UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 9, 2023

Erasca, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-40602**	**83-1217027**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

3115 Merryfield Row Suite 300 San Diego, California	**92121**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (858) 465-6511

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.0001 par value per share	ERAS	NASDAQ Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On January 9, 2023, representatives of Erasca, Inc. (the Company) will be presenting at the J.P. Morgan Healthcare Conference and will be attending meetings with investors and analysts during the week in connection with the conference. During the presentation and the meetings, the Company will present the corporate presentation attached as Exhibit 99.1 to this report, which is incorporated herein by reference.

The Company's updated corporate presentation will be posted to the Company's website, www.erasca.com. The Company plans to use its website to disseminate future updates to its corporate presentation and does not intend to file or furnish a Form 8-K alerting investors each time the presentation is updated.

The information set forth in this Item 7.01 is being furnished pursuant to Item 7.01 and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the Exchange Act), or otherwise subject to the liabilities of that section, and it shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or under the Exchange Act, whether made before or after the date hereof, except as expressly provided by specific reference in such a filing.

By filing this report and furnishing the information in this Item 7.01, the Company makes no admission as to the materiality of Item 7.01 in this report or the presentation available on the Company's website. The information contained in the presentation is summary information that is intended to be considered in the context of the Company's filings with the Securities and Exchange Commission (the SEC) and other public announcements that the Company makes, by press release or otherwise, from time to time. The Company undertakes no duty or obligation to publicly update or revise the information contained in this report, although it may do so from time to time as its management believes is appropriate or as required by applicable law. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases, by updating the Company's website or through other public disclosure.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Erasca, Inc. Corporate Presentation, dated January 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Erasca, Inc.

Date: January 9, 2023

By: /s/ Ebun Garner
Ebun Garner, General Counsel

Exhibit 99.1

ERASCA

On a Journey to Erase Cancer

Erasca Corporate Presentation

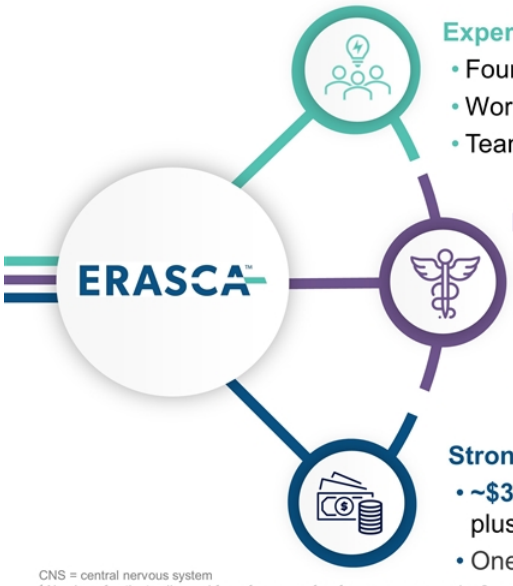
January 2023

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, 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, 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 are early in our development efforts and have only five product candidates in clinical development and all of our other development efforts are in the preclinical or development stage; the retrospective analysis of pooled clinical data for ERAS-007 and ERAS-601 covers multiple clinical trials with different designs, inclusion criteria, and dosing regimens, which cannot be directly compared, and therefore may not be a reliable indicator of efficacy and safety data; interim 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; 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 and acquisitions 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; our ability to fund our operating plans with our current cash, cash equivalents, and investments; our ability to maintain undisrupted business operations due to the COVID-19 pandemic, including delaying or disrupting our clinical trials, manufacturing, and supply chain; unstable market and economic conditions having serious adverse consequences on our business, financial condition and stock price; 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, 2021, 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 potential for NRASm & other MAPK tumors
- **ERAS-007 ERKi & ERAS-601 SHP2i** with best-in-class potential for MAPK tumors
- **ERAS-801, CNS-penetrant EGFRi** with first-in-class potential for EGFR-driven rGBM
- **ERAS-3490, CNS-penetrant KRAS G12Ci** with best-in-class potential in NSCLC

Strong financial position with high quality investor base and industry visibility

- **~$365M in cash, cash equivalents, and short-term marketable securities[2];** plus **$100M equity financing** announced on 12/9/2022
- 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] Unaudited, as of September 30, 2022

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

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)

Kevan Shokat, PhD

UCSF University of California San Francisco

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

Stephen Blacklow MD, PhD

HARVARD MEDICAL SCHOOL · Dana-Farber Cancer Institute

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

Ryan Corcoran, MD, PhD

HARVARD MEDICAL SCHOOL · MASSACHUSETTS GENERAL HOSPITAL CANCER CENTER

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

Pablo Rodriguez-Viciana, PhD

UCL CANCER INSTITUTE · UCL

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

Karen Cichowski, PhD

HARVARD MEDICAL SCHOOL · BWH BRIGHAM AND WOMEN'S HOSPITAL

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

George Demetri, MD

HARVARD MEDICAL SCHOOL · Dana-Farber Cancer Institute

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

Michael Varney, PhD

Genentech

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~5.5m 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	AML	US	EU	ROW	Global
EGFR*/FLT3	125	513	184	338	-	-	-	61	82	222	917	1,220
NF1	25	58	98	34	33	1.9	434	3.2	75	159	453	687
KRAS G12C	-	2.8	240	57	-	5.1	45	0.1	36	82	232	350
KRAS G12D	0.2	4.7	68	238	0.5	178	201	1.3	65	171	456	692
RAS Q61X	0.4	23	35	80	69	32	155	4.1	51	106	242	399
RAS G13R	-	9.4	5.9	5.5	2.1	-	14	0.5	3.6	8.1	26	37
Other RAS	0.6	31	162	452	4.4	211	331	13	112	291	800	1,203
BRAF V600E/K	2.0	1.9	23	180	93	1.4	158	0.4	63	127	271	461
BRAF Class 2	0.4	3.8	18	6.9	5.3	0.5	57	-	11	23	58	92
BRAF Class 3	0.1	0.9	12	17	2.5	-	29	0.2	6.1	15	40	61
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	3.0	33	69	162	264
US	12	29	93	114	77	51	153	11	542			
EU	34	76	194	398	116	124	324	18		1,285		
Rest of World	109	555	635	964	60	264	1,053	57			3,696	
Global	155	660	923	1,476	253	438	1,530	86				5,522

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

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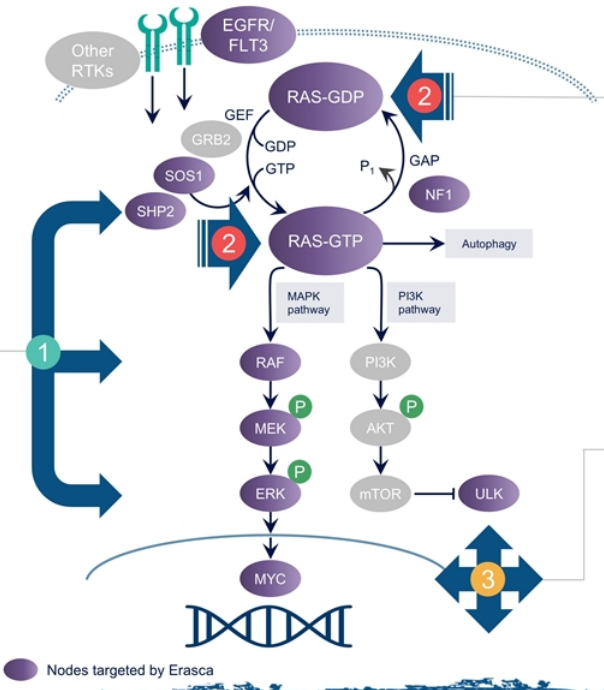
Our singular focus is on the RAS/MAPK pathway

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

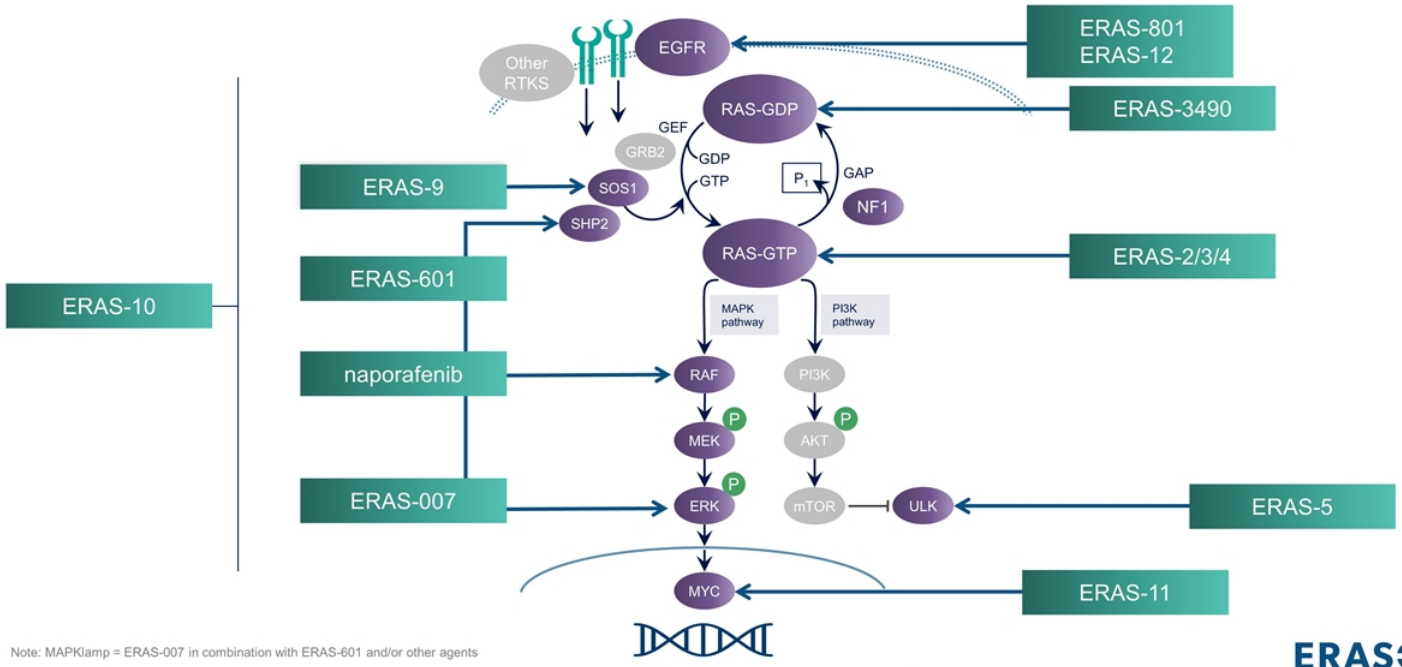
Erasca's deep modality-agnostic RAS/MAPK pathway-focused pipeline

Program/ Company	Target	Modality	Indication	Discovery	IND-enabling	Phase 1	Phase 2	Phase 3	Erase Cancer Strategy	Worldwide Rights
			Pan-RAS Q61X tissue agnostic			SEACRAFT-1 (planned)			1	ERASCA
Naporafenib	BRAF/CRAF		NRASm melanoma			SEACRAFT-2 (planned)			1	ERASCA
			NF1 LOF, pan-RAS G13R, KRAS G12C, BRAF Class 2/3 solid tumors			SEACRAFT-3 (planned)			1	ERASCA
ERAS-007*‡	ERK1/2		RAS/MAPK altered tissue agnostic, NSCLC and GI Tumors			HERKULES-1 / -2 / -3			1	ERASCA
ERAS-601*	SHP2		RAS/MAPK altered tumors			FLAGSHP-1			1	ERASCA
ERAS-801	EGFR		EGFR altered GBM			THUNDERBBOLT-1			1	ERASCA
ERAS-3490	KRAS G12C		KRAS G12C solid tumors			AURORAS-1			2	ERASCA
ERAS-2/3	RAS-GTP		RASm solid tumors						2	ERASCA
ERAS-4	KRAS G12D		KRAS G12D solid tumors						2	ERASCA
ERAS-5	ULK		RASm solid tumors						3	ERASCA
ERAS-9	SOS1		RAS/MAPK altered solid tumors						1	ERASCA
ERAS-10	RAS/MAPK		RAS/MAPK altered cancers						1 2 3	ERASCA
ERAS-11	MYC		MYC & RAS/MAPK altered solid tumors						3	ERASCA
ERAS-12	EGFR D2/D3		EGFR & RAS/MAPK altered solid tumors						1	ERASCA
Affini-T	KRAS G12V/D		KRASm solid tumors						2	affini T

small molecule | protein degrader | large molecule | TCR T cell therapy | ERASCA investment

