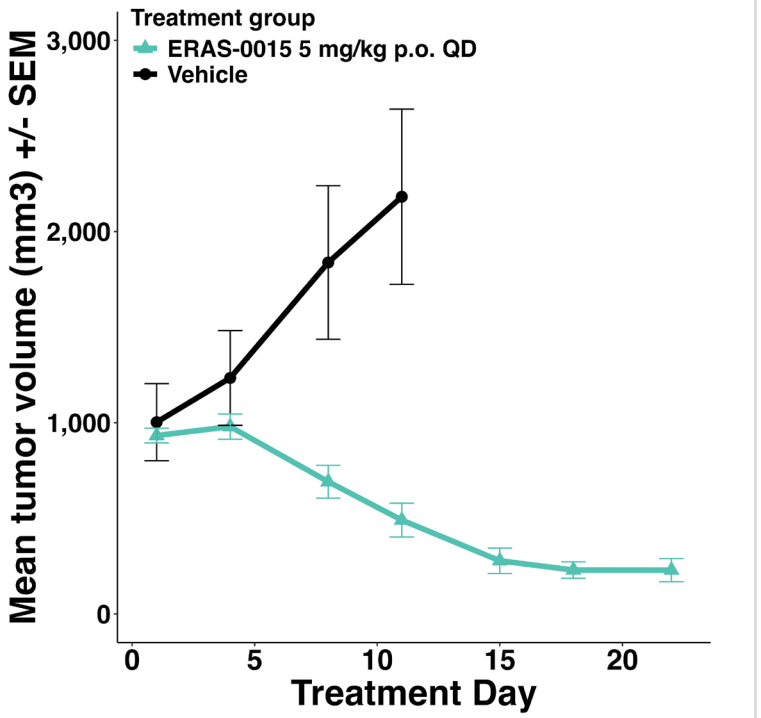
ERAS-0015: Achieved tumor regression in a KRAS G12R PDAC CDX model

TGI in KRAS G12R PSN-1



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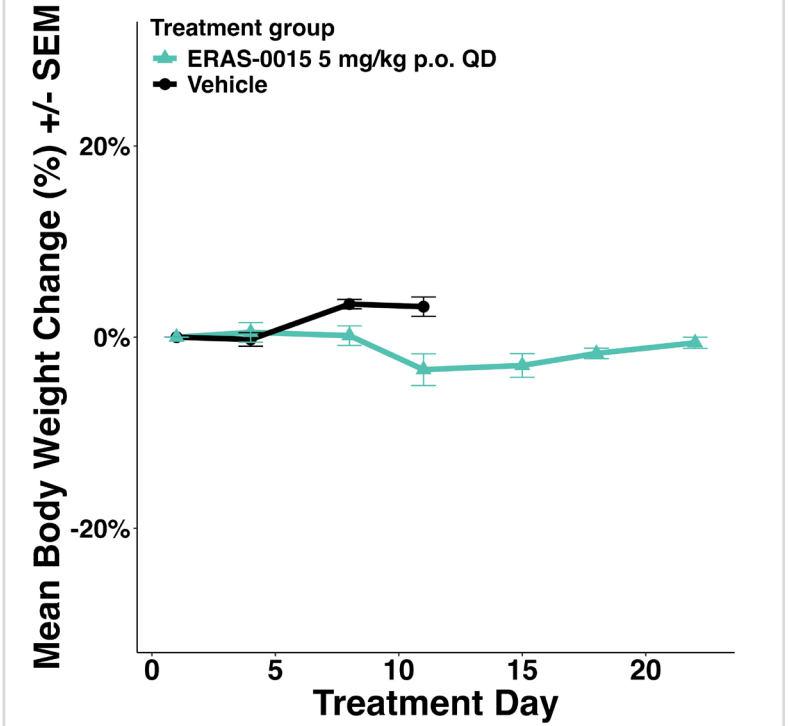


TGI Summary

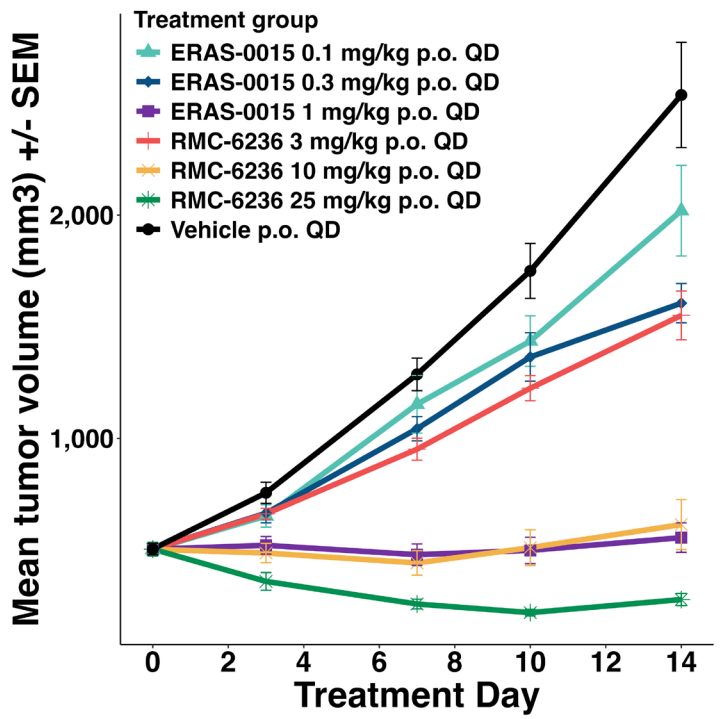
Therapy	Dose	TGI on Day 11
ERAS-0015	5 mg/kg	138%

- ERAS-0015 tumor regression observed at 5 mg/kg p.o. QD
- No dose reductions or holidays and body weight loss < 1% for ERAS-0015 at 5 mg/kg p.o. QD
- TGI assessed on last day where vehicle and ERAS-0015 tumors were both measured (i.e., day 11)

p.o.: orally administered; QD: once daily; CDX: cell line-derived xenograft; TGI: tumor growth inhibition

ERAS-0015: Showed 10x higher potency than RMC-6236, achieving >95% TGI in a KRAS G12R PDAC CDX model

TGI in KRAS G12R CDX PSN-1



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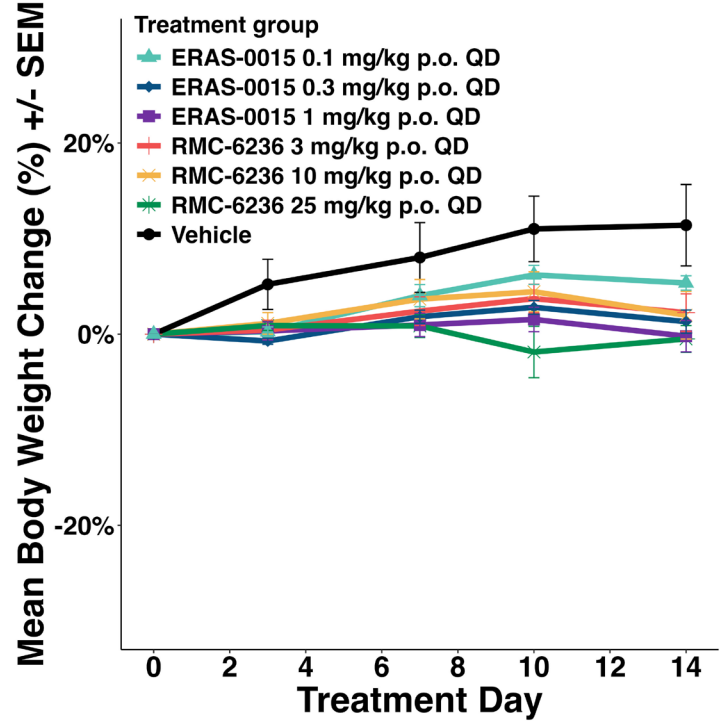


TGI Summary

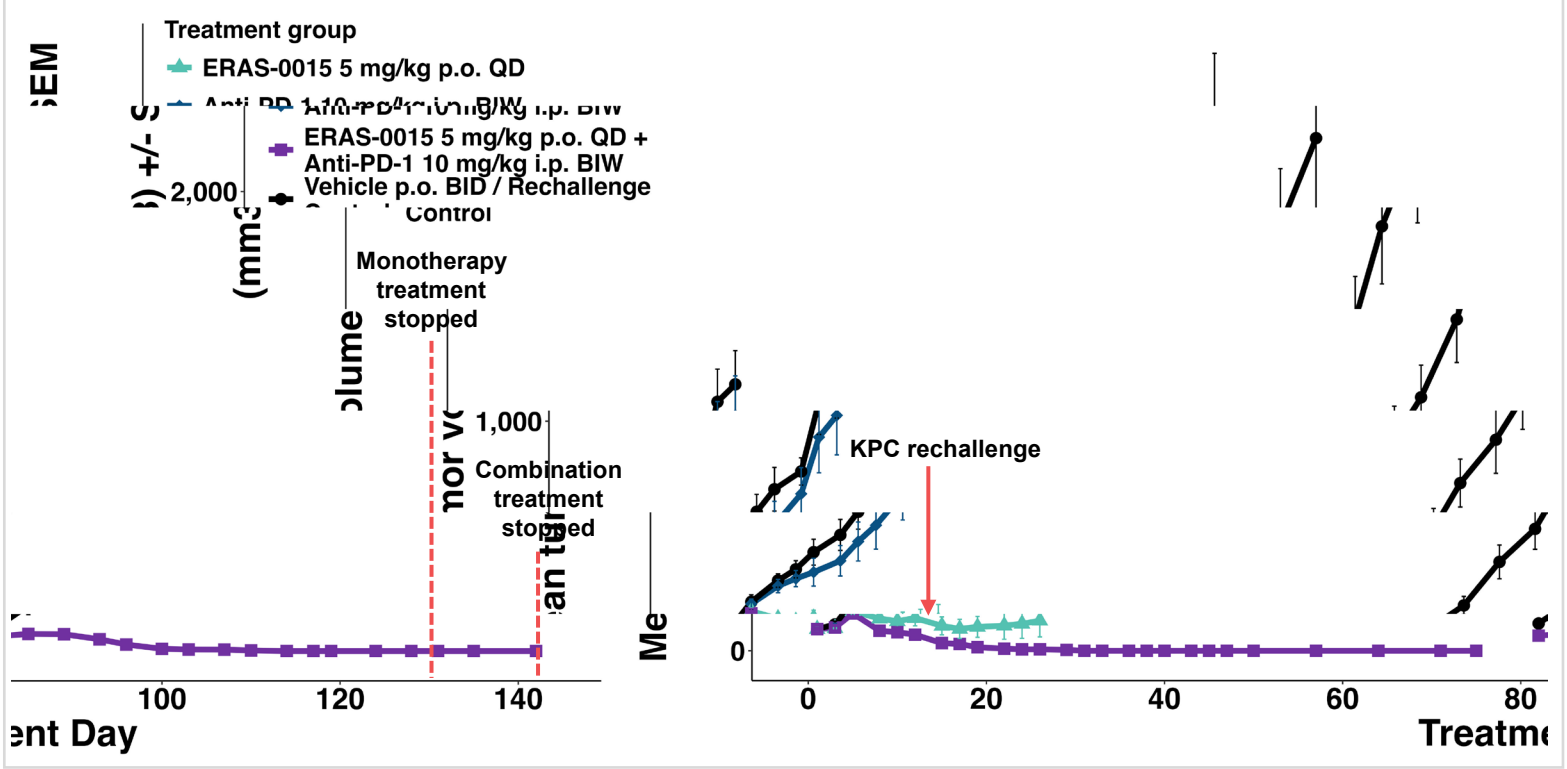
Therapy	Dose	TGI on Day 14
ERAS-0015	0.1 mg/kg	25%
	0.3 mg/kg	46%
	1 mg/kg	97%
RMC-6236	3 mg/kg	49%
	10 mg/kg	95%
	25 mg/kg	111%

- ERAS-0015 achieved comparable TGI to RMC-6236 in this model at 1/10th the dose starting at 0.3 mg/kg p.o. QD
- No dose reductions or holidays and body weight loss < 2% for ERAS-0015

p.o.: orally administered; QD: once daily; CDX: cell line-derived xenograft; TGI: tumor growth inhibition

ERAS-0015 + anti-PD-1: Compelling combination benefit in a syngeneic KRAS G12D PDAC model