* Together, ERAS-007 and ERAS-601 comprise our first innovative MAPKlamp
‡ Also being evaluated in combo w/ G12Ci in KRAS G12C NSCLC and GI Tumors under Stand Up to Cancer grant

Our pipeline targets every node of the RAS/MAPK pathway



Note: MAPKlamp = ERAS-007 in combination with ERAS-601 and/or other agents

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Focus of presentation

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

Indication	RAS Q61X solid tumors	NRASm melanoma post-IO	RAS/MAPK altered solid tumors	EGFRm NSCLC post-osi	KRAS G12C NSCLC	BRAFm CRC EC-naïve	BRAFm CRC EC-treated	RASm CRC + KRASm PDAC	KRASwt/ NRASwt/ BRAFwt CRC	HPV-negative HNSCC	EGFR altered rGBM
Benchmark	SOC is largely chemo	ORR 7%, mDOR 4.1 mos.	SOC is largely chemo	ORR 29%, mDOR 4.2 mos.	ORR 36%, mDOR 10 mos.	ORR 20%, mDOR 6.1 mos.	ORR ~2%, mDOR NA	ORR ~2%, mDOR NA	ORR 20%, mDOR 5.4 mos.	ORR 13%, mDOR 5.8 mos.	ORR 7-8% mDOR 3.9 mos.
Regimen tested	naporafenib + trametinib	naporafenib + trametinib	ERAS-007 + ERAS-601 (our first MAPKlamp)	ERAS-007 + osimertinib	ERAS-601 + sotorasib ERAS-3490	ERAS-007 + encorafenib + cetuximab	ERAS-007 + encorafenib + cetuximab	ERAS-007 + palbociclib	ERAS-601 + cetuximab	ERAS-601 + cetuximab	ERAS-801 monotherapy
Erasca trial(s)	SEACRAFT-1	SEACRAFT-2	HERKULES-1	HERKULES-2 Sub-study 1[1]	HERKULES-2 Sub-study 2[2] AURORAS-1	HERKULES-3 Sub-study 1[3]	HERKULES-3 Sub-study 1[3]	HERKULES-3 Sub-study 2[4]	FLAGSHP-1[5]	FLAGSHP-1[5]	THUND-ERBBOLT-1

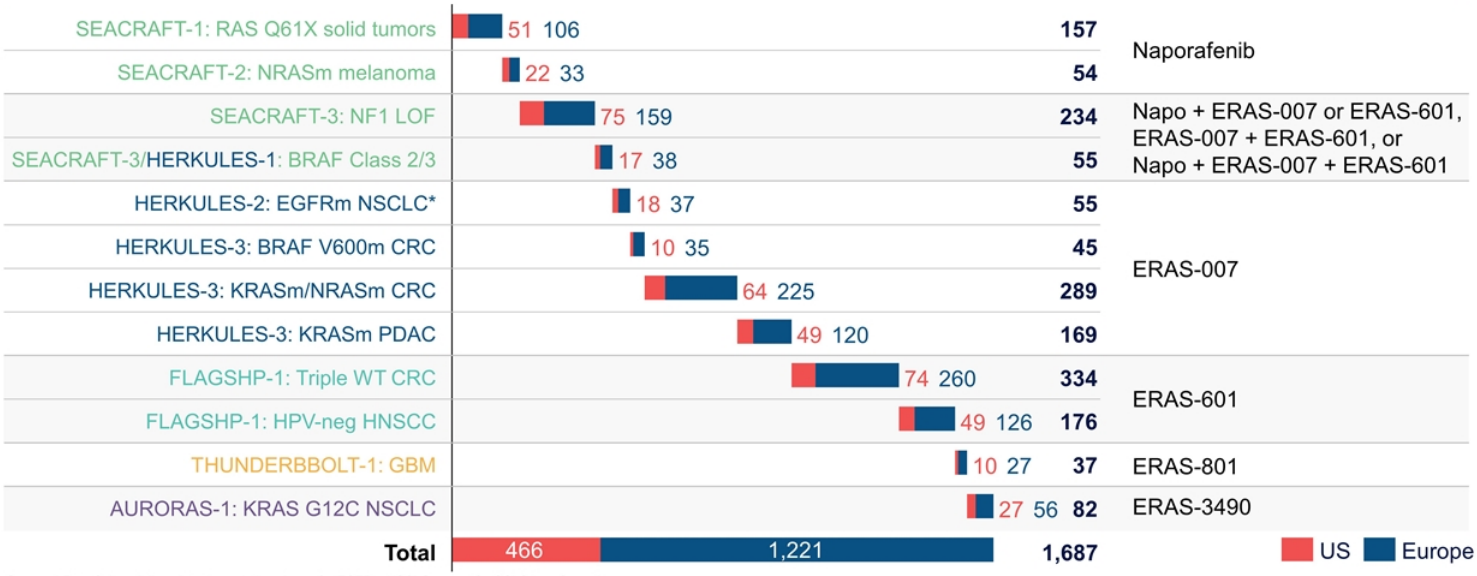
100% of CRC

[1] Completed enrollment; data in H1 2023
[2] Closed from further enrollment due to prioritization of other opportunities

[3] Sep. 2021: Announced CTCSA with Pfizer for encorafenib (Braftovi®)
Mar. 2022: Announced CTCSA with Lilly for cetuximab (Erbitux®)
Nov. 2022: Announced CTCSA with Pierre Fabre for encorafenib (Braftovi®)

[4] Oct. 2022: Announced CTCSA with Pfizer for palbociclib (Ibrance®)
[5] Jul. 2022: Announced CTCSA with Lilly for cetuximab (Erbitux®)

Erasca's clinical-stage programs could address unmet needs in up to 1.7 million patients annually in the US and Europe



Source: * Post-Osimertinib resistant population shown for EGFRm NSCLC except for SCLC transformation
Source: SEER database (2020), ECIS 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

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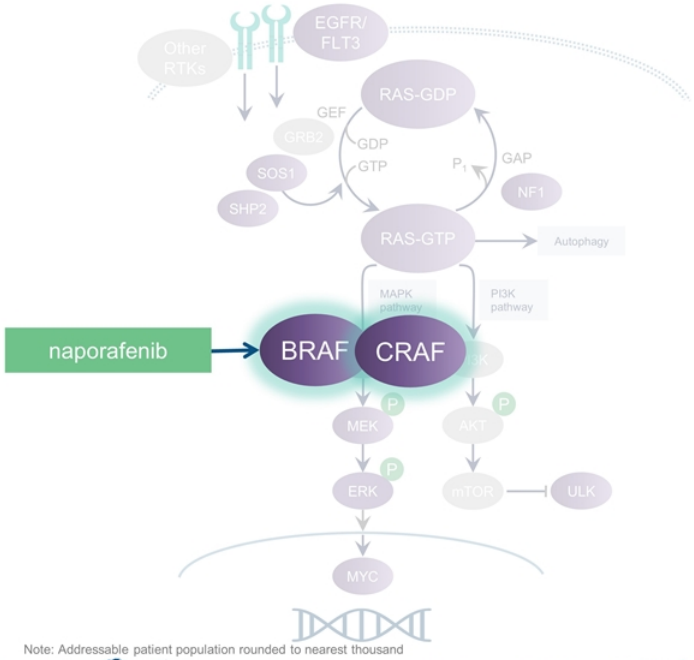
Erasca's naporafenib pan-RAFi could address unmet needs in approximately 500k patients in the US and Europe



Tumor Type	Addressable Patient Pop.
RAS Q61X Solid Tumors	157,000
NRASm Melanoma	54,000
NF1 Loss-of-Function	234,000
BRAF Class II/III Solid	55,000
TOTAL	**500,000**

Note: Addressable patient population rounded to nearest thousand

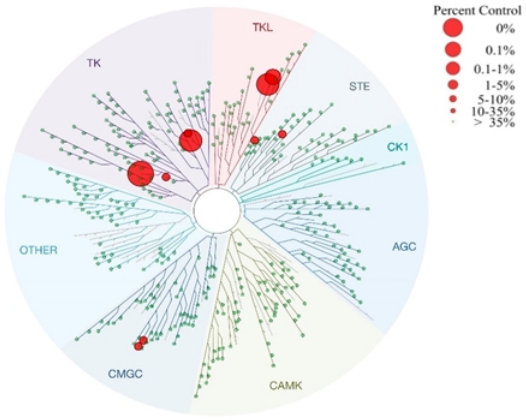
tissue agnostic indication

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

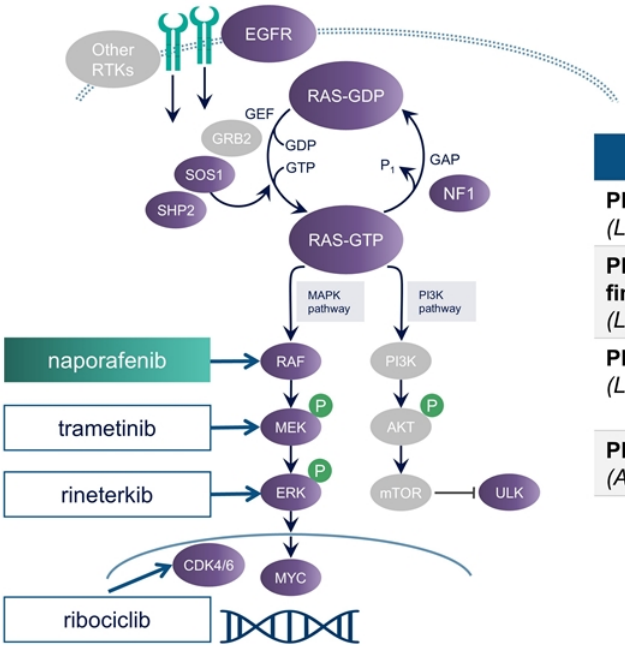
Assay	Value (nM)
Biochemical CRAF IC50 (IC_{50})	0.1
Biochemical BRAF IC50 (IC_{50})	0.2
Biochemical ARAF Inhibition (IC_{50})	6.4

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
Platform study *(ADPT01C12101)*	Exploring triplet combination of naporafenib + dabrafenib + rineterkib in BRAF V600X CRC	7

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

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

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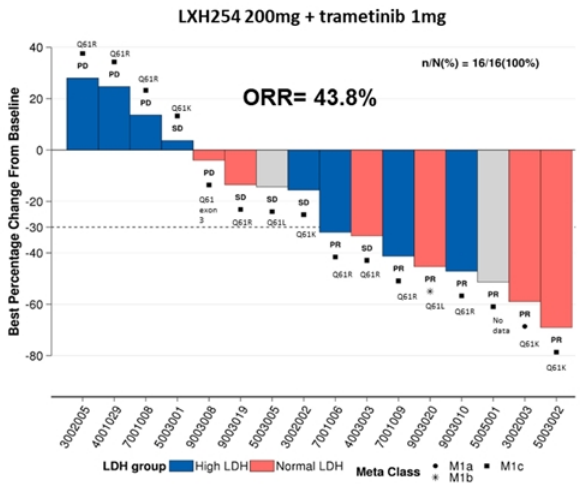
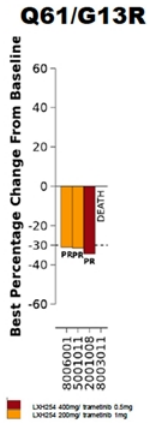
Preliminary clinical PoC in NRAS Q61X melanoma and KRAS Q61X NSCLC supports development in RAS Q61X tissue agnostic solid tumors (SEACRAFT-1)

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

Current standard of care post-IO for NRASm metastatic melanoma is chemotherapy with 7% ORR and 1.5m PFS

Front line

- IO mono or combo
  - Ex: nivolumab, pembrolizumab, nivolumab + ipilimumab

Second line plus

- Post-IO therapy is predominantly chemo
  - Binimetinib (MEKi) is not approved; recommended by US NCCN but not by EU guidelines

SOC[1]	ORR	DCR	PFS	OS
Dacarbazine	7%	24%	1.5m	10.1m
Binimetinib	15%	56%	2.8m	11.0m

- ***Improvement in ORR and DCR of binimetinib vs. dacarbazine translated to improvement in PFS***

[1] NEMO trial (*Lancet Oncol* (2017) 18: 435-445.); IO = immuno-oncology

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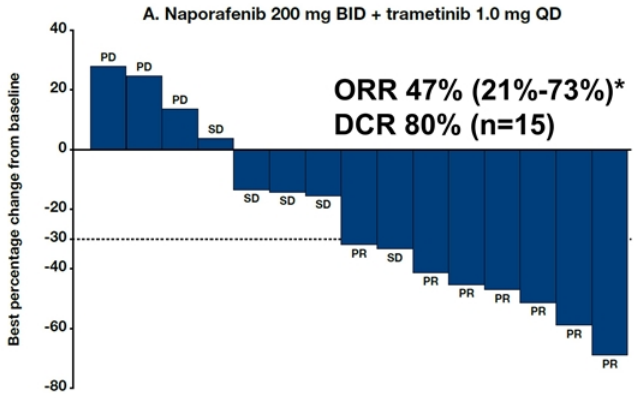
Phase 1 in NRASm melanoma: naporafenib 200mg BID + trametinib 1mg QD showed strong anti-tumor activity



BID, twice daily; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease.

Regimen (n)	Median Prior Therapy ^	ORR *	DCR
Dacarbazine (133)	1	7% (3-13)	25%
Binimetinib (269)	1	15% (11-20)	58%
Napo 200mg BID + Trame 1mg QD (15)	2 (1-7)	47% (21-73)	80%

De Braud et al AACR 2022 (Trial LXH254X2102, NCT02974725). ^ NEMO trial initially limited to 1 prior therapy later amended to allow more than 1 line. Range not available. * 95% confidence interval. ORR: objective response rate. DCR: disease control rate (ORR + stable disease).

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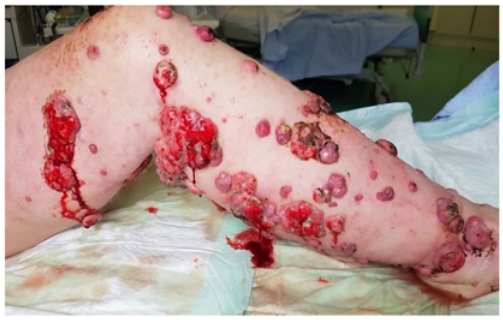
Case Study: Partial response with naporafenib 200mg BID + trametinib 1mg QD in a patient with NRASm melanoma

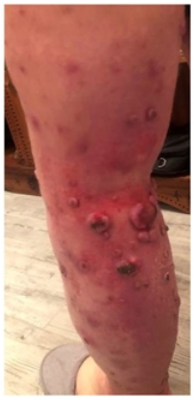
Pre-treatment

C1D1

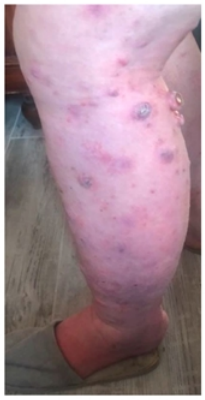


On treatment

C3D1

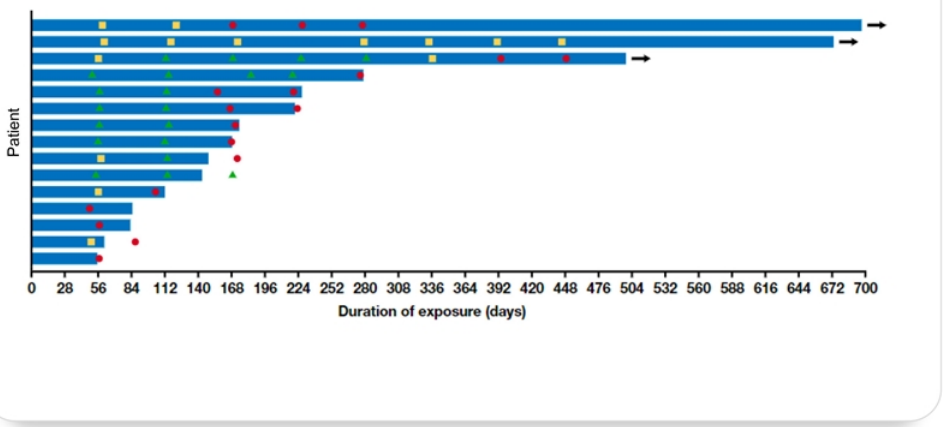


C6D1



Source: Novartis Non-Confidential Materials

Phase 1 in NRASm melanoma: naporafenib and trametinib exhibited durable time on treatment



- Responses observed in patients with normal or high LDH
- Median DOR was 3.75 months
- ***Median PFS was 5.03 months*** (95% CI: 3.42–5.62)*

Ongoing →

Response
- ◆ CR
- ▲ PR
- □ Non-CR/Non-PD
- ■ SD
- ● PD
- ⊠ UNK

Treatment
- Naporafenib 200 mg BID + trametinib 1.0 mg QD

De Braud et al AACR 2022 (Trial LXH254X2102, NCT02974725)
* Median PFS was calculated based on two RDEs: napo 200mg BID + trame 1.0mg QD and napo 400mg BID + trame 0.5mg QD

DOR, duration of response; BID, twice daily; CR, complete response; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease; UNK, unknown.

ERASCA

Clinical activity of naporafenib + trametinib in NRASm melanoma at the likely Recommended Dose was reproducible across Phase 1 and Phase 2 studies

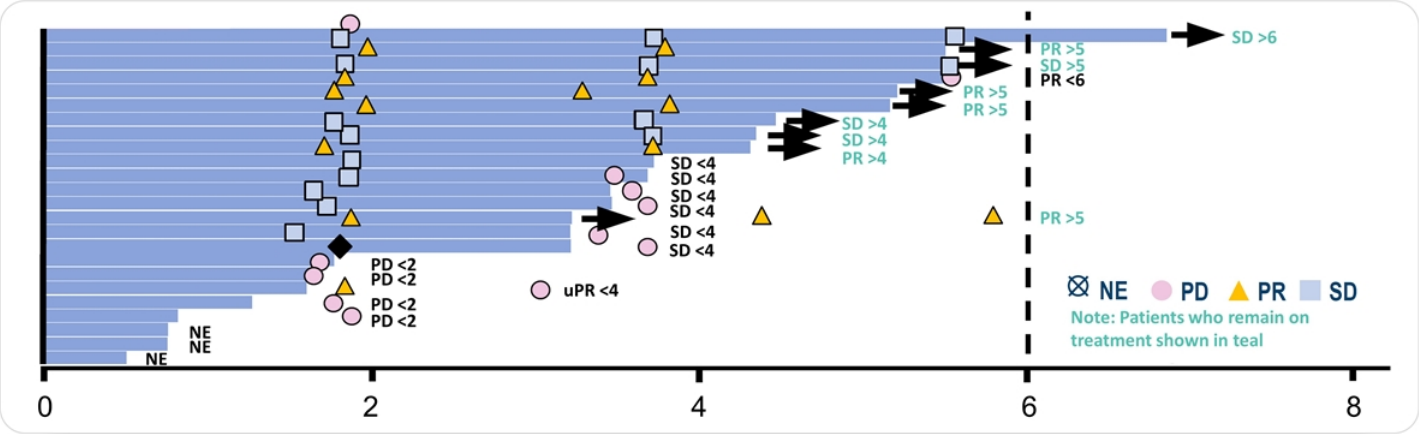
Study/Indication	Data Cutoff	Naporafenib (200 mg BID) + trametinib (1.0 mg QD)			Source
		ORR	DCR	DOR	
Phase 1 (LXH254X2102*)	9 Dec 2021	7/15 (46.7%)	12/15 (80.0%)	3.75 mo	AACR 2022
Phase 2 (LXH254C12201#)	4 July 2022	6/24 (25.0%)	17/24 (70.8%)	NA	ESMO 2022

Total of 13/39 responses
33.3% ORR

*De Braud et al AACR 2022
Lebbe et al ESMO 2022

Phase 2 in NRASm melanoma: Analysis of pts who remain on treatment show potential for naporafenib + trametinib to demonstrate PFS benefit

Duration of Exposure (months) for naporafenib 200 mg BID + trametinib 1 mg QD



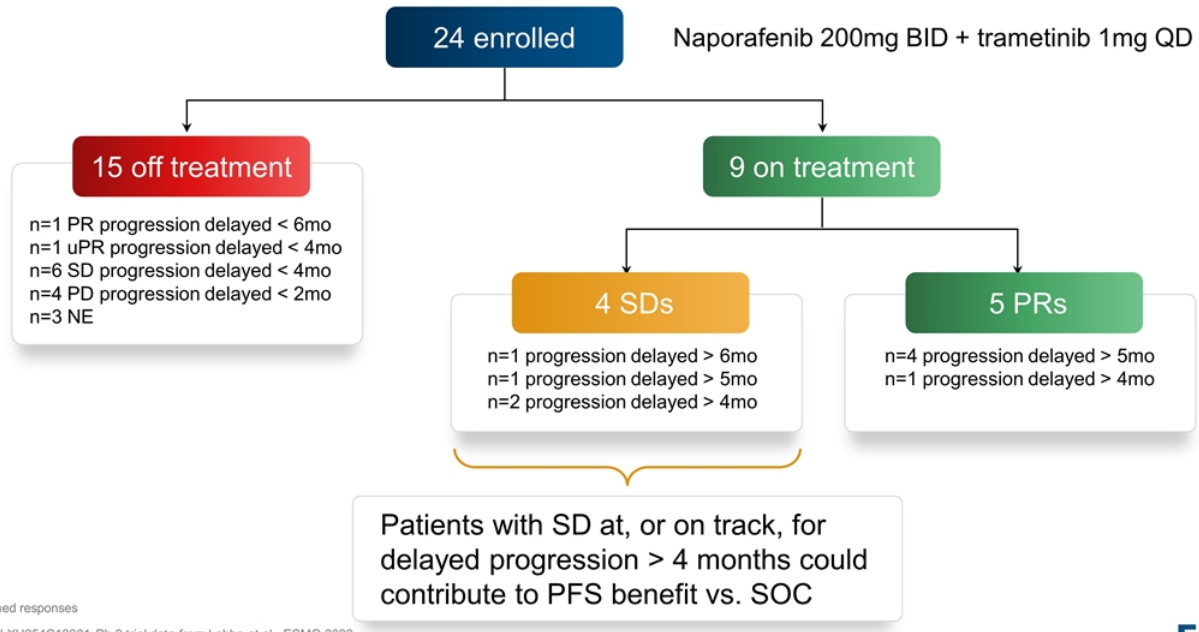
9/24 patients remain on treatment as of data cutoff

- 1 of these has already delayed progression by >6 months
- 8 other patients have possibility of continuing on treatment for >6 months (5 are at >5 mos., 3 are at >4 mos.; 5 of them have PRs, 3 of them have SDs) and could extend PFS

Source: annotated LXH254C12201 Ph 2 trial data from Lebbe et al, ESMO 2022

ERASCA

Ph 2 patients continuing on treatment on naporafenib + trametinib = potential for confirmation of Ph 1 DOR and PFS advantage in SEACRAFT-2

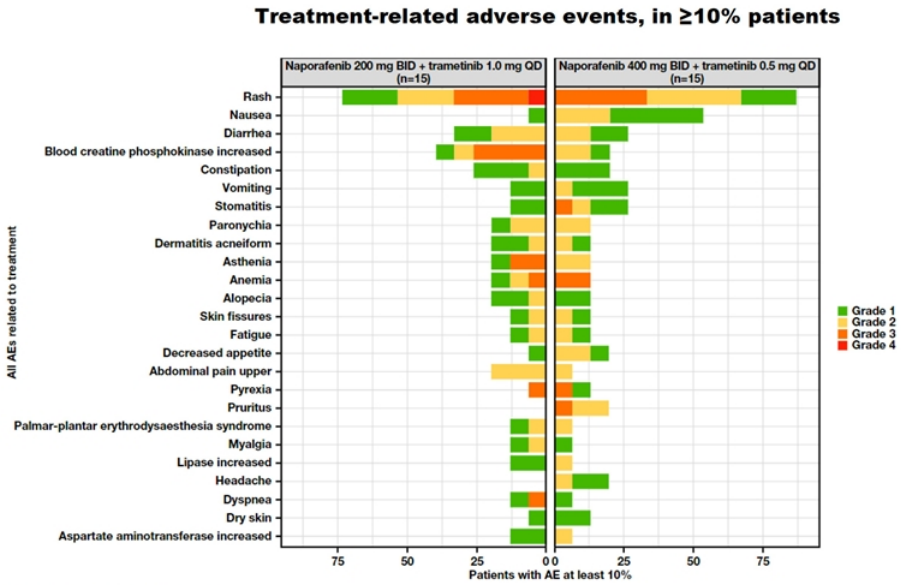


Patients with SD at, or on track, for delayed progression > 4 months could contribute to PFS benefit vs. SOC

*includes unconfirmed responses

Source: annotated LXH254C12201 Ph 2 trial data from Lebbe et al, ESMO 2022

Naporafenib + trametinib demonstrated a favorable and manageable safety profile



AE, adverse event; BID, twice daily; QD, once daily.