TGI in syngeneic KRAS G12D KPC



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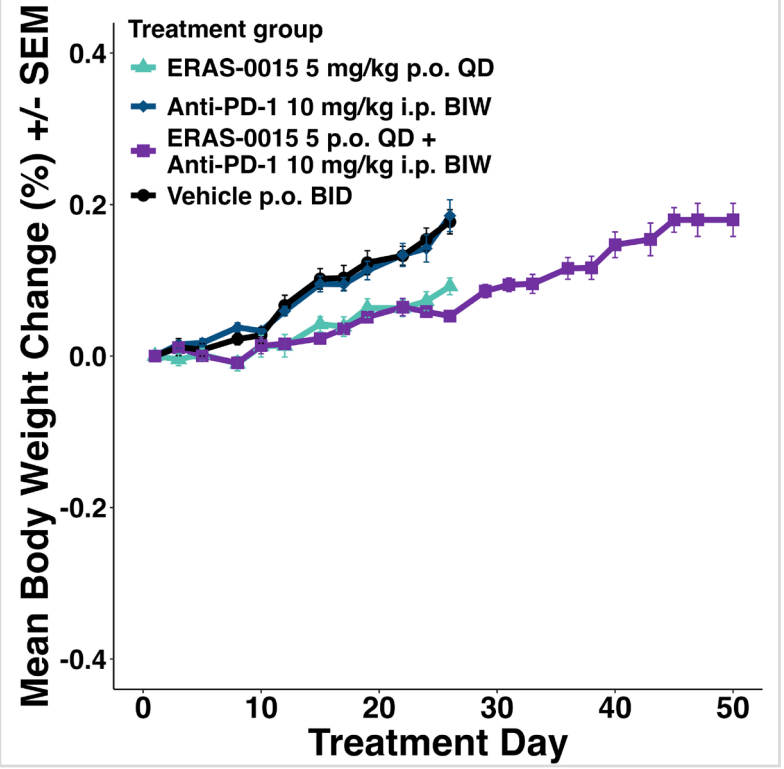
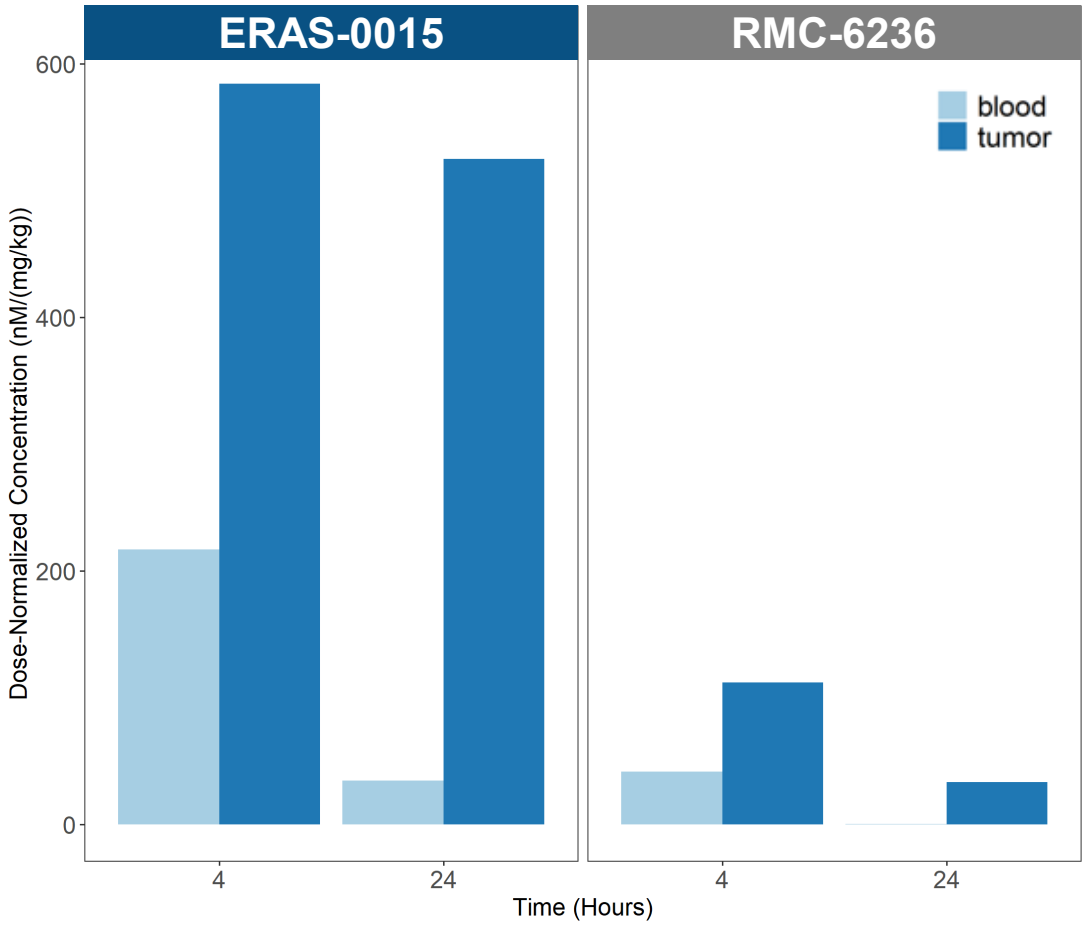


- ERAS-0015 in combination with anti-PD-1 therapy resulted in a sustained complete response in 7 out of 7 treated mice starting on day 31
- ERAS-0015 as a monotherapy and in combination with an anti-PD-1 was well tolerated
- Monotherapy treatments stopped on study day 26 and combination treatment stopped on study day 38
- Tumor formation was not observed up to 60 days after KPC rechallenge (KPC tumor cells were reinoculated on day 79)

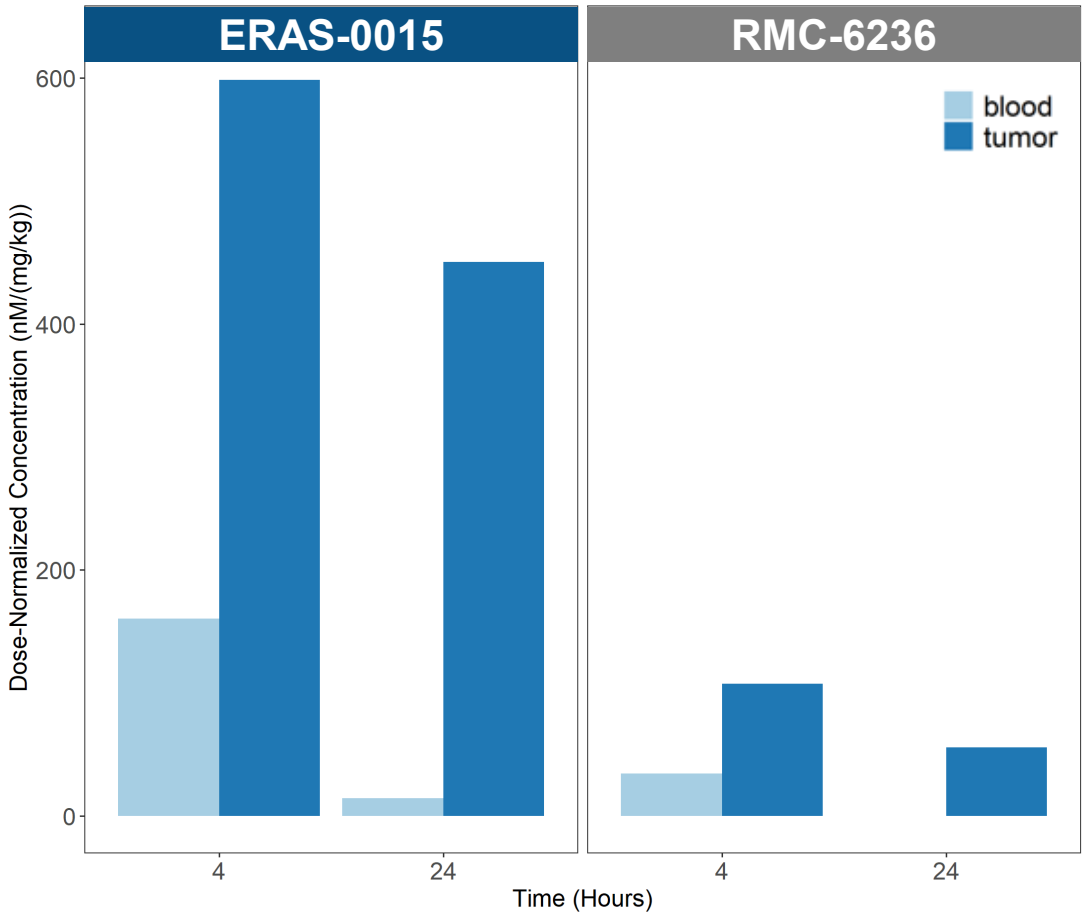
p.o.: orally administered; BIW: twice a week; BID: twice a day; QD: once daily; CDX: cell line-derived xenograft; TGI: tumor growth inhibition

ERAS-0015 demonstrated preferential tumor distribution and longer residence time vs. RMC-6236 in vivo

Tumor PK Distribution Assessment in the KRAS G12D PDAC CDX Model, PK-59



Tumor PK Distribution Assessment in the KRAS G12R PDAC CDX Model, PSN-1



PDAC: pancreatic ductal adenocarcinoma; CDX: cell-line derived xenograft

ERAS-0015 showed promising IV and oral PK in mouse, rat, dog, and monkey

		Mouse		Rat		Dog		Monkey	
		ERAS-0015	RMC-6236	ERAS-0015	RMC-6236	ERAS-0015	RMC-6236	ERAS-0015	RMC-6236
IV	Dose (mpk)	**1**	1	**1**	1	**1**	1	**1**	No Data
	$T_{1/2}$ (h)	**5.0**	1.7	**5.7**	1.5	**24.5**	7.6	**15.2**	No Data
	Vd_{ss} (L/kg)	**5.3**	1.9	**1.9**	1.9	**3.8**	3.7	**1.8**	No Data
	Cl (mL/Kg/min)	**12.8**	15.6	**4.6**	19.2	**1.9**	7.9	**1.6**	No Data
	$AUC_{0\text{-last}}$ (nM*h)	**1,337**	1,274	**4,125**	1,123	**7,910**	2,630	**11,479**	No Data
Oral	Dose (mpk)	**10**	10	**10**	10	**5**	5	**5**	No Data
	C_{max} (nM)	**745**	1,443	**1,620**	339	**472**	377	**723**	No Data
	$T_{1/2}$ (h)	**6.3**	1	**6.1**	2.5	**22.4**	7.8	**12.3**	No Data
	$AUC_{0\text{-last}}$	**6,786**	4,467	**15,213**	1,427	**8,720**	2,755	**10,004**	No Data
	Bioavailability (F %)	**48%**	33%	**38%**	14%	**22%**	21%	**17%**	No Data

ERAS-0015 demonstrated good overall ADME and toxicology properties

Assay	Value
Kinetic Solubility (FaSSIF, FeSSIF) (µg/mL)	127, 156
MDR1(A/B,B/A ER)	0.3, 1.7, 5.5
PPB (% Unbound)	0.4 (h), 2.1 (c), 0.4 (d), 0.2 (r), 0.6 (m)
WBS $T_{1/2}$(min)	>289 (h), >289 (d), >289 (r), >289 (m)
BPR, $K_{B/P}$	3.5 (h), 14.2 (c), 1.7 (d), 3.0 (r), 5.3 (m)
MMS(CL_{int} (liver)(mL/min/kg))	87 (h), 287 (c), 23 (d), 31 (r), 197 (m)
HMS(CL_{int} (liver)(mL/min/kg))	51 (h), 272 (c), 73 (d), 104 (r), 408 (m)
CYP450 IC50 (µM) 1A2 / 2C9 / 2C19 / 2D6 / 3A4	50, 1.3, 25, 50, 4.4
GLP Ames	Negative
GLP hERG (IC_{50} µM)	6.0
GLP 28-day repeat dose studies in rat and dog	Completed; finalizing reports

Recent data[1]

[1] Data added since Erasca Nov. 2024 Corporate Presentation
h: human; c: cynomolgus monkey; d: dog; r: rat; m: mouse

ERAS-0015 and ERAS-4001 exhibit competitive profiles that exceed our TPP

ERAS-0015
Pan-RAS
Molecular Glue

Potential best-in-class Pan-RAS molecular glue

- ~5x – 10x greater potency vs. pan-RAS MG in development
- Favorable ADME properties and PK performance in animals vs. pan-RAS MG in development
- Designed to address RASwt activation to prevent resistance vs. mutant-selective inhibitors

ERAS-4001
Pan-KRAS
Inhibitor

Potential first-in-class and best-in-class KRAS inhibitor

- Designed to spare H/NRAS WT
- Wider therapeutic window predicted vs. pan-RAS MG for KRASm solid tumors
- Designed to address KRASwt activation to prevent resistance vs. mutant-selective inhibitors

TPP = target product profile; MG: molecular glue; ADME: absorption, distribution, metabolism, and excretion; PK: pharmacokinetic; WT: wild type; KRASm: KRAS mutant

ERASCA

ERAS-4001 selectively bound KRAS with high affinities, long residence times

SPR-based kinetic biophysical binding characterization of ERAS-4001

Target	KD (nM)	$t_{1/2}$ (s)
KRAS G12D	0.0006	273,079
KRAS G12V	0.0069	30,159
KRAS G12C	0.016	7,724
KRAS WT	0.058	3,409
HRAS WT	117	18.1
NRAS WT	2,660	1.2

ERAS-4001 showed potent activity against both GTP- and GDP-bound KRAS

Assay Class	Assay	Target	ERAS-4001 IC50 (nM)
Biochemical Functional	RAS-RAF Binding Assay (RBD)	RBD KRAS G12D GDP	**1.6**
		RBD KRAS G12D GMPPNP*	**6.8**

* GMPPNP is a nonhydrolyzable GTP analogue intended to approximate GTP-bound KRAS

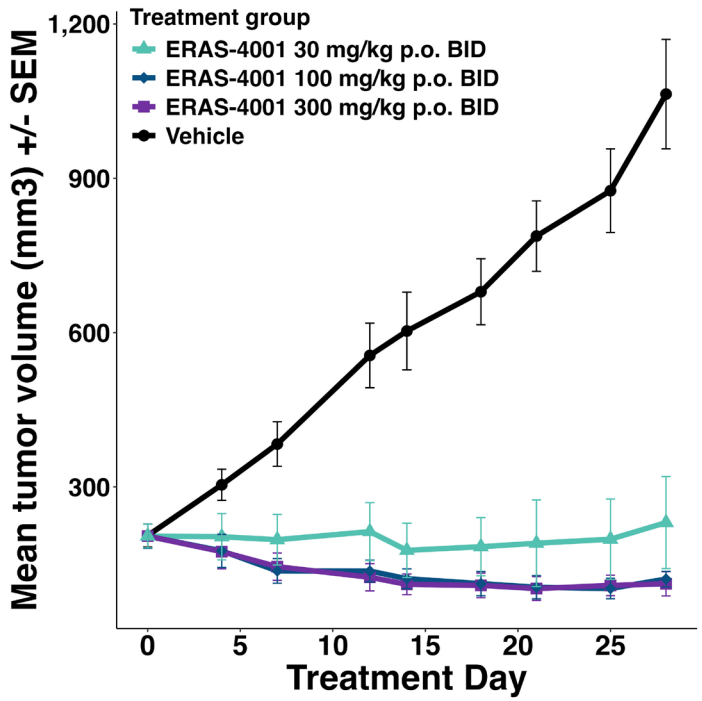
ERAS-4001 potently and selectively inhibited cell growth in KRAS G12X, G13D and WT cell lines

KRAS Mutation	Tumor type	Cell line	ERAS-4001 cell growth inhibition (nM)
KRAS G12D	Pancreatic	AsPC-1	**1.8**
	Pancreatic	Panc 04.03	**1.9**
	Pancreatic	HPAC	**1.0**
	Pancreatic	PK-59	**2.6**
KRAS G12V	Lung	NCI-H727	**3.5**
	Lung	NCI-H441	**0.7**
	Ovary	RKN	**2.3**
	Colorectal	SW620	**9.1**
KRAS G12C	Lung	LU99	**2.7**
	Pancreatic	MIA PaCa-2	**1.1**
	Lung	NCI-H2030	**4.5**
KRAS G12A	Multiple Myeloma	RPMI-8226	**6.5**
	Lung	NCI-H1573	**37.7**
KRAS G13D	Colorectal	LoVo	**5.8**
	Colorectal	HCT-116	**56**
KRAS WT	Lung	NCI-H1975	**10.8**
	Stomach	MKN-1	**3.6**
KRAS Independent	Melanoma	A375	**>2,000**
	Lung	NCI-H226	**3,497**

ERASCA

ERAS-4001: Achieved tumor regression in a KRAS G12D PDAC CDX model at doses at or above 100 mg/kg BID

KRAS G12D CDX Panc 04.03
TGI curves from 28 day repeat dose study



TGI, PD (pERK) and PK ($AUC_{0\text{-last}}$) Summary

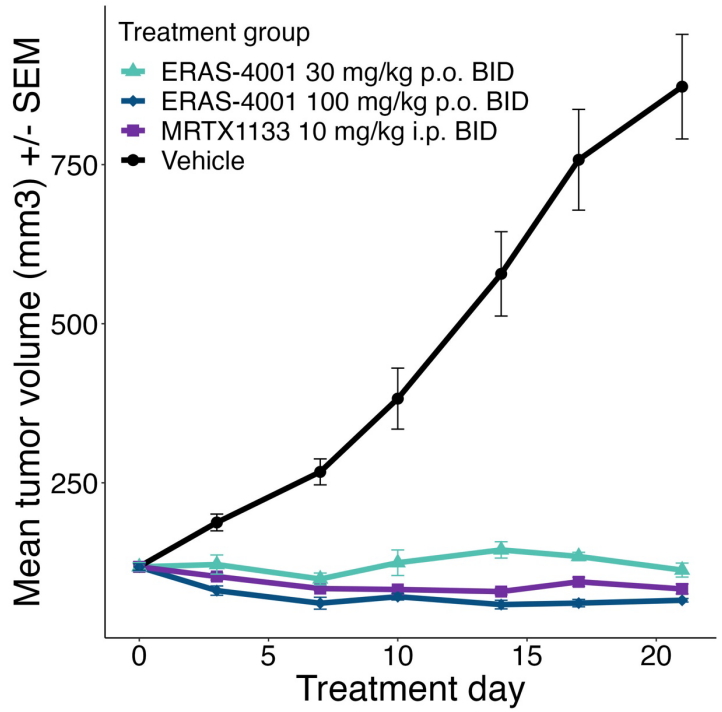
Therapy	Dose	TGI on Day 28	pERK Inhibition at 8 hr	$AUC_{0\text{-last}}$ (nmol/L·h)
ERAS-4001	30 mg/kg	97%	17%	1,547
	100 mg/kg	110%	64%	5,153
	300 mg/kg	111%	80%	12,971

- ERAS-4001 was well tolerated at doses up to 300 mg/kg BID for 28 days (i.e., no dose reductions or holidays; no body weight loss or significant health observations)

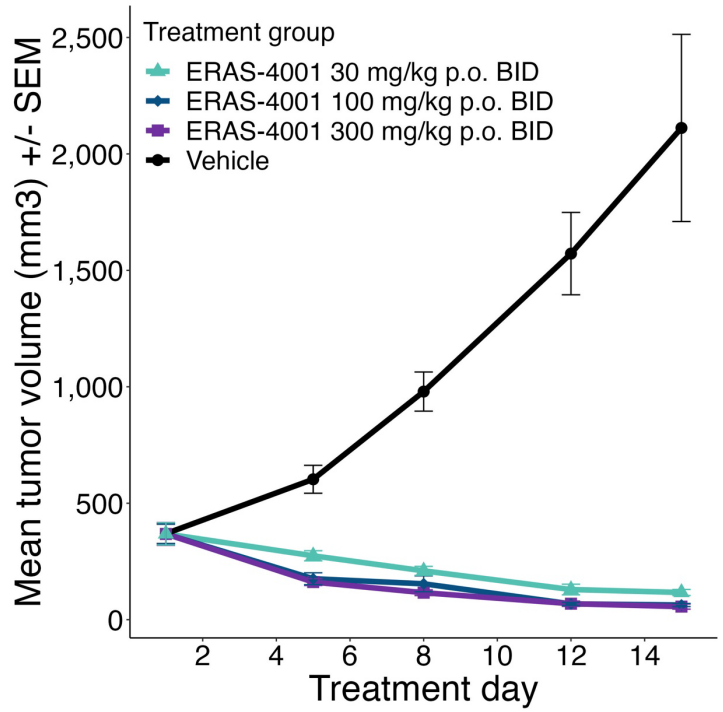
p.o.: orally administered; BID: twice a day; CDX: cell line-derived xenograft; TGI: tumor growth inhibition

ERAS-4001: Achieved tumor regressions in KRAS G12D and G12V CDX models at doses as low as 30 mg/kg BID

TGI in KRAS G12D PDAC CDX PK-59



TGI in KRAS G12V Ovarian CDX RKN

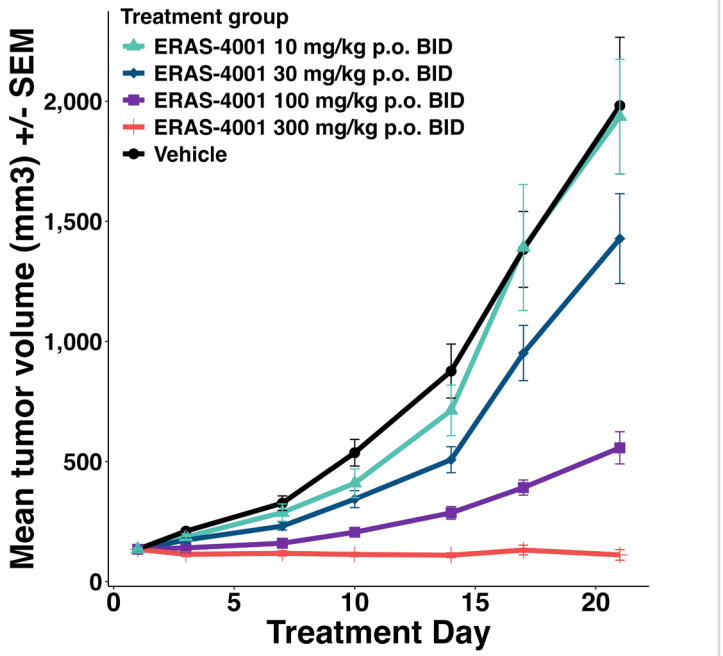


- ERAS-4001 was well tolerated in both studies at doses up to 300 mg/kg BID (i.e., no dose reductions or holidays; no body weight loss or significant health observations)

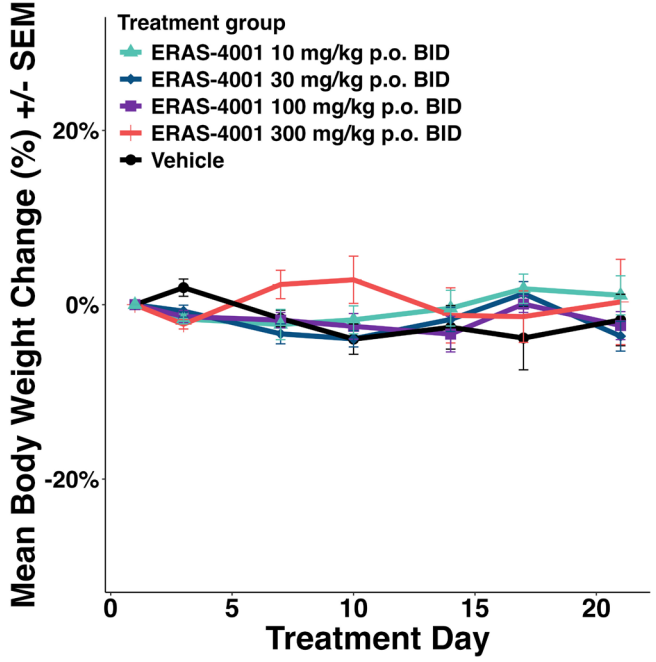
p.o.: orally administered; BID: twice a day; CDX: cell line-derived xenograft; TGI: tumor growth inhibition

ERAS-4001: Achieved tumor regression in a pan-KRASi insensitive KRAS G12V NSCLC CDX model

TGI in KRAS G12V NCI-H727



% Body Weight Change



TGI Summary

Therapy	Dose	TGI on Day 21
ERAS-4001	10 mg/kg	3%
	30 mg/kg	30%
	100 mg/kg	77%
	300 mg/kg	101%

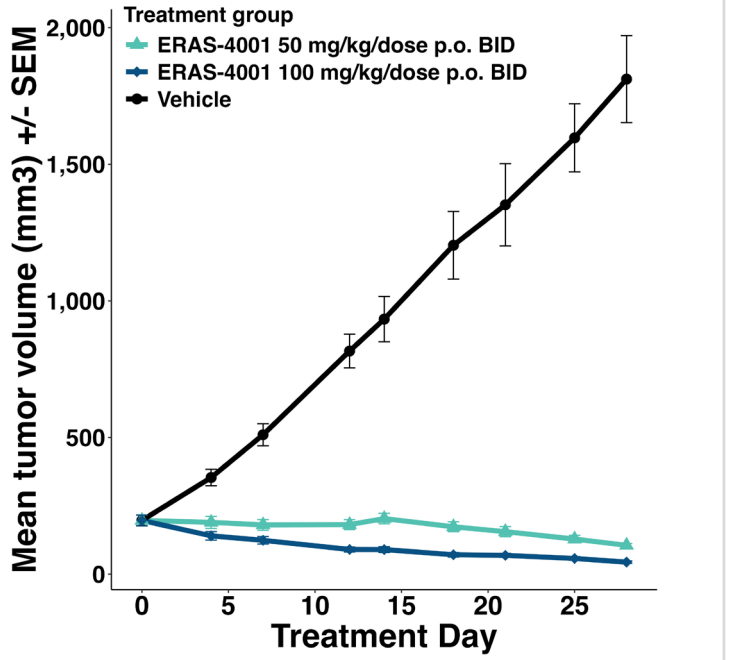
- ERAS-4001 was well tolerated at doses ranging from 10 mg/kg p.o. BID to 100 mg/kg p.o. BID (i.e., no dose holidays or mortality)
- ERAS-4001 at 300 mg/kg p.o. BID showed borderline tolerability with 4 out of 6 mice receiving continuous treatment, one mouse receiving a dose holiday due to body weight loss on days 16-21, and one mouse death on day 13
- Observed borderline tolerability may be model and/or study specific; ERAS-4001 at 300 mg/kg p.o. BID was well tolerated in the Panc 04.03 CDX TGI study (no dose holidays or mortality)

p.o.: orally administered; BID: twice a day; CDX: cell line-derived xenograft; TGI: tumor growth inhibition