Phase 1 data in NRASm melanoma from De Braud et al AACR 2022

ERASCA

Proposed pivotal & Phase 2 trial designs: Creative CDP strategy includes high PTS randomized NRASm melanoma trial and tissue agnostic indication

Initiate single-arm and randomized trials in quick succession. NRASm melanoma is the lead indication. Tissue agnostic registration will be supported by melanoma and other solid tumor data, based on regulatory feedback.

Single-Arm Phase 2 Trial (SEACRAFT-1)

Solid Tumors
(Age 12+)
Post-available therapy
RAS Q61X
(NRAS, HRAS, KRAS)

naporafenib + trametinib

Study Endpoints
ORR, DOR

N~30 - 100

Randomized Phase 3 Trial (SEACRAFT-2)

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

R
1:1

naporafenib + trametinib

TBD (e.g., dacarbazine, physician's choice)

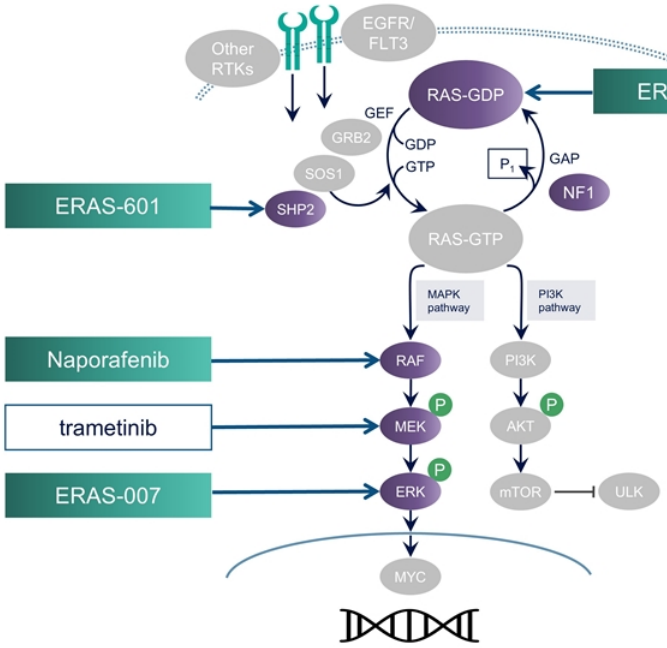
Study Endpoints
PFS, OS (dual primary) ORR, DOR (secondary)

N~350 - 400

Note: Preliminary plan subject to global health authority feedback. Assumes CoC for naporafenib monotherapy in melanoma from FIH trial; CoC in solid tumors is not needed.

ERASCA

SEACRAFT-3: Naporafenib could combine synergistically with the rest of our pipeline



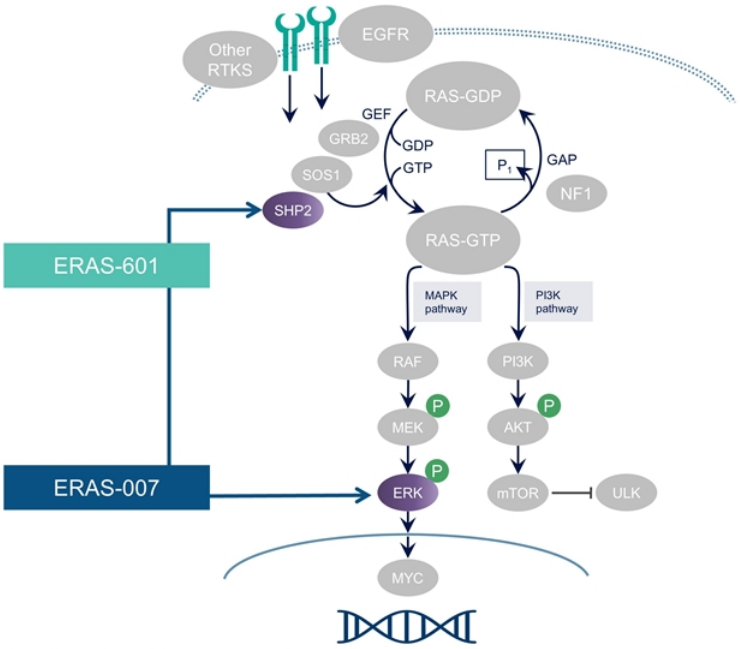
Potential Naporafenib combos with Erasca Pipeline

- **naporafenib + ERAS-007**
- **naporafenib + ERAS-601**
- **naporafenib + ERAS-007 + ERAS-601**
- **naporafenib + ERAS-3490**

Target Tumor Types
NF1 LOF Tissue Agnostic
RAS G13R Tissue Agnostic
KRAS G12C NSCLC
BRAF Class 2 Tissue Agnostic
BRAF Class 3 Tissue Agnostic

ERAS-007 ERKi and ERAS-601 SHP2i could address unmet needs in over 1.1 million patients in the US and Europe

Focus of this section



Tumor Type	Addressable Patient Pop.
BRAF Class II/III Solid	55,000
EGFRm NSCLC	55,000
BRAF V600m CRC	45,000
KRASm/NRASm CRC	289,000
KRASm PDAC	169,000
Triple WT CRC	334,000
HPV-neg HNSCC	176,000
TOTAL	**1,123,000**

tissue agnostic indication

Note: Addressable patient population rounded to nearest thousand

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

We believe ERAS-601 is a potential best-in-class SHP2 inhibitor that demonstrates high potency and selectivity against SHP2

Compound	Biochemical SHP2 inhibition IC50 (nM)
ERAS-601	4.6

ERAS-601 demonstrated no off-target activity in 300 kinase (<30% inhibition @ 1μM) and 12 phosphatase panels (IC50 >10μM)

	Cell Line	Cancer Type	IC_{50} (nM)	
			ERAS-601	RMC-4550[1]
KRAS G12C	HCC44	NSCLC	↑ 48	95
	MIA PaCa-2	Pancreatic	↑ 6	17
	NCI-H1373	NSCLC	↑ 64	474
	NCI-H1792	NSCLC	↔ 40	27
	NCI-H2122	NSCLC	↑ 259	1,876
	NCI-H358	NSCLC	↑ 12	49
	SW1573	NSCLC	↑ 104	298
BRAF class III	NCI-H1666	NSCLC	↑ 19	51
	NCI-H508	CRC	↑ 95	208
NF1 LoF	MeWo	Melanoma	↑ 56	241
wtEGFR amplification	KYSE-520	Esophageal	↑ 119	440

[1]RMC-4550 is Revolution Medicine's SHP2i tool compound and is believed to behave similarly to their clinical compound, RMC-4630 (per company disclosure); LoF = loss of function; wtEGFR = wildtype EGFR

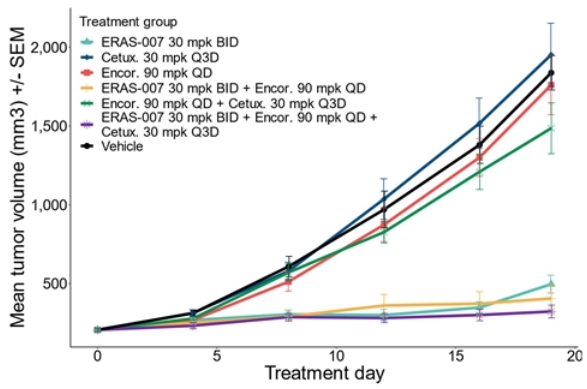
ERASCA

ERAS-007 + EC in BRAFm CRC:

ERAS-007 showed strong in vivo combination activity in BRAF V600E CRC

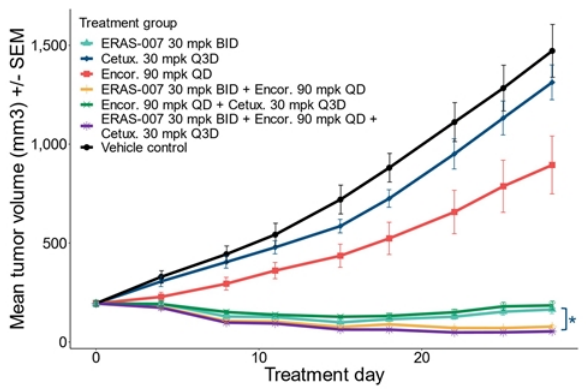
TGI in RKO (BRAF V600E CRC)

EC-resistant CDX Model



TGI in WiDr (BRAF V600E CRC)

EC-sensitive 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

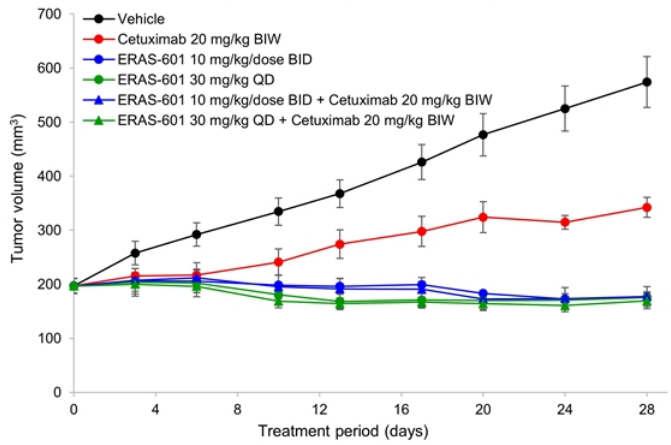
Note: Cetux. = cetuximab; encor. = encorafenib; EC = encorafenib plus cetuximab (BEACON regimen)

ERASCA

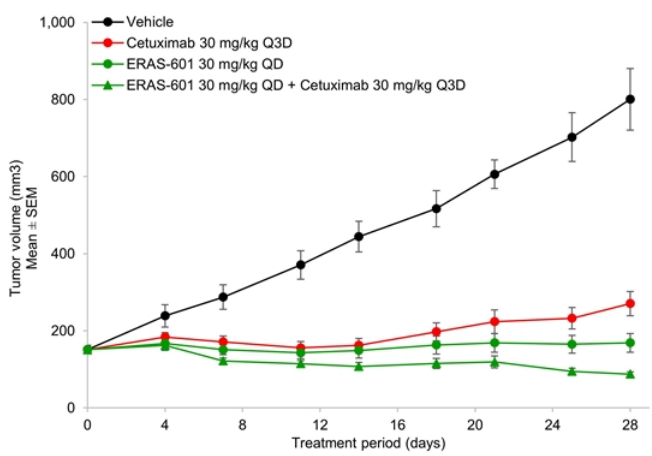
ERAS-601 + cetuximab in triple wildtype CRC and HPV-negative HNSCC:

Combo demonstrated significantly greater tumor inhibition vs. cetuximab alone in both models

TGI in Triple WT CRC PDX model CRC1021



TGI in HPV-negative HNSCC PDX HN3411



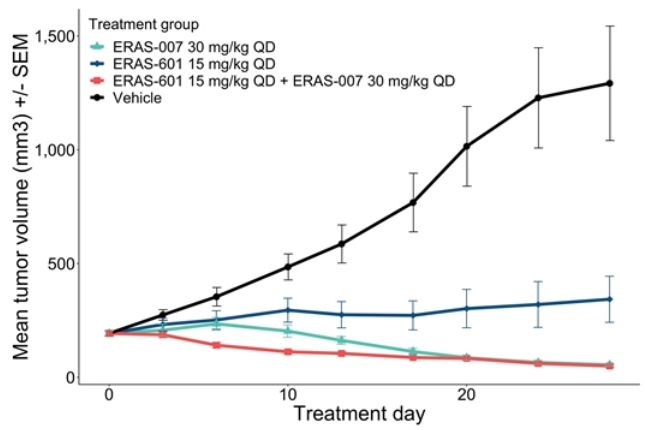
- Combination was tolerated in mice (e.g., no dose holidays, deaths, or euthanizations)
- ERAS-601 was dosed orally and cetuximab was dosed intraperitoneally