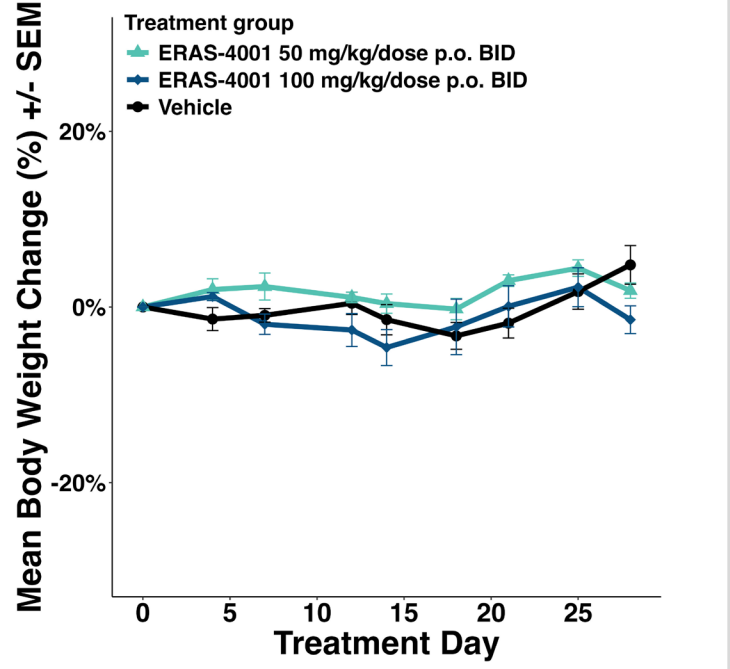
ERASCA

ERAS-4001: Achieved tumor regression in KRAS G12D PDAC CDX model

TGI in KRAS G12D HPAC



% Body Weight Change



TGI Summary

Therapy	Dose	TGI on Day 28
ERAS-4001	50 mg/kg	106%
	100 mg/kg	109%

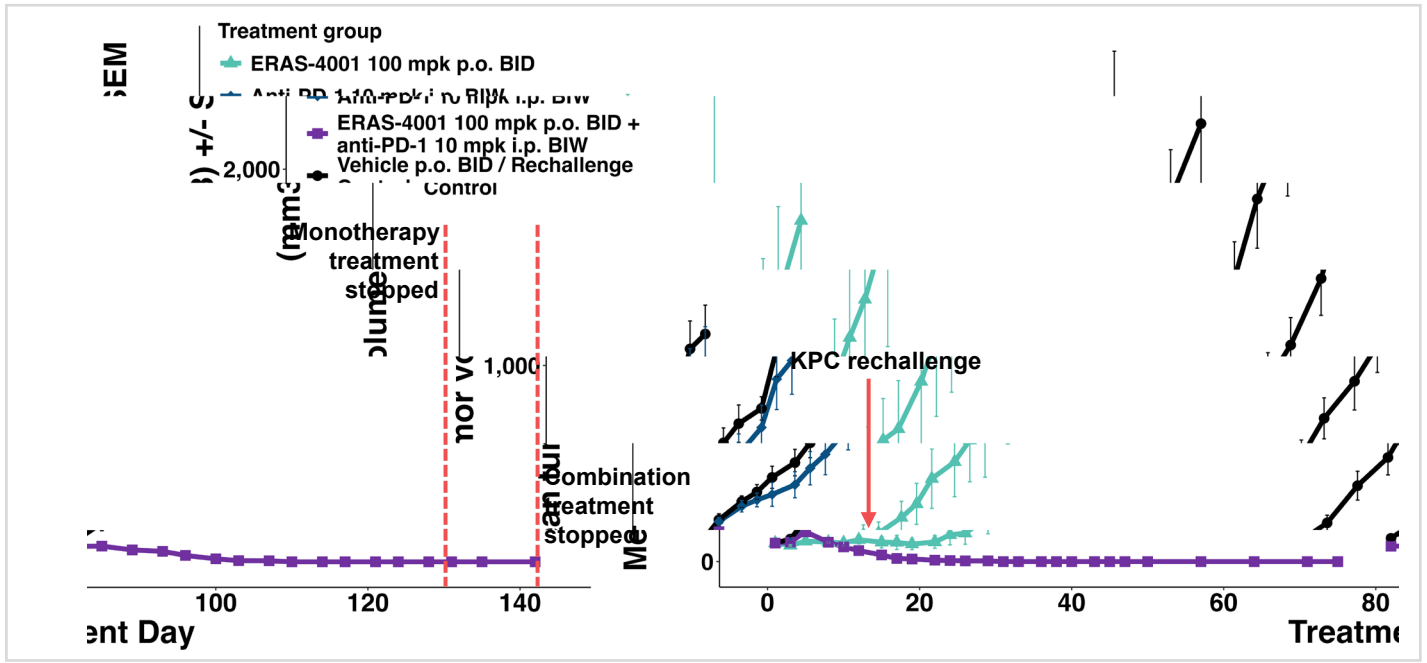
- ERAS-4001 achieved tumor regressions at 50 and 100 mg/kg p.o. BID doses, reproducing the in vivo activity previously observed in external studies
- ERAS-4001 was well tolerated at doses up to 100 mg/kg BID (i.e., no dose reductions or holidays; no body weight loss or significant health observations)

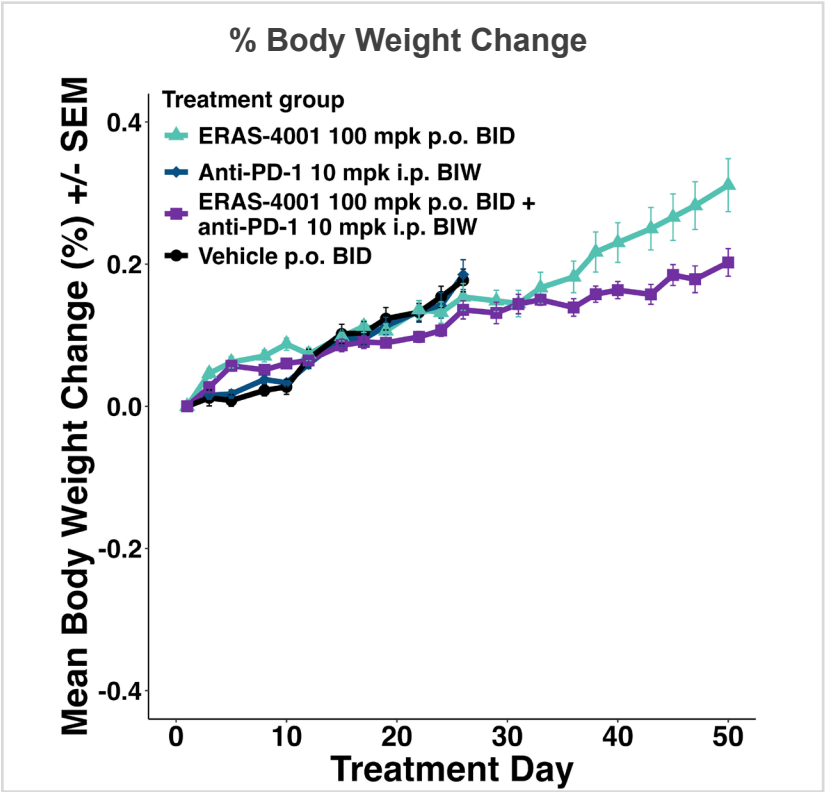
p.o.: orally administered; BID: twice a day; CDX: cell line-derived xenograft; TGI: tumor growth inhibition

ERAS-4001 + anti-PD-1: Combination benefit in a syngeneic KRAS G12D PDAC model

TGI of ERAS-4001 +/- anti-PD-1 in KRAS G12D PDX model

All treatment stopped by day 38. KPC rechallenge demonstrated immune memory effect by a contralateral inoculation of KPC cells in combination treatment groups that resulted in tumor formation.





	Anti-PD-1	ERAS-4001	Anti-PD-1 + ERAS-4001
TGI at day 26	12.7%	95.3%	108.5%
Complete response rate at day 50	0% (0/7)	29% (2/7)	100% (7/7)

PDX: patient-derived xenograft; p.o.: orally administered; i.p. intraperitoneally; BID: twice a day; BIW: twice a week; TGI: tumor growth inhibition

ERASCA

ERAS-4001 showed promising PK and oral bioavailability in mouse, rat, and dog

	PK Parameter	Mouse	Rat	Dog
IV	Dose (mpk)	1.7	2	2.1
	C_0 (nM)	1,722	1,083	1,669
	$T_{1/2}$ (h)	1.9	3	5.8
	V_d (L/kg)	5.16	10.1	14.1
	Cl (mL/Kg/min)	45.5	70.9	53.1
	$AUC_{0\text{-last}}$ (nM·h)	938	615	827
Oral	Dose (mpk)	30.3	30.9	15.3
	C_{max} (nM)	2,090	584	323
	T_{max} (h)	1.5	4	0.5
	$T_{1/2}$ (h)	1.5	2.3	5.4
	$AUC_{0\text{-last}}$ (nM·h)	4,498	2,562	962
	Bioavailability (F %)	27	27	16

ERASCA

ERAS-4001 demonstrated good overall ADME and toxicology properties

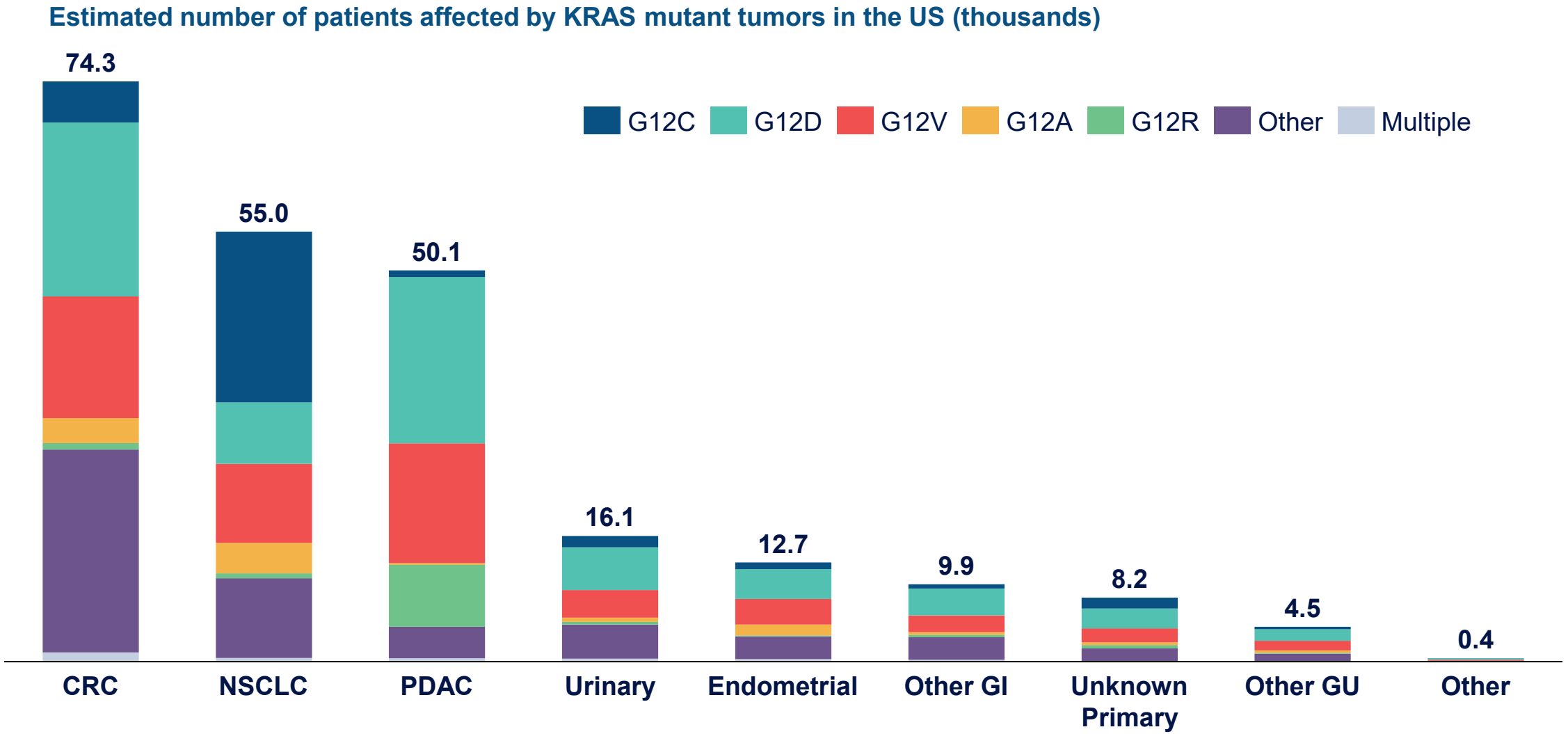
Assay	Value
CLogP / tPSA	3.7 / 111.6
pKa / Kinetic Solubility (pH@7.4)	9.0 / 113.0 µM
PPB (Unbound %)	1.3 (h) / 1.6 (d) / 0.8 (r) / 1.5 (m)
HMS CL_{int} (mL/min/kg)	38.8 (h) / 212.3 (d)/ 511.6 (r)/ 830 (m)
IS9 CL_{int} (mL/min/kg)	<9.6 (h) / 12.5 (d) / - / -
MDR1 A to B (P_{app} (10^{-6} cm/s) /Efflux Ratio	0.9 / 26.7
$K_{B/P}$ H / D / M (blood/plasma)	0.6 / 0.7 / 0.9
CYP450 IC50 (µM) 1A2 / 2C9 / 2C19 / 2D6 / 3A4	>50 / 37.7 / 24.4 / 9.9 / 6.6
GLP Ames	Negative
GLP hERG IC_{50} (µM)	<1
GLP cardiovascular study in dogs	No observed QTc prolongation
GLP 28-day repeat dose studies in rat and dog	Completed; finalizing reports