ERASCA

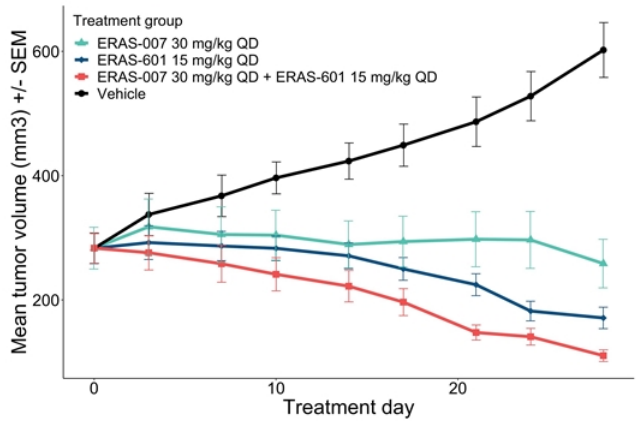
ERAS-007 + ERAS-601 MAPKlamp in BRAF Class 3 and NF1 loss of function:

Combination showed consistent activity in both models

TGI in BRAF Class 3 NSCLC PDX LUN023



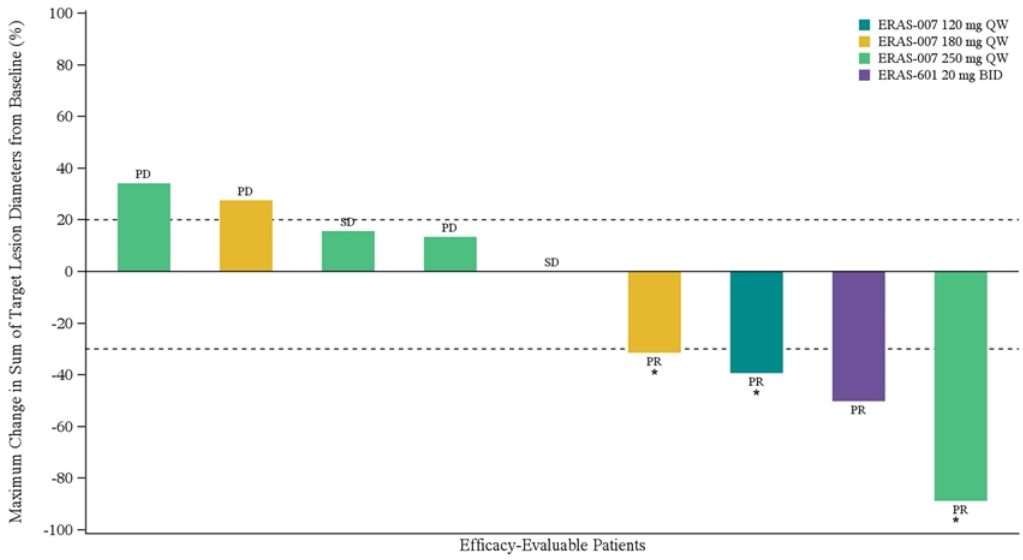
TGI in NF1 LoF NSCLC NCI-H1838



- MAPKlamp combination showed activity in both models and was tolerated in mice (e.g., no dose holidays, deaths, or euthanizations)
- ERAS-007 and ERAS-601 were dosed orally and continuously

Note: LoF. = loss of function

Best Overall Response Observed with ERAS-007 or ERAS-601 in BRAF-driven Blue Ocean Indications across lines of therapy



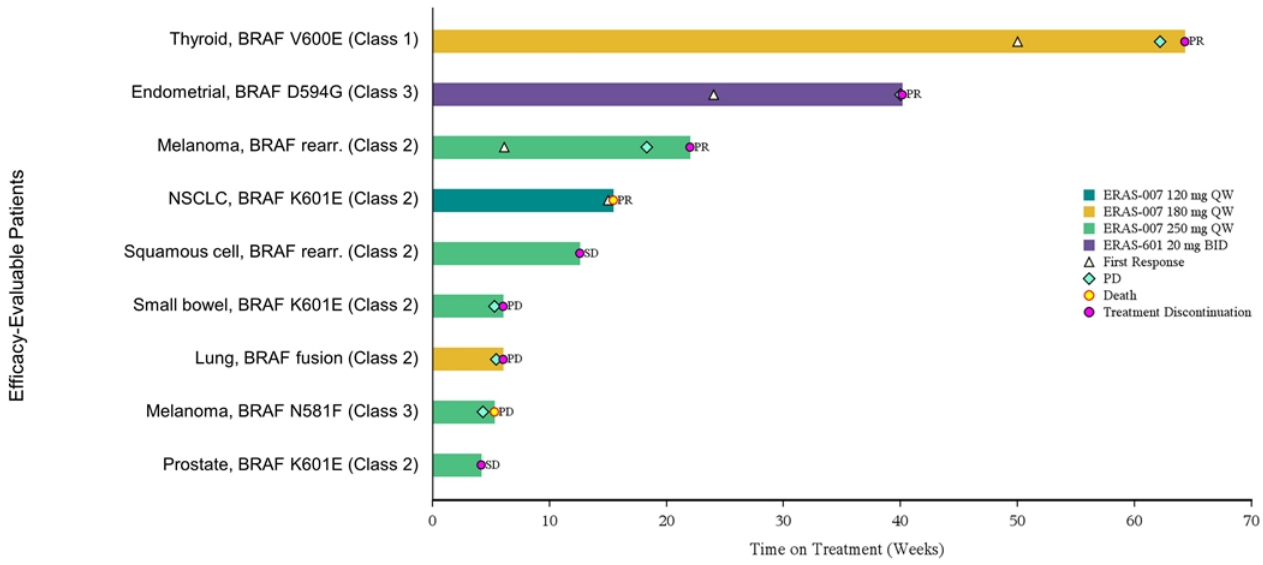
44% (4 out of 9) of patients responded (confirmed and unconfirmed PR) to single agent ERAS-007 or ERAS-601

* Unconfirmed partial responses indicated with an asterisk

NOTE: Blue Ocean Indications defined as populations of unmet need with relevant tumor types and RAS/MAPK alterations where no targeted therapies are approved; Biologically relevant dose defined as weekly monotherapy dose intensity between 120mg and 250mg for ERAS-007 and daily monotherapy dose intensity of 40mg (40mg QD or 20mg BID) for ERAS-601; data extraction date: 6NOV2020 for ASN007-101, 11JUL2022 for ERAS-601-01, 16May2022 for ERAS-007-01.

ERASCA

Duration of Treatment Observed with ERAS-007 or ERAS-601 in BRAF-driven Blue Ocean Indications

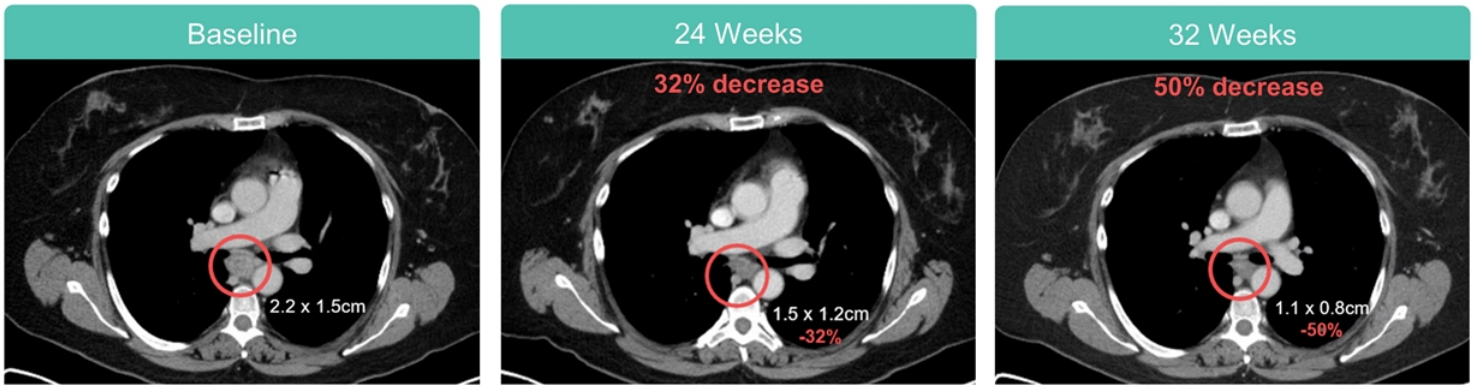


NOTE: Blue Ocean Indications defined as populations of unmet need with relevant tumor types and RAS/MAPK alterations where no targeted therapies are approved; Biologically relevant dose defined as weekly monotherapy dose intensity between 120mg and 250mg for ERAS-007 and daily monotherapy dose intensity of 40mg (40mg QD or 20mg BID) for ERAS-601; data extraction date: 6NOV2020 for ASN007-101, 11JUL2022 for ERAS-601-01, 16May2022 for ERAS-007-01.

ERASCA

FLAGSHP-1 Case Study: Single agent ERAS-601 response
63-year-old female (Patient 0009) with BRAF Class 3 metastatic endometrial cancer

Diagnosis	Stage III/IV endometrial cancer, metastatic disease, BRAF Class 3, initially diagnosed in September 2018
Sites of Metastases	Lung, lymph nodes
Prior Therapy	Surgery, chemotherapy, pembrolizumab
Dosing	ERAS-601 20 mg BID



Per RECIST 1.1: ≥30% = objective response

Tumor assessment (5) (Jan 4, 2022): patient had radiologic progressive disease (PD) due to a new lesion Peri-Esophageal lesion, shrinkage in non-target lesions also noted (not shown)

ERASCA

Likely recommended dose of ERAS-007 for combinations was well tolerated

Treatment-related Adverse Events Occurring in ≥ 20% and ≥ 2 Patients at Any Dose
(arranged by descending frequency in the 250mg QW any grade column)

System Organ Class/ Preferred Term	50 mg BID-QW (n=4)		100 mg BID-QW (n=11)		125 mg BID-QW (n=8)		250 mg QW (n=29)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
At least one TRAE	4 (100.0%)	1 (25.0%)	9 (81.8%)	2 (18.2%)	8 (100.0%)	3 (37.5%)	27 (93.1%)	10 (34.5%)
Eye Disorders*	1 (25.0%)	0	6 (54.5%)	1 (9.1%)	5 (62.5%)	2 (25.0%)	16 (55.2%)	5 (17.2%)
Diarrhea	0	0	2 (18.2%)	0	3 (37.5%)	0	16 (55.2%)	1 (3.4%)
Nausea	2 (50.0%)	0	5 (45.5%)	0	5 (62.5%)	0	14 (48.3%)	0
Vomiting	1 (25.0%)	0	3 (27.3%)	0	3 (37.5%)	0	9 (31.0%)	2 (6.9%)
Dermatitis acneiform	1 (25.0%)	0	4 (36.4%)	0	3 (37.5%)	0	6 (20.7%)	0
Rash maculopapular	0	0	1 (9.1%)	0	1 (12.5%)	0	6 (20.7%)	1 (3.4%)
Dehydration	2 (50.0%)	0	1 (9.1%)	0	1 (12.5%)	0	4 (13.8%)	0
Fatigue	1 (25.0%)	1 (25.0%)	4 (36.4%)	0	4 (50.0%)	1 (12.5%)	5 (17.2%)	1 (3.4%)

Likely recommended dose between 50 – 100mg BID-QW for combinations was well tolerated

*includes uniocular blindness (one patient in 250mg QW cohort), chorioretinopathy, papilloedema, retinal detachment, retinal oedema, retinopathy, serous retinal detachment, subretinal fluid, vision blurred, visual impairment, and vitreous floaters. Data extraction for ASN-007-101 was on 6 Nov. 2020; data cutoff for HERKULES-1 was 23 May 2022

ERASCA

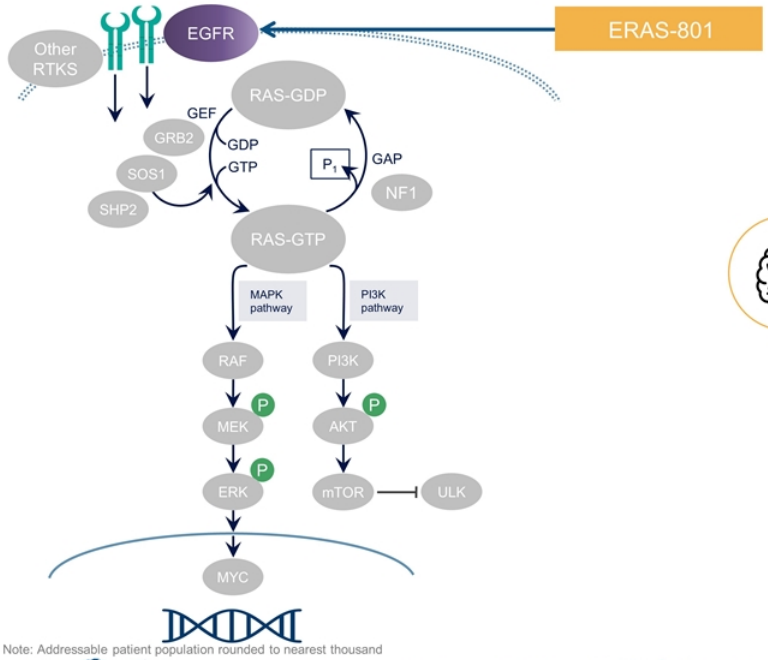
ERAS-601 QD and BID regimens were well tolerated with acceptable safety profile

Treatment-related Adverse Events occurring in ≥ 20% of patients in QD and BID cohorts

System Organ Class/ Preferred Term	QD (20-80 mg) N=15		QD MTD (40 mg) N=3		BID (20 and 40 mg) N=13		BID MTD (40 mg) N=9		QD + BID N=28	
	ALL	Gr ≥ 3	ALL	Gr ≥ 3	ALL	Gr ≥ 3	ALL	Gr ≥ 3	ALL	Gr ≥ 3
At least one TRAE	14 (93.3)	6 (40)	3 (100)	2 (66.7)	13 (100)	6 (46.2)	9 (100)	4 (44.4)	27 (96.4)	12 (42.9)
Thrombocytopenia*	7 (46.7)	2 (13.3)	2 (66.7)	1 (33.3)	3 (23.1)	2 (15.4)	2 (22.2)	2 (22.2)	10 (35.7)	4 (14.3)
AST increased	6 (40.0)	2 (13.3)	1 (33.3)	0	2 (15.4)	1 (7.7)	2 (22.2)	1 (11.1)	8 (28.6)	3 (10.7)
ALT increased	6 (40.0)	1 (6.7)	1 (33.3)	0	2 (15.4)	0	2 (22.2)	0	8 (28.6)	1 (3.6)
Diarrhea	4 (26.7)	0	1 (33.3)	0	4 (30.8)	1 (7.7)	2 (22.2)	0	8 (28.6)	1 (3.6)
Oedema peripheral	3 (20.0)	0	2 (66.7)	0	4 (30.8)	0	2 (22.2)	0	7 (25.0)	0

* Includes thrombocytopenia and platelet count decrease
Source: ENA 2022

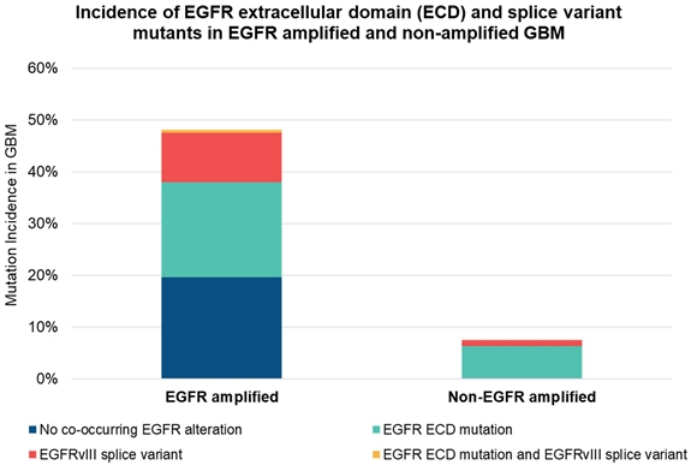
ERAS-801 EGFRi could address high unmet need in 37k patients in US and EU



Tumor Type	Addressable Patient Pop.
Glioblastoma multiforme	37,000
TOTAL	**37,000**

Note: Addressable patient population rounded to nearest thousand

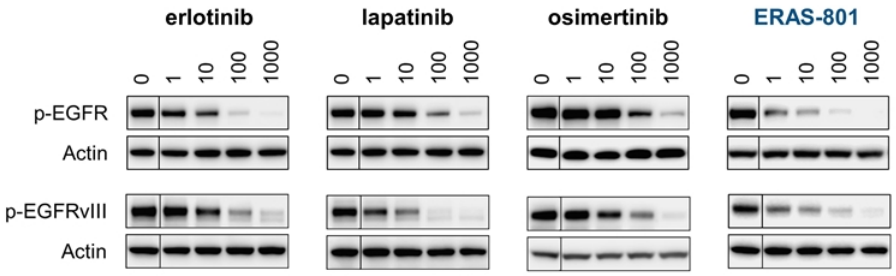
Poor activity of legacy EGFRi in GBM due to minimal activity against GBM-specific EGFR alterations and poor CNS penetration



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)

TCGA *Cell*, 2013

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



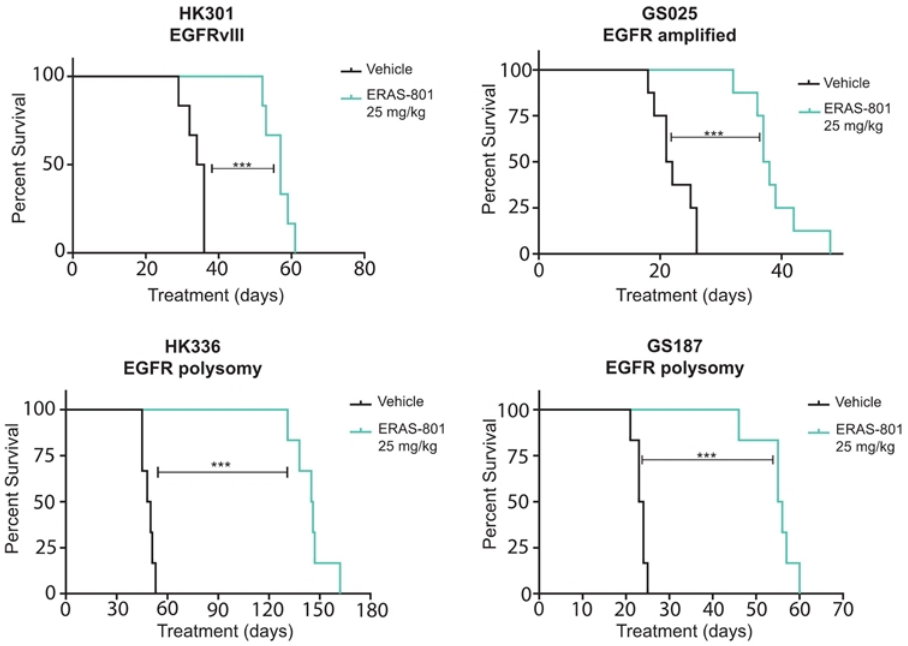
Compound (Brand Name)	Company	K_p, brain (mouse)	$K_{p,uu}$, brain (mouse)[1]
ERAS-801	**Erasca**	**3.7**	**1.2**
osimertinib	AstraZeneca	0.99	0.29
afatinib	Boehringer Ingelheim	0.25	0.05
erlotinib	Genentech	0.06	0.13
gefitinib	AstraZeneca	0.36	0.10
dacomitinib	Pfizer	0.61	0.49

1 $K_{p,uu}$ is a measure of the ratio of unbound brain concentration to unbound plasma concentration

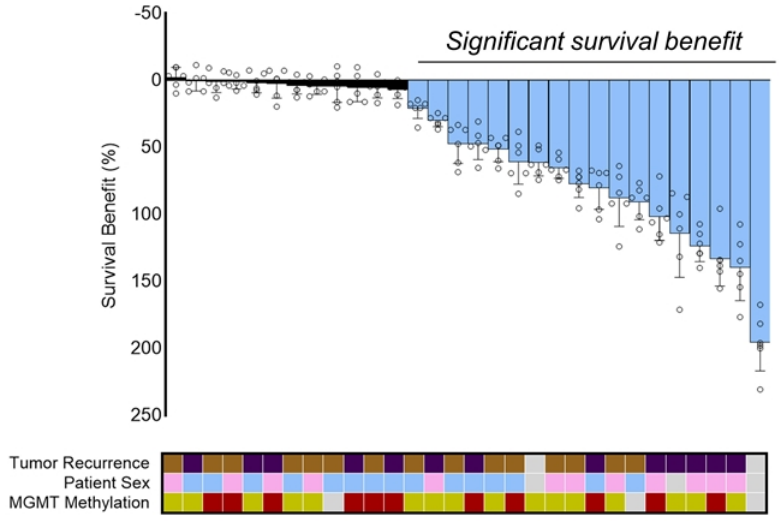
Kim M, et al. Brain Distribution of a Panel of Epidermal Growth Factor Receptor Inhibitors Using Cassette Dosing in Wild-Type and Abcb1/Abcg2-Deficient Mice. Drug Metab. Dispos., 2019. PMID: 30705084

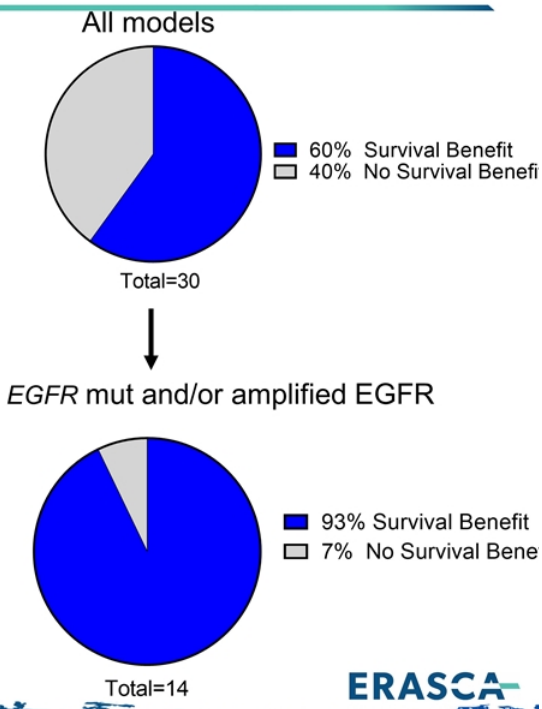
ERASCA

ERAS-801 shows significant survival benefit in multiple glioma PDX models harboring a variety of EGFR alterations



ERAS-801 improves outcomes of >90% of EGFR mutant and/or amplified GBM PDXs across a diverse range tested





All of Erasca's 2022 milestones were achieved on or ahead of schedule

Program *Mechanism*	Trial Name *Indication*	2022 milestone guidance	Status
ERAS-007 and/or ERAS-601 (MAPKlamp[1]) *ERK1/2 inhibitor and/or SHP2 inhibitor*	**HERKULES-1** *Advanced Solid Tumors*	**H2 2022** Ph 1b data (achieved)	Achieved Sept. 2022
		H1 2023 MAPKlamp FPD (achieved)	Achieved Dec. 2022 – one half early
ERAS-601 *SHP2 inhibitor*	**FLAGSHP-1** *Advanced Solid Tumors*	**H2 2022** Ph 1 data (achieved)	Achieved Sept. 2022
ERAS-801 *CNS-penetrant EGFR inhibitor*	**THUNDERBBOLT-1** *Glioblastoma Multiforme*	**Q1 2022** FPD (achieved)	Achieved Feb. 2022
ERAS-3490 *CNS-penetrant KRAS G12C inhibitor*	**AURORAS-1** *KRAS G12Cm NSCLC*	**H2 2022** File IND (achieved)	Achieved Nov. 2022

[1] ERAS-007 (oral ERK1/2 inhibitor) and ERAS-601 (oral SHP2 inhibitor) together comprise our first innovative MAPKlamp

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Anticipated key milestones and clinical trial readouts