Recent data[1]

[1] Data added since Erasca Nov. 2024 Corporate Presentation
h: human; d: dog; r: rat; m: mouse

ERASCA

KRAS alterations found most commonly in CRC, PDAC and NSCLC



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.
CRC: colorectal cancer; NSCLC: non-small cell lung cancer; PDAC: pancreatic ductal adenocarcinoma; GI: gastrointestinal; GU: genitourinary

ERASCA

Innovative CDP designed to maximize efficiency and POS

01

Patients

Focus on tumor types with largest number of potential patients to allow efficient clinical trial enrollment and potential for maximum patient benefit

02

Early combo assessment

Parallel pursuit of monotherapy proof-of-concept & combination dose finding to expedite development

03

Data-driven

Efficiently use clinical data to prioritize mono and combo approaches
De-risk subsequent trials by using RWD to understand benchmarks, contribution of components

04

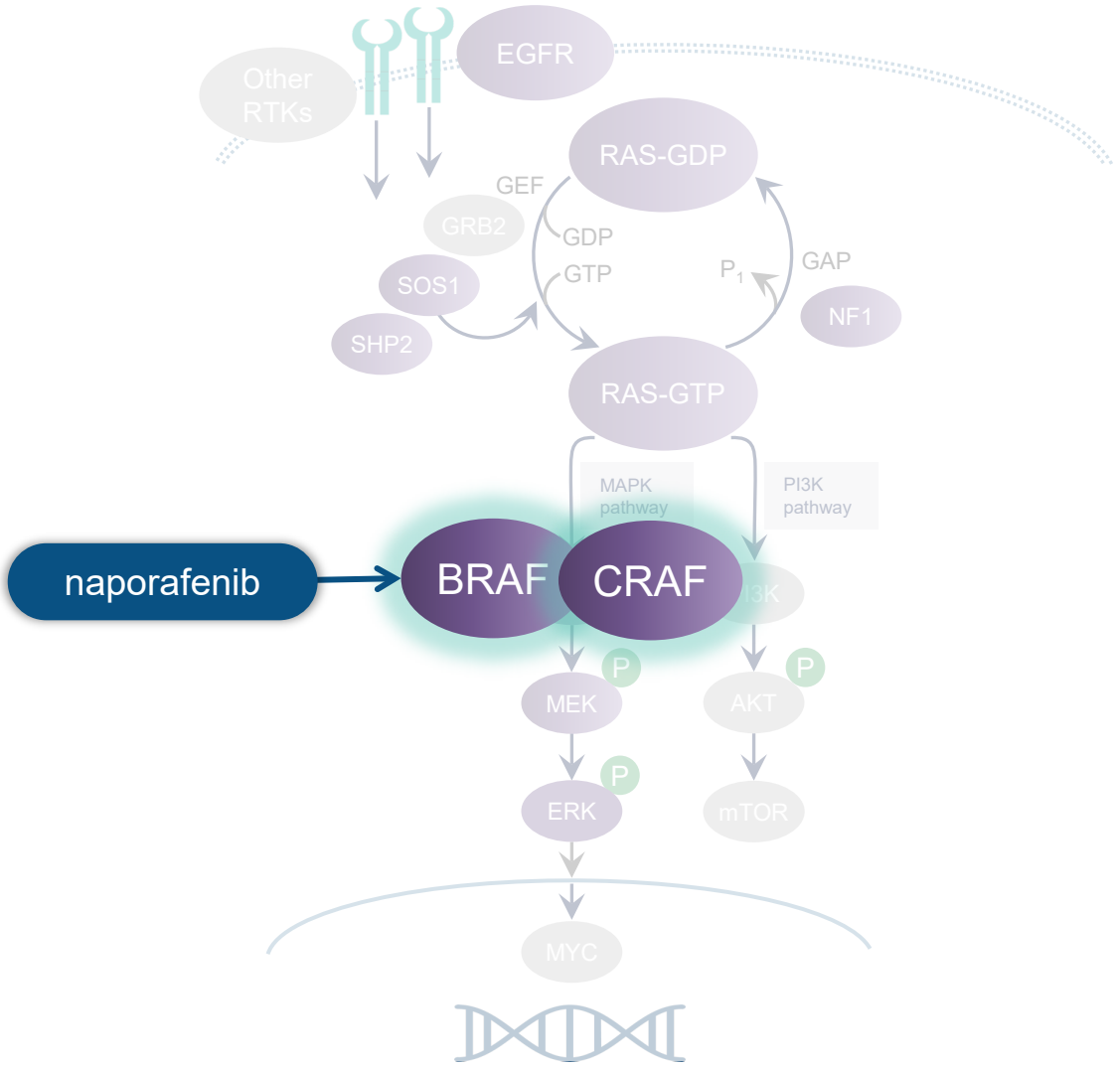
Portfolio

Capitalize on unique portfolio of molecules with complementary RAS inhibitory mechanisms (S-IIP binding vs. MG) and target profiles (pan-KRAS vs. pan-RAS)

POS: probability of success; CDP: clinical development plan; RWD: real world data; MG: molecular glue; S-IIP: Switch-II pocket

ERASCA

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



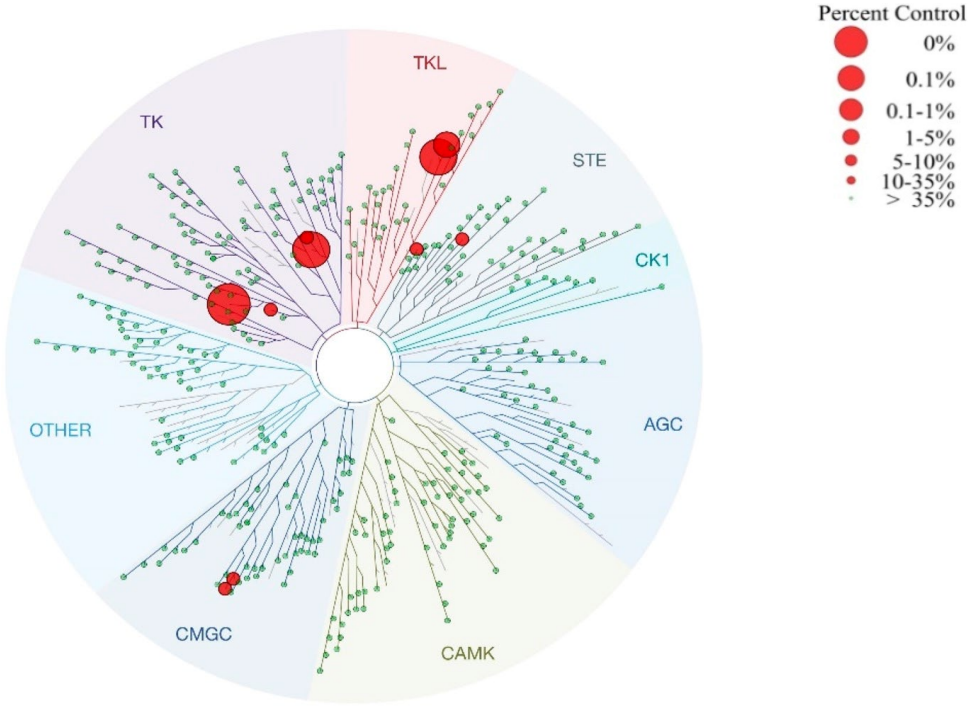
- Potently **inhibits CRAF and BRAF** and blocks downstream RAS/MAPK pathway signaling
- **Synergizes with trametinib** which targets MEK, the immediate downstream node of RAF
- Selectivity for BRAF and CRAF over ARAF is predicted to enable a **better therapeutic window**
- **Does not result in paradoxical 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 Inhibition (IC_{50})	**0.1**
Biochemical BRAF Inhibition (IC_{50})	**0.2**
Biochemical ARAF Inhibition (IC_{50})	**6.4**

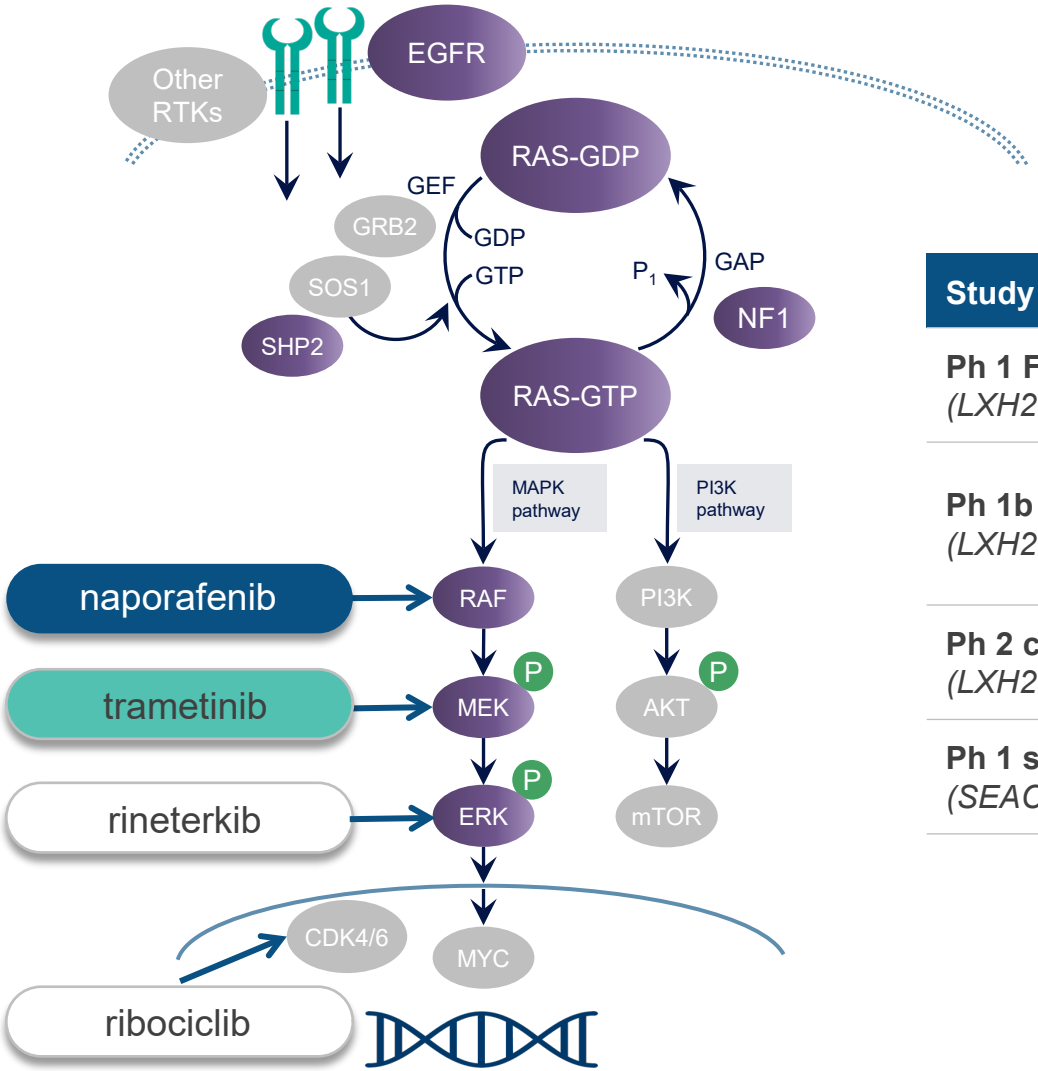
Biochemical activity of naporafenib across 456 kinases (KINOMEscan)



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

ERASCA

Naporafenib has been dosed in more than 600 patients to date, establishing its safety, tolerability, and proof of concept in NRASm melanoma



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
Ph 1 study *(SEACRAFT-1)*	Evaluating safety and efficacy (+ trametinib) in patients with RAS Q61X solid tumors	52*

Total size of safety database > 600 patients
(includes monotherapy and combinations)

* As of SEACRAFT-1 DCO 03Sep2024

ERASCA

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)