Program *Mechanism*	Trial Name *Indication*	2023	2024
Naporafenib *Pan-RAF inhibitor*	**SEACRAFT-1** *RAS Q61X Solid Tumors*	**H2 2023** Ph 2 FPD[3]	**H2 2024 – H1 2025** Ph 2 combo data
	SEACRAFT-2 *NRASm Melanoma*		**H1 2024** Ph 3 pivotal FPD[3]
ERAS-007 and/or ERAS-601 (MAPKlamp[1]) *ERK1/2 inhibitor and/or SHP2 inhibitor*	**HERKULES-1** *Advanced Solid Tumors*		**H1 2024** Ph 1b combo data[4]
	HERKULES-2 *Lung Cancers*	**H1 2023** Ph 1b combo data	
	HERKULES-3 *BRAFm CRC and RASm GI Cancers*	**H1 2023** Ph 1b combo data	**H2 2023 – H1 2024** Ph 1b combo data in BRAFm CRC and/or RASm GI cancers
ERAS-601 *SHP2 inhibitor*	**FLAGSHP-1** *Triple WT CRC[2] and HPV-neg HNSCC*	**H1 2023** Ph 1b dose escalation (incl. MTD) data	**2024** Ph 1b combo data in triple WT CRC and/or HPV-neg HNSCC
ERAS-801 *CNS-penetrant EGFR inhibitor*	**THUNDERBBOLT-1** *Glioblastoma Multiforme*	**H2 2023** Ph 1 data in rGBM	
ERAS-3490 *CNS-penetrant KRAS G12C inhibitor*	**AURORAS-1** *KRAS G12Cm NSCLC*		**2024** Ph 1 data

[1] ERAS-007 (oral ERK1/2 inhibitor) and ERAS-601 (oral SHP2 inhibitor) together comprise our first innovative MAPKlamp
[2] Triple wildtype CRC is KRASwt, NRASwt, and BRAFwt
[3] FPD = first patient dose
[4] Data to include preliminary combination safety and pharmacokinetics to support combination dose expansion

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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
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 believe we have built the deepest pipeline in the industry to comprehensively shut down RAS/MAPK pathway, with the potential to address unmet needs in over 5 million patients globally

FIVE CLINICAL-STAGE COMPOUNDS
Differentiated profiles including naporafenib, a phase 2, pivotal-ready pan-RAF inhibitor for NRASm melanoma and Q61X tissue agnostic solid tumors and our first, innovative MAPKlamp comprising compelling ERK and SHP2 inhibitors

MULTIPLE POTENTIAL NEAR-TERM AND LONG-TERM VALUE DRIVERS
Robust clinical development plan with multiple combination and monotherapy readouts in 2023 and beyond and a strong Research engine to drive novel compounds into the clinic

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Thank You!

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

Company	Program	Stage
ERASCA	**naporafenib**	**Ph 2**
Day One Biopharmaceuticals	tovarafenib	Ph 2 *Lead indication in pediatric low-grade glioma; novel-novel*
Roche	belvarafenib	Ph 1b
Fore	FORE-8394	Ph 1
BeiGene	lifirafenib	Ph 1
Mapkure	BGB-3245	Ph 1 *Combo w/ mirdametinib starting 2023*
KINNATE BIOPHARMA	KIN-2787	Ph 1 *Unclear whether non-clinical parameters will translate in clinic*
Jazz Pharmaceuticals	JZP815	Ph 1 *Ph 1 FPD Nov 2022*
Black Diamond Therapeutics	BDTX-4933	Preclinical
cullgen	CUL-BRAF	Preclinical

Most advanced pan-RAF inhibitor

- Dosed in the most patients (500+) of any pan-RAF inhibitor in development
- Potential to be first-to-market and raise SoC in prioritized indications

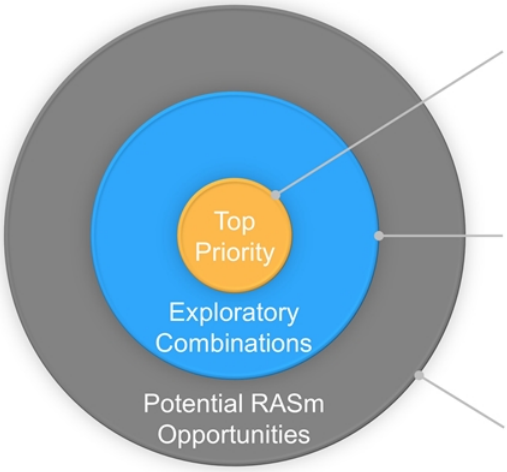
PoC established

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

Strong complementarity with Erasca pipeline

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

Erasca is well positioned to advance naporafenib through a focused development plan that leverages RAS/MAPK pipeline synergies



Top priority to address unmet needs in ~395,000 patients WW

Focus on securing regulatory approval for naporafenib + trametinib in RAS Q61X tissue agnostic solid tumors (SEACRAFT-1) and/or NRASm melanoma (SEACRAFT-2) as soon as possible

Exploratory combos to address unmet needs in ~1.2m patients WW

Explore novel combination(s) in NF1 LOF, RAS G13R, KRAS G12C, and BRAF Class 2 and 3 altered solid tumors (SEACRAFT-3); combos include naporafenib with ERAS-007, ERAS-601, ERAS-007 + ERAS-601, or ERAS-3490

Potential RASm opportunities to address unmet needs for ~1.9m patients WW

Ungate potential opportunities in other RASm indications if well tolerated combinations are identified above and/or supported by evolving data

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

Company	Program	Stage
BioMed Valley Discoveries	ulixertinib	Ph 2 (combo w/ HCQ, palbo) *Safety concerns (disfiguring rash); CoM patent through 2025*
ERASCA	**ERAS-007**	**Ph 2 (multiple combos)**
astex pharmaceuticals	ASTX029	Ph 2 (combo w/ internal SHP2)
Lilly	temuterkib	Ph 1 *Reported monotherapy ORR[1] of 0%*
NOVARTIS	rineterkib	Ph 1 (combo w/ napo, TNO155) *Reported monotherapy ORR of 2%*
JSI	JSI-1187	Ph 1 (combo w/ dabrafenib)
ATG ANTENGENE	ATG-017	Ph 1 (combo w/ nivolumab)
MERCK	MK-8353	Ph 1 (combo w/ pembro)
Genentech A Member of the Roche Group	GDC-0994	Terminated *Significant tolerability issues*
KURA ONCOLOGY	KO-947	Terminated *Placed on partial clinical hold; IV administered*
Celgene	CC-90003	Terminated *MTD "did not offer sufficiently encouraging profile to proceed"*

[1] ORR = objective response rate

Hit-and-run profile optimizing efficacy, tolerability

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

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 studies indicating areas of focus for combination development

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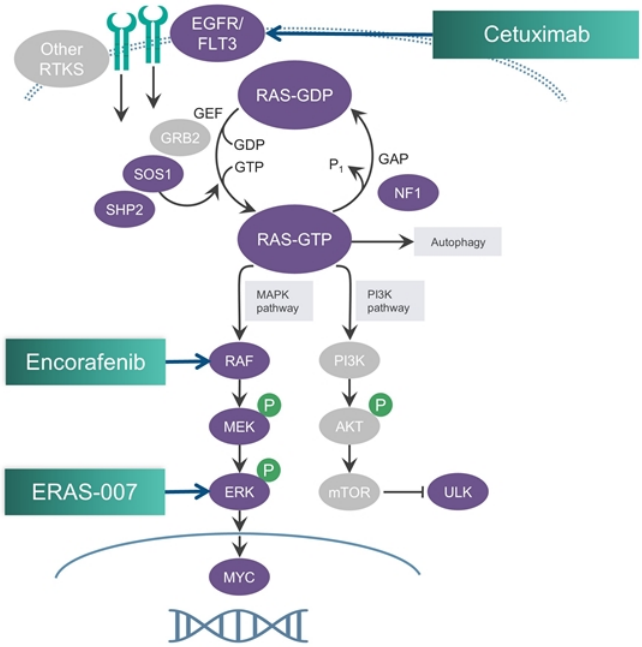
Scientific rationale: Triple blockade of BRAF, EGFR and ERK in BRAFm CRC



- ERK inhibition may **overcome treatment-induced resistance to BRAF/EGFR inhibition** by adding ERAS-007 to encorafenib + cetuximab (EC)
- Combined blockade of ERK plus BRAF/EGFR could more effectively inhibit the RAS/MAPK pathway, as well as **prevent MAPK feedback reactivation** in BRAFm CRC, representing approximately 10% of patients with CRC

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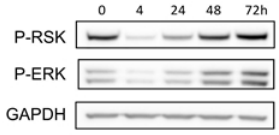
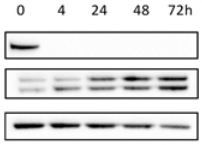
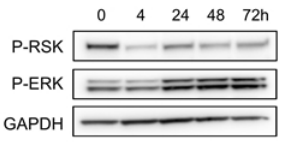
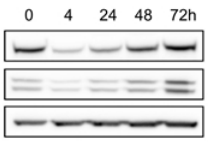
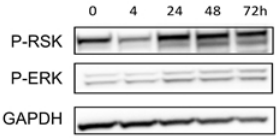
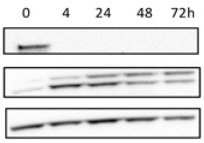
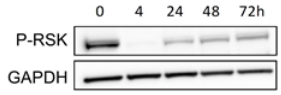
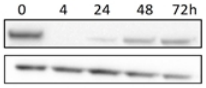
ERAS-007 blocked the MAPK feedback reactivation observed with MEK or other ERK plus BRAF inhibitor combinations

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

HERKULES and SU2C clinical trial series – ERAS-007 master protocols

HERKULES-1		HERKULES-2		HERKULES-3		Stand Up To Cancer	
Tissue Agnostic		Lung Cancer		GI Cancer		Lung and GI Cancer	
Regimen	**Indication**	**Regimen**	**Indication**	**Regimen**	**Indication**	**Regimen**	**Indication**
ERAS-007	Exploring safety & PK of various intermittent dosing schedules for combinations	ERAS-007 + osimertinib (Tagrisso®)	EGFR-mutant NSCLC	ERAS-007 + encorafenib (Braftovi®)[1,4] and cetuximab (Erbitux®)[2]	BRAF V600E-mutant CRC (EC naïve and treated)	ERAS-007 + adagrasib	KRAS G12C-mutant NSCLC and CRC
ERAS-007 + ERAS-601 (our first MAPKlamp)	RAS/MAPK-altered Solid Tumors (potential tissue agnostic)	ERAS-007 or ERAS-601 + sotorasib (Lumakras™)	KRAS G12C-mutant NSCLC	ERAS-007 + palbociclib[3] (Ibrance®)	KRAS- or NRAS-mutant CRC; KRAS-mutant PDAC		
		ERAS-007 in combination with other agents	Mutational subtypes of NSCLC	ERAS-007 in combination with other agents	Mutational subtypes of GI cancers		

Pfizer / Lilly / Pfizer / Pierre Fabre

1 Sep. 2021: Announced CTCSA with Pfizer for encorafenib (Braftovi®)
2 Mar. 2022: Announced CTCSA with Lilly for cetuximab (Erbitux®)
3 Oct. 2022: Announced CTCSA with Pfizer for palbociclib (Ibrance®)
4 Nov. 2022: Announced CTCSA with Pierre Fabre for encorafenib (Braftovi®)

Ongoing sub-study
Future sub-study

Note: CTCSA = clinical trial collaboration and supply agreement

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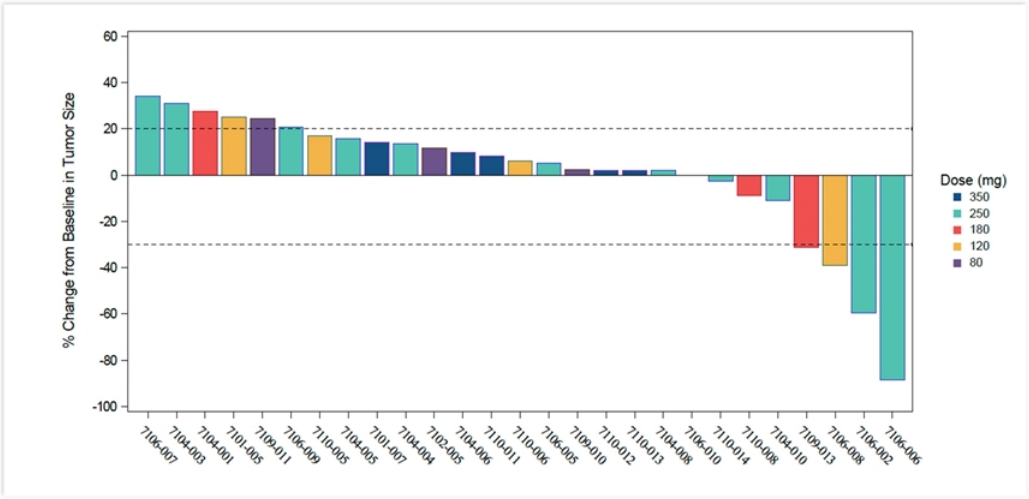
ERAS-007 Phase 1: Responses observed in patients with RAS and RAF alterations in diverse tumor types with single agent QW schedule