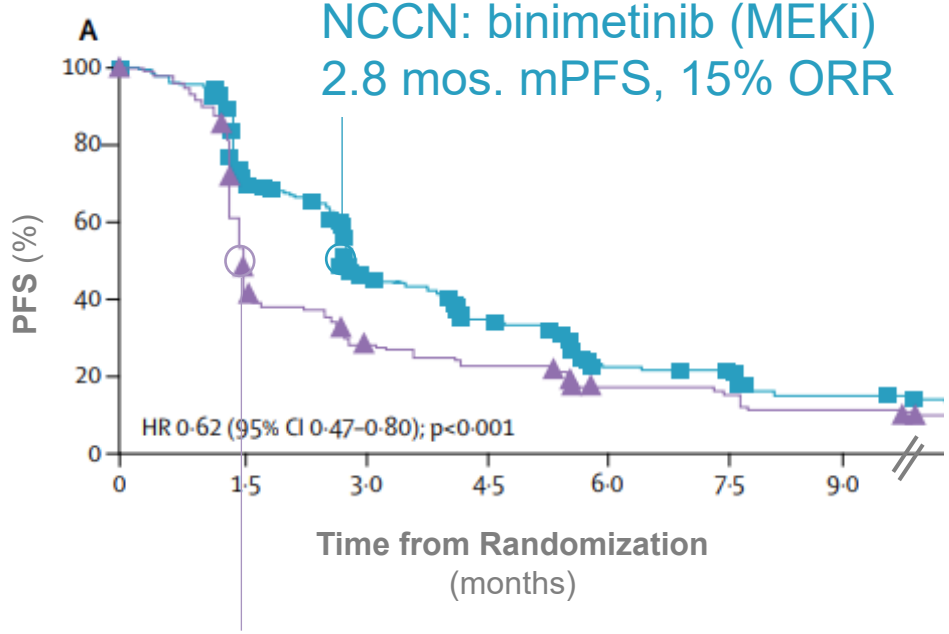
Naporafenib (pan-RAFi)

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

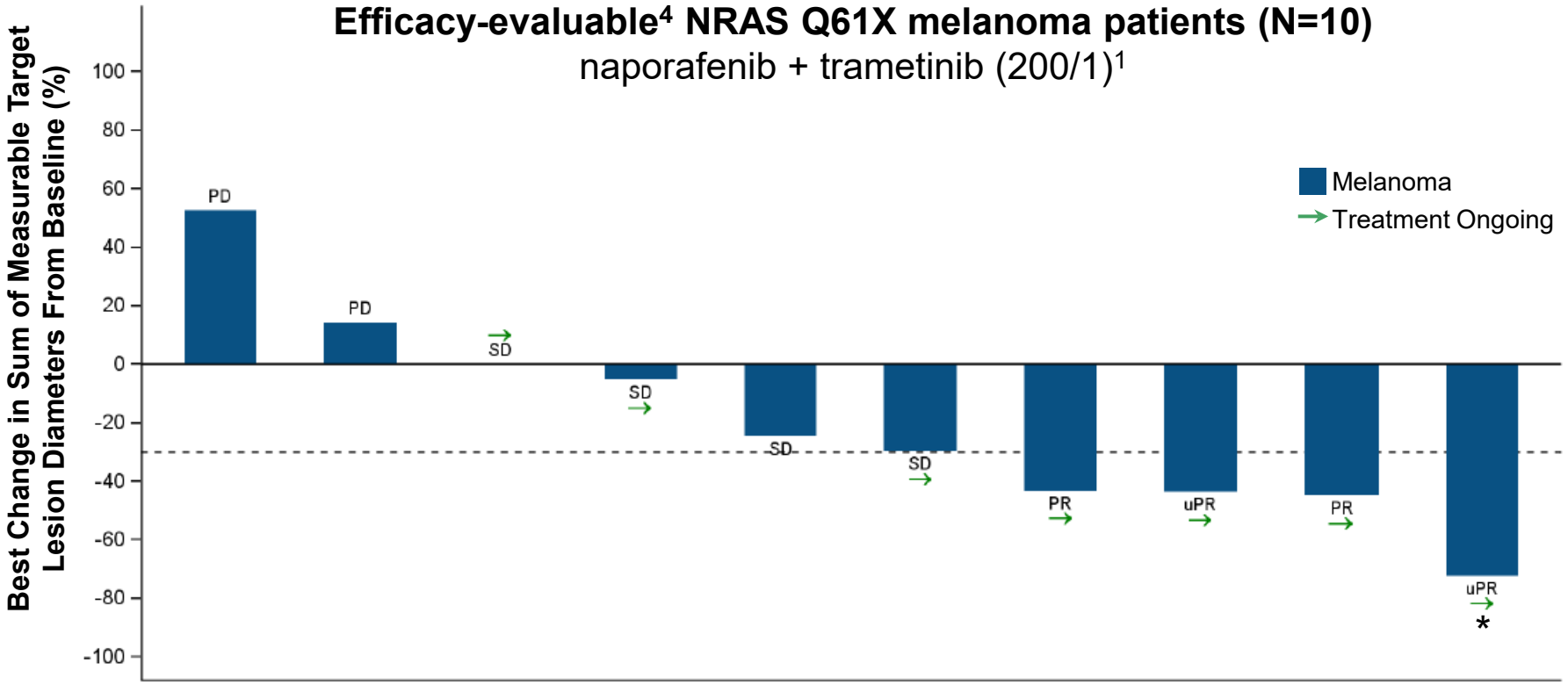


Adapted from Dummer et al. (Lancet Oncol (2017) 18:435-445)
Note: Benchmarks are most relevant for SC-2 mPFS, although study was conducted in a 1/2L setting

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

ERASCA

Positive preliminary efficacy observed in SEACRAFT-1 melanoma cohort bolsters rationale for pursuing tissue-specific NRASm melanoma indication in SEACRAFT-2



40% (4/10) response rate (3 confirmed PRs, 1 uPR[2])

80% (8/10) disease control rate[3]

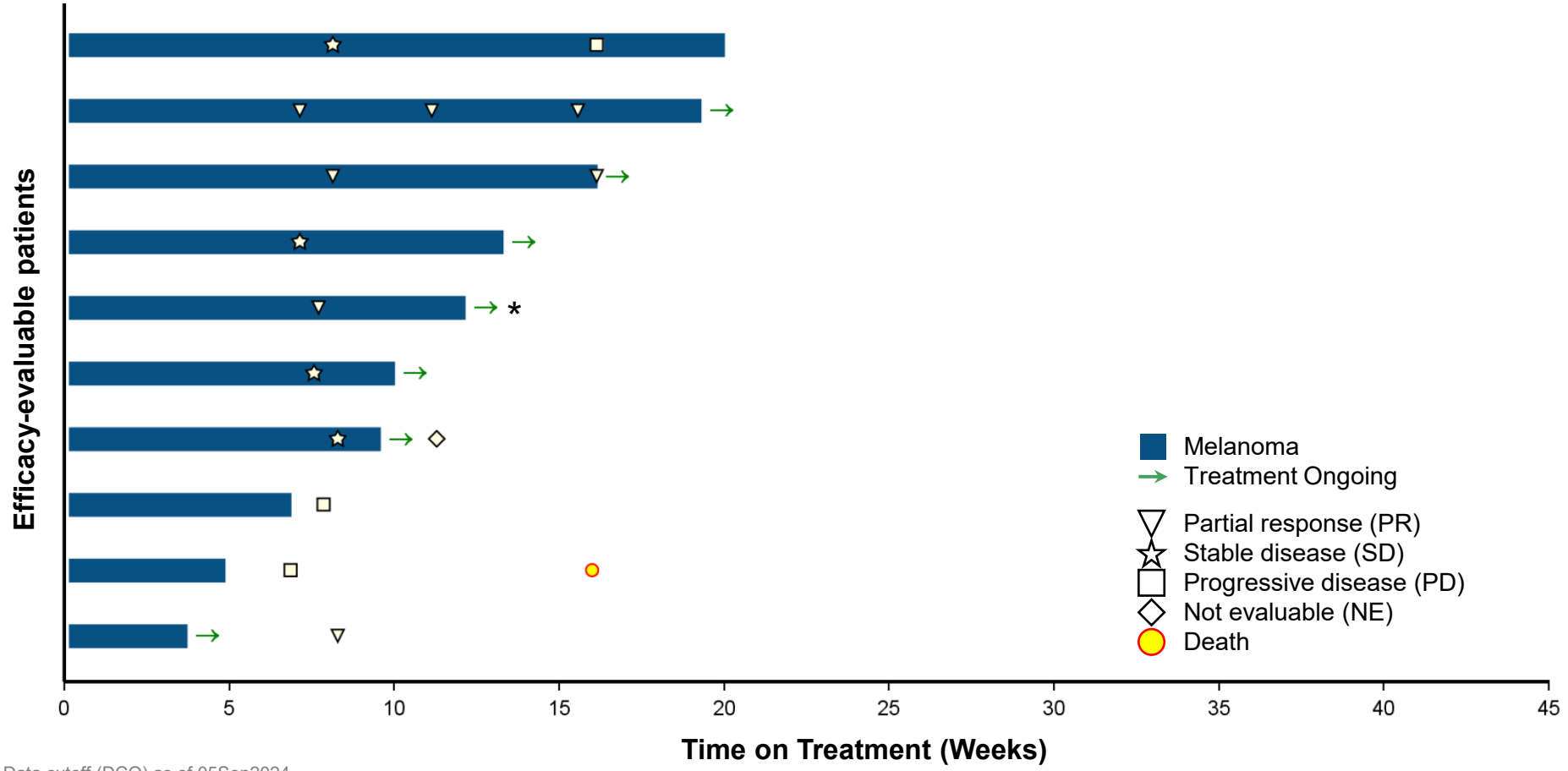
Response observed in patient with mucosal melanoma, a population that had not been enrolled in previous studies

Data cutoff (DCO) as of 05Sep2024
* Patient response was confirmed after DCO
[1] naporafenib 200 mg BID + trametinib 1 mg QD (BID: twice a day; QD: once a day)
[2] Melanoma patient with uPR continuing study treatment with next scan pending as of the time of data disclosure
[3] Disease control rate (DCR) = CR + PR + SD; uPR is included
[4] Defined as patients who received at least one dose of study drug, had measurable disease at baseline per RECIST, and had at least one post-baseline response assessment
NRASm: NRAS mutant; PR: partial response; uPR: unconfirmed partial response; PD: progressive disease: SD: stable disease

Early but encouraging durability observed in SEACRAFT-1 melanoma cohort

Duration of treatment in efficacy-evaluable[2] NRAS Q61X melanoma patients (N=10)

naporafenib + trametinib (200/1)[1]



70% (7/10) of patients remained on treatment as of data cutoff, including **all confirmed and unconfirmed responders**

Data cutoff (DCO) as of 05Sep2024

* Patient response was confirmed after DCO

[1] naporafenib 200 mg BID + trametinib 1 mg QD (BID: twice a day; QD: once a day)

[2] Defined as patients who received at least one dose of study drug, had measurable disease at baseline per RECIST, and had at least one post-baseline response assessment

ERASCA

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

	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
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**
mOS months	~7 months+			**~13 months**	**~14 months**

ORR 40% observed in SEACRAFT-1 NRASm melanoma cohort[5]

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

US FDA Fast Track Designation:

Compelling efficacy for both doses evaluated to date

High unmet medical need for NRASm melanoma patients post-IO

* Assumes trametinib efficacy is similar published binimetinib efficacy results
+ Data disclosed and further described in Erasca's Annual Report on Form 10-K, filed with the SEC on 27 Mar 2024 (p 21)
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 Data disclosed and further described in an oral presentation on 27 Oct 2024 at the 36th EORTC-NCI-AACR (ENA) Symposium
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

Mandatory primary rash prophylaxis in SEACRAFT-1 significantly decreased incidence/ severity of derm tox, reduced drug discontinuations due to AEs, and improved RDI

	CLXH254X2102 [200/1]	CLXH254C12201 [200/1]	SEACRAFT-1 [200/1]
	N = 54	N = 30	N = 52
Pts with dermatologic* toxicities, n(%)	49 (90.7)	26 (86.7)	38 (73.1)
Pts with G≥3 dermatologic* toxicities, n(%)	20 (37.0)	11 (36.7)	6 (11.5)
Pts with dermatitis acneiform, n(%)	17 (31.5)	9 (30.0)	11 (21.2)
Pts with G≥3 dermatitis acneiform, n(%)	4 (7.4)	1 (3.3)	1 (1.9)
Pts with rash, n(%)	23 (42.6)	11 (36.7)	22 (42.3)
Pts with G≥3 rash, n(%)	9 (16.7)	4 (13.3)	3 (5.8)
TEAE leading to permanent discontinuation of study treatment n(%)	10 (18.5)	6 (20.0)	5 (9.6)
	5/10 for skin tox TEAE	5/6 for skin tox TEAE	0 for skin tox TEAE
Median RDI, % [naporafenib / trametinib]	66.3 / 59.2	57.5 / 62.4	98.5 /100

With mandatory primary prophylaxis in SEACRAFT-1:

Decreased overall and Grade ≥3 frequency of dermatologic toxicities (including dermatitis acneiform and rash)

No patient has permanently discontinued naporafenib (or trametinib) due to dermatologic toxicity TEAE

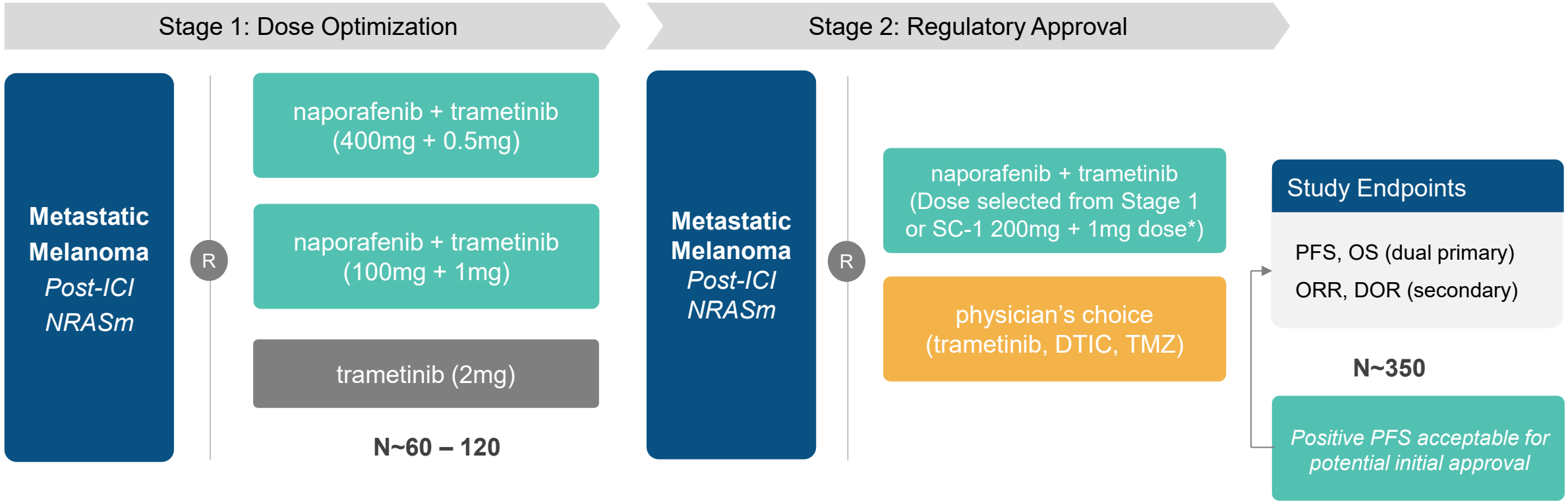
Improved relative dose intensity (RDI)

200/1 = 200mg naporafenib BID + trametinib 1mg QD; G=CTCAE grade; Pts=patients; RDI=relative dose intensity; TEAE=treatment emergent adverse event
*"Dermatologic" includes MedDRA HLTs (rashes, eruptions and exanthems NEC; bullous conditions; dermatitis and eczema; exfoliative conditions) and the following PTs: dermatitis acneiform, drug eruption, drug reaction with eosinophilia and systemic symptoms, palmar-plantar erythrodysaesthesia, severe cutaneous adverse reaction, toxic skin eruption, photosensitivity reaction, skin fissures, pruritis
Data cut offs- CLXH254C12201 30Dec2022; CLXH254X2102 04Aug2022; SEACRAFT-1 03Sep2024
Due to differences between trial designs and subject characteristics, comparing data across different trials may not be a reliable indicator of data

ERASCA

Pivotal Phase 3 trial design capitalizes on promising efficacy signals and potentially support successful registration

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



* 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 (SC-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

Anticipated key milestones and clinical trial readouts

Program *Mechanism*	**Trial Name** *Indication* *(Combo partner if applicable)*	**Completed or Anticipated Milestone**
ERAS-0015 *Pan-RAS molecular glue*	**AURORAS-1** *RASm solid tumors*	• **Q4 2024:** IND filed with China CDE[1] • **Mid-Q2 2025:** IND filing with US FDA • **2026:** Ph 1 monotherapy data[2]
ERAS-4001 *Pan-KRAS inhibitor*	**BOREALIS-1** *KRASm solid tumors*	• **Q2 2025:** IND filing with US FDA • **2026:** Ph 1 monotherapy data[2]
Naporafenib *Pan-RAF inhibitor*	**SEACRAFT-2** *NRASm Melanoma* *(+ trametinib)*	• **H2 2025:** Ph 3 stage 1 randomized dose optimization data[2]

[1] IND filed by Joyo Pharmatech; CDE = Center for Drug Evaluation of China's National Medical Products Administration (NMPA)
[2] 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 the RAS/MAPK pathway (Shokat, UCSF; Lito, MSKCC; Rodriguez-Viciana, UCL; Cichowski, HMS; Blacklow, HMS; Corcoran, MGH), precision oncology (Demetri, DFCI; Bernards, NKI), 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

PHASE 3 COMPANY WITH TWO ADDITIONAL PROGRAMS ENTERING CLINIC IN 2025

Differentiated programs including naporafenib, a Phase 3 pan-RAF inhibitor for NRASm melanoma, and a potential best-in-class RAS franchise composed of a pan-RAS molecular glue and pan-KRASi

MULTIPLE POTENTIAL NEAR-TERM AND LONG-TERM VALUE DRIVERS

Focused clinical development plan with multiple clinical readouts

ERASCA


ERASCA
THANK YOU!

ERAS-0015 and ERAS-4001 exhibit competitive profiles that exceed our TPP

	Preclinical (in vitro and in vivo) Potency[1]		OBA[2]	IP[3]
ERAS-0015 Pan-RAS Molecular Glue	KRAS G12D: 0.2 – 13.3 nM KRAS G12V: 0.4 – 2.5 nM KRAS G12C: 0.8 – 1.4 nM KRAS G12X: 4.1 – 7.4 nM KRAS G13D: 2.8 – 5.5 nM KRAS WT: 4.1 – 13.8 nM H/NRAS WT: Active	***KRAS G12D:*** Tumor regression in PK-59 CDX model at 0.3 mpk PO QD ***KRAS G12V:*** Tumor regression in NCI-H727 CDX model at 1 mpk PO QD ***KRAS G12R:*** Tumor regression in PSN1 CDX model at 5 mpk PO QD	Mouse: 48% Rat: 38% Dog: 22% Monkey: 17%	• IP exclusivity expected through **2043** • No patentability roadblocks identified to date
ERAS-4001 Pan-KRAS Inhibitor	KRAS G12D: 1.0 – 2.6 nM KRAS G12V: 0.7 – 9.1 nM KRAS G12C: 1.1 – 4.5 nM KRAS G12X: 6.5 – 37.7 nM KRAS G13D: 5.8 – 56.0 nM KRAS WT: 3.6 – 10.8 nM H/NRAS WT: No activity	***KRAS G12D:*** Tumor regression in Panc04.03, PK-59, and LU-01-1381 CDX/PDX models at 30 – 100 mpk PO BID; combo with anti-PD-1 achieved complete disappearance of tumors in all mice (7/7) on D31 at 100 mpk PO BID ***KRAS G12V:*** Tumor regression in RKN and NCI-H727 CDX models at 30 – 300 mpk PO BID	Mouse: 27% Rat: 5 – 27% (variable PK in rat) Dog: 16%	• IP exclusivity expected through **2043** • No patentability roadblocks identified to date

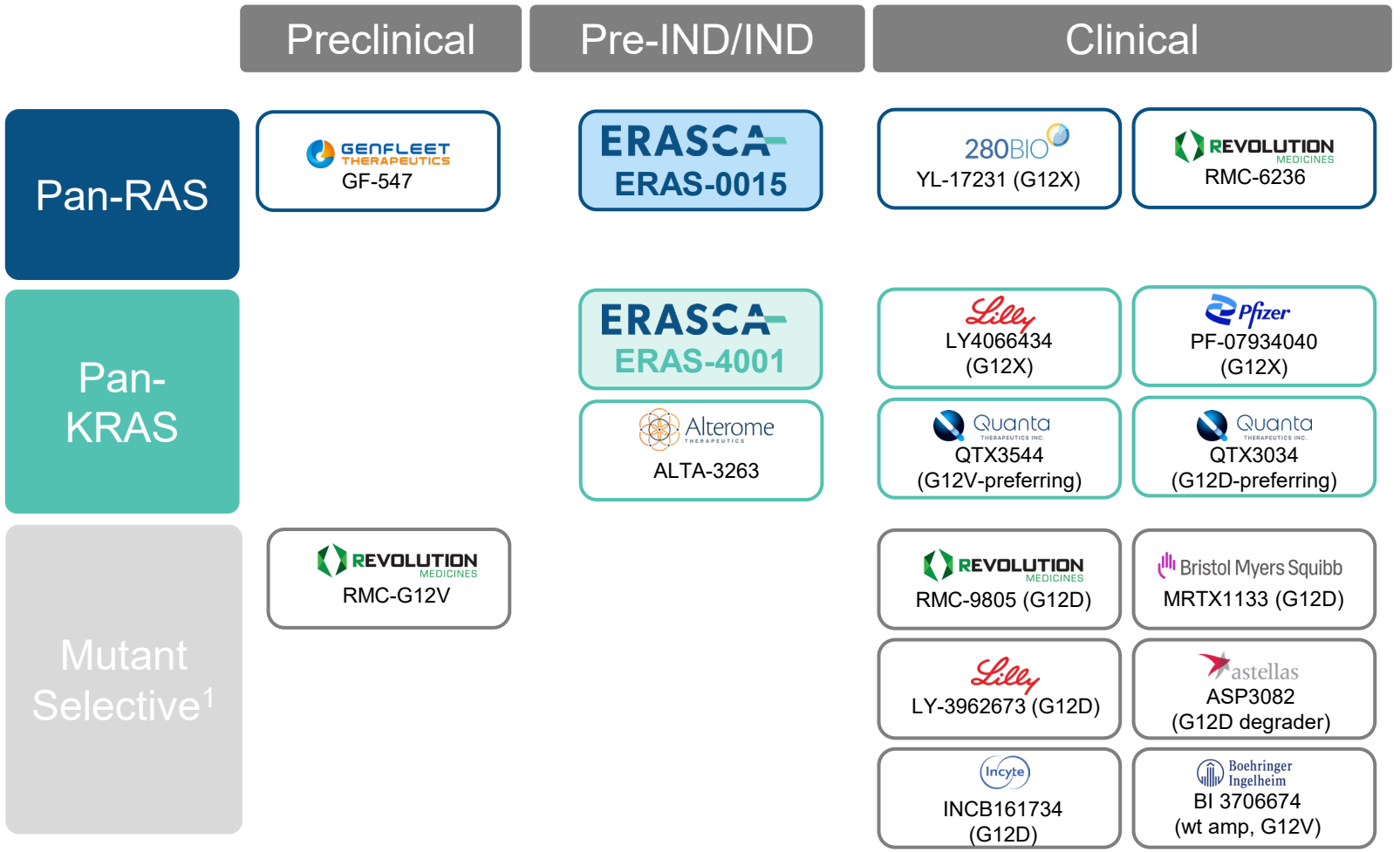
Potential BIC **Pan-RAS MG** for RASm solid tumors, which showed ~5x – 10x greater potency and favorable ADME properties and PK performance in animal species (vs. current Pan-RAS MG in development)

Potential FIC/BIC **Pan-KRAS** or **"KRAS-selective" SMi** that spared H/NRAS WT, predicted to provide a wider therapeutic window (vs. Pan-RAS MG) for KRASm solid tumors and address KRASwt activation to prevent resistance (vs. mutant-selective inhibitors)

KRAS-selective SMi + **Pan-RAS MG** "RASKlamp" combo could uniquely shut down MAPK signaling in KRASm solid tumors

TPP: target product profile; OBA: oral bioavailability; IP: intellectual property; FIC: first-in-class; BIC: best-in-class; WT: wildtype; SMi: small molecule inhibitor; MG: molecular glue; [1] in vitro potency assessed by CTG 2D and 3D-cell proliferation assay IC50s; [2] OBA assessed by %F; [3] IP includes composition of matter, methods of use, and methods of making licensed compounds; date is absent any patent term adjustments or extensions

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



Comments on Class

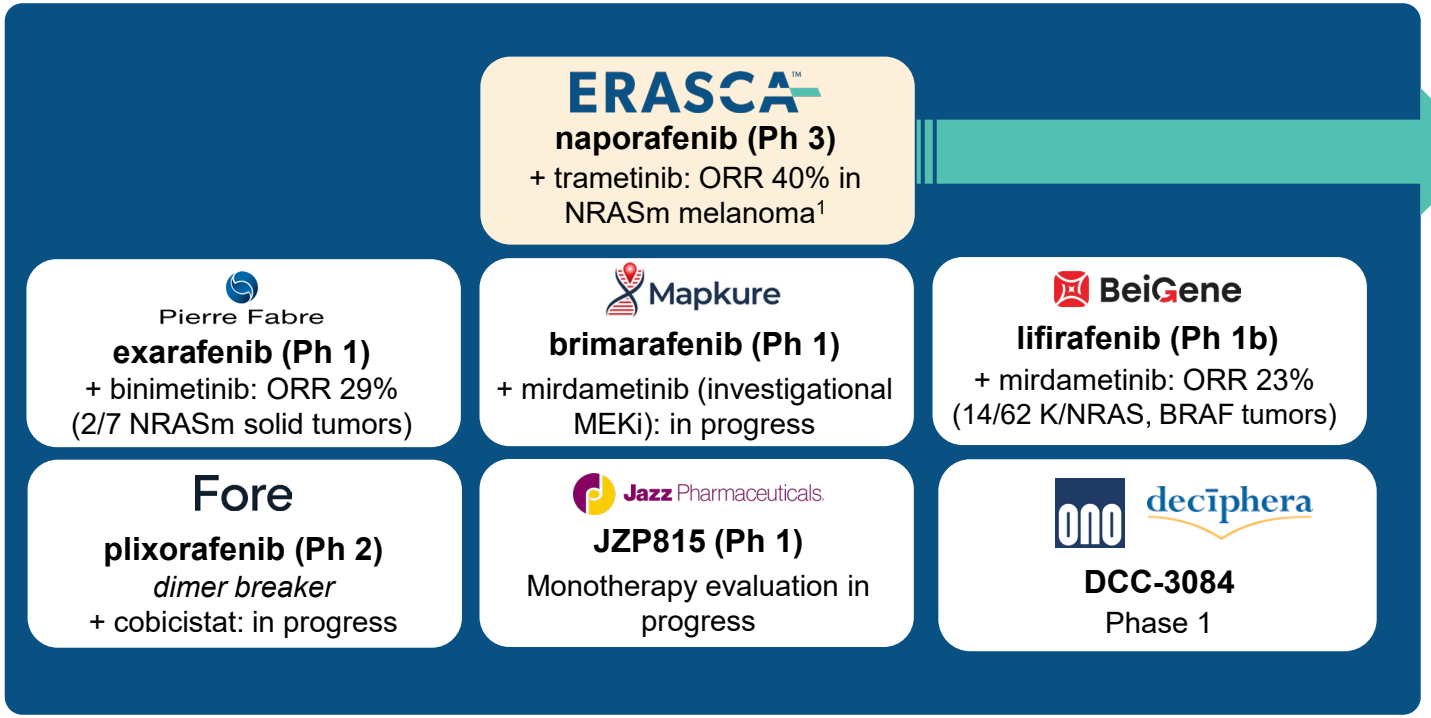
- ⊕ Encouraging preliminary clinical data
- ⊕ Inhibition of the GTP state has potential to better address pERK rebound
- ⊖ Tolerability, combinability may be challenging

- ⊕ Opportunity for a wider 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 and wt-sparing
- ⊖ Oral bioavailability has 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

Naporafenib has the potential to be a first-in-class targeted therapy to address unmet need in NRASm melanoma



Most advanced pan-RAF inhibitor

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

PoC established

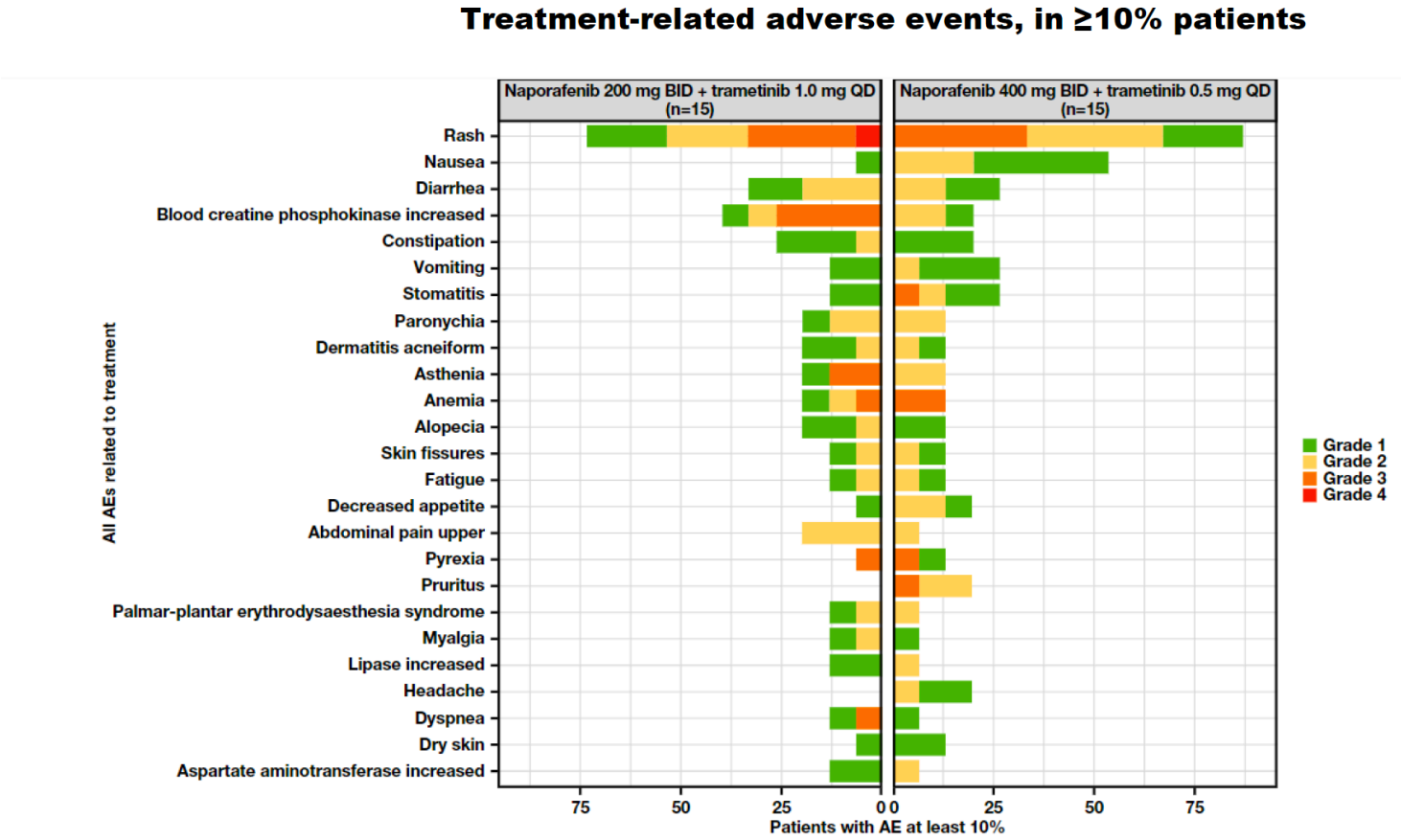
- Evaluating naporafenib where it has already shown PoC (NRASm melanoma)

Strong complementarity with Erasca pipeline

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

ORR: overall response rate; SOC: standard of care; PoC: proof-of-concept
1 Data disclosed and further described in an oral presentation on 27 Oct 2024 at the 36th EORTC-NCI-AACR (ENA) Symposium

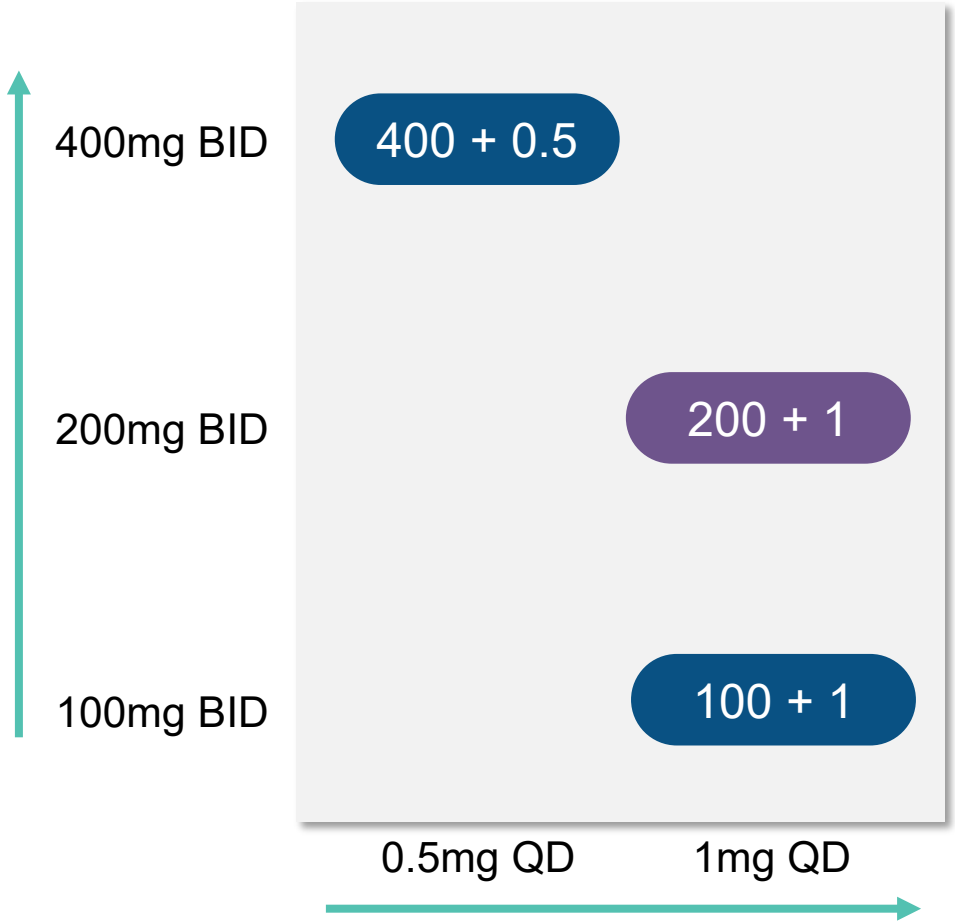
Naporafenib + trametinib demonstrated a favorable, manageable AE profile



- 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



naporafenib
range of potentially efficacious doses*

trametinib
range of potentially efficacious doses*

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

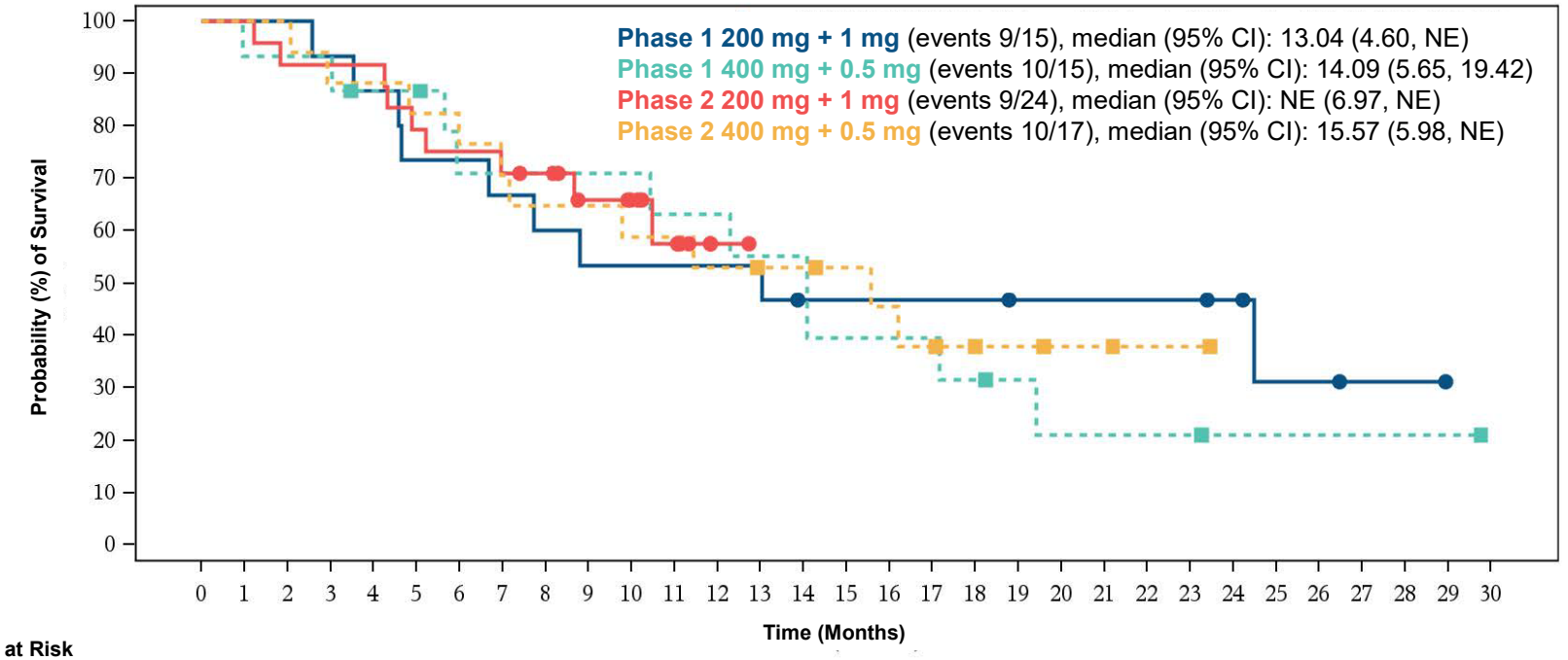
SEACRAFT-1 dose

SEACRAFT-2 dose

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

ERASCA

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.