Waterfall Plot of Tumor Response by Patient for Once Weekly Schedule Efficacy-Evaluable Analysis Set



Four responses seen in patients with:

- **BRAF V600E thyroid CA** (180mg)
- **BRAF K601E NSCLC** (120mg)
- **HRAS salivary gland CA** (250mg)
- **BRAF rearranged melanoma** (250mg)

Source: ASN007-101 study; as of the November 6, 2020, data extraction
Note: Best percent change from baseline in tumor lesions is defined as the maximum reduction in post-baseline tumor lesion diameter compared to baseline tumor lesion diameter. Prior treatments in patients with objective responses: HRAS salivary gland – radiation; BRAF rearranged melanoma – nivolumab/ipilimumab, radiation; BRAF V600E thyroid – radiation; BRAF K601E NSCLC – carbo/pemetrexed, carbo-paclitaxel + durvalumab

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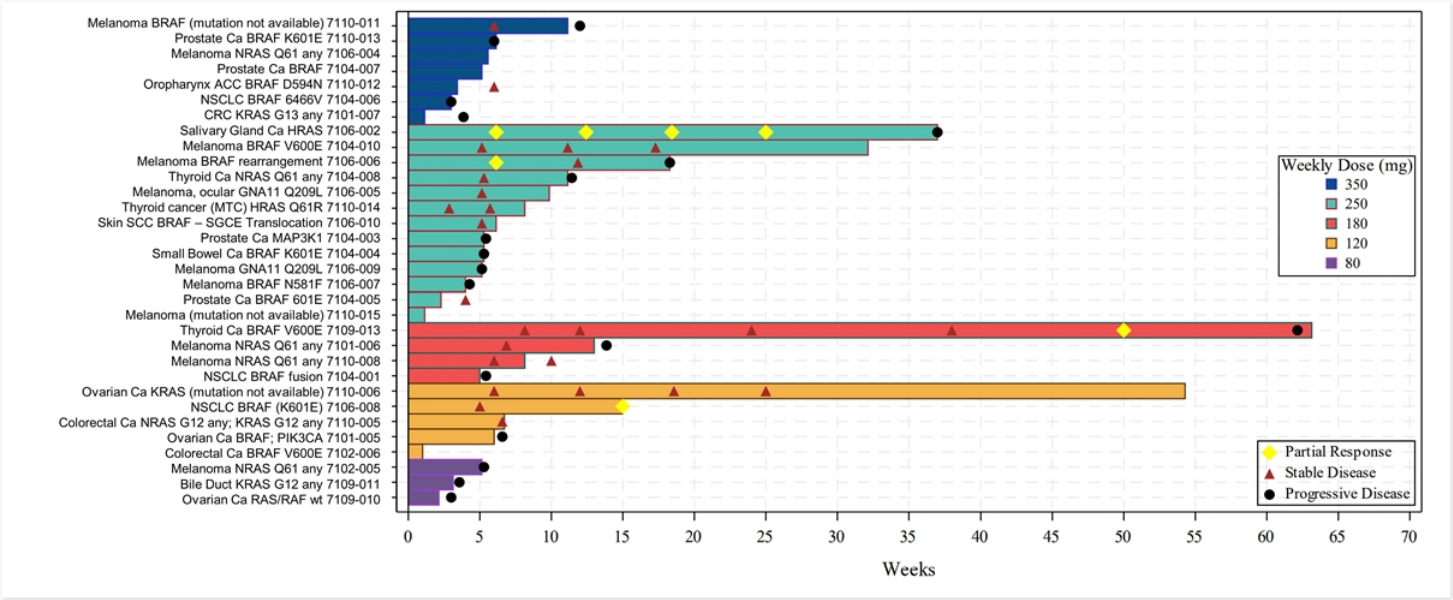
ERAS-007 swimmer plot demonstrated encouraging duration of treatment



One patient with BRAF V600E melanoma (7104-010) received ERAS-007 for a total of 71 weeks before experiencing disease progression

Source: ASN007-101 study; as of the November 6, 2020, data extraction

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Sept. 2022 R&D Day highlights*: MAPKlamp has potential to meaningfully impact BRAF Class II and III patients

Efficacy

- **ERAS-007** and **ERAS-601** are **active drugs** – monotherapy responses
  - **23% (6/26) of patients** with **RAS/MAPK-altered non-CRC solid tumors** and **44% (4/9)** with **BRAF-driven non-CRC solid tumors responded** (confirmed and unconfirmed PR) to single agent ERAS-007 or ERAS-601
  - **ERAS-007**: uPR in KRAS G12V PDAC on new BID-QW dosing
  - **ERAS-601**: cPR in BRAF Class III endometrial cancer—only second company to show monotherapy response with SHP2 inhibitor
- **Validated hypotheses** for combo of upstream + downstream RAS/MAPK pathway inhibition (MAPKlamp) and combo of RAS/MAPK + cell cycle inhibition

Safety

- Both compounds appear **safe and tolerable**, with **limited overlapping tox** (diarrhea)
- Diarrhea should be able to be managed with prophylaxis or supportive care

PK

- **Well behaved PK characteristics** for both drugs
- **ERAS-007**: data from PK modeling is nearly superimposable with observed data
- **ERAS-007**: **good exposure above IC90** for tumor cell killing and **below IC50** for normal cell recovery enables "hit and run" profile
- **ERAS-601**: **good exposure above IC50** for sustained target coverage

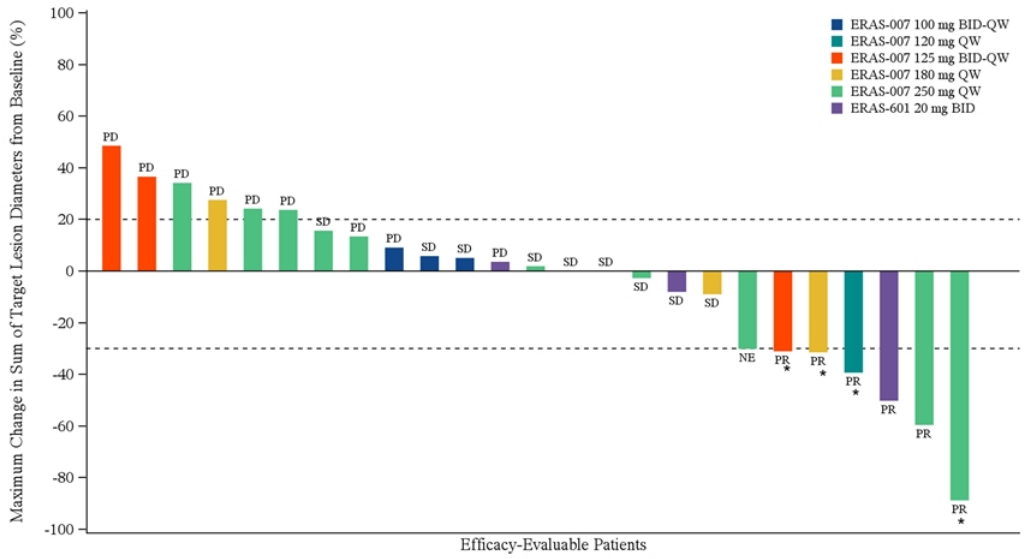
Future directions:

- Erasca identified a meaningful and targetable population—**specifically BRAF Class II and III**—that could benefit from MAPKlamp (ERAS-007 + ERAS-601)
- This patient population currently has no approved targeted therapy

Note: PK = pharmacokinetics; u/cPR = unconfirmed/confirmed partial response; PDAC = pancreatic ductal adenocarcinoma; BID-QW = two doses on one day each week

* The clinical data presented in the following slides are based on a retrospective analysis of pooled data across multiple clinical trials with different designs, inclusion criteria, and dosing regimens. Results across such clinical trials cannot be directly compared.

Best overall response with ERAS-007 or ERAS-601 in 15 RAS/MAPK-altered Blue Ocean Indications across lines of therapy



23% (6 out of 26) of patients responded (confirmed and unconfirmed PR) to single agent ERAS-007 or ERAS-601

* Unconfirmed partial responses indicated with an asterisk.
NOTE: Blue Ocean Indications defined as populations of unmet need with relevant tumor types and RAS/MAPK alterations where no targeted therapies are approved; Biologically relevant dose defined as weekly monotherapy dose intensity between 120mg and 250mg for ERAS-007 and daily monotherapy dose intensity of 40mg (40mg QD or 20mg BID) for ERAS-601; data extraction date: 6NOV2020 for ASN007-101, 11JUL2022 for ERAS-601-01, 16May2022 for ERAS-007-01. One patient without measurable disease at baseline and at least one post baseline target lesion measurement was excluded from the waterfall plot

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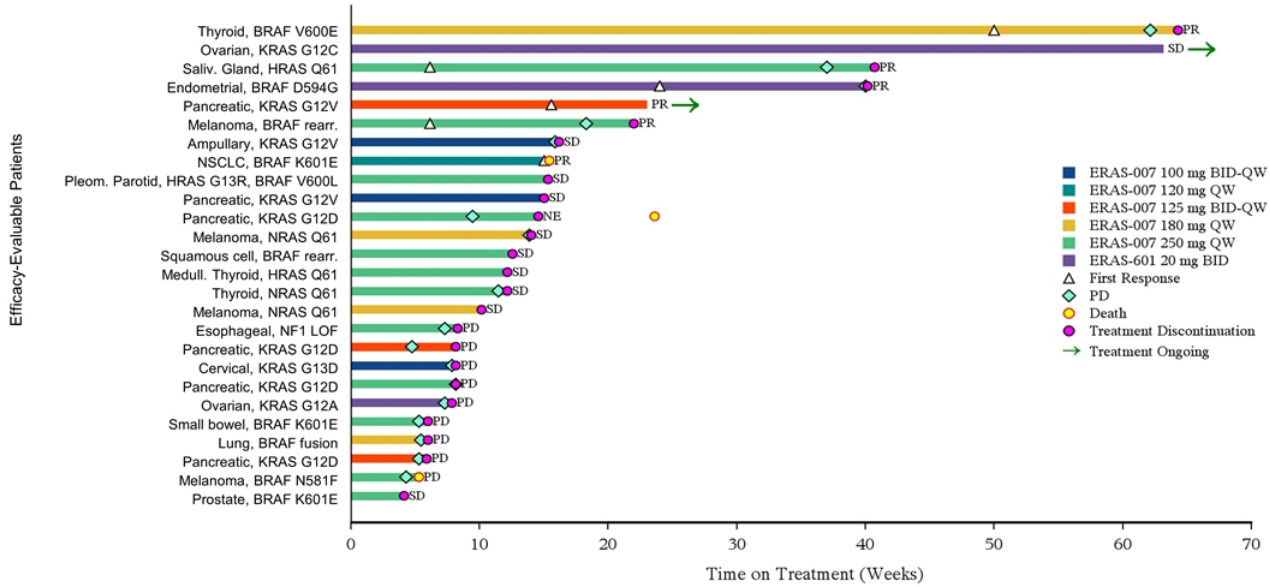
Duration of treatment observed with ERAS-007 or ERAS-601 in 15 RAS/MAPK-altered Blue Ocean Indications across lines of therapy



NOTE: Blue Ocean Indications defined as populations of unmet need with relevant tumor types and RAS/MAPK alterations where no targeted therapies are approved; Biologically relevant dose defined as weekly monotherapy dose intensity between 120mg and 250mg for ERAS-007 and daily monotherapy dose intensity of 40mg (40mg QD or 20mg BID) for ERAS-601; data extraction date: 6NOV2020 for ASN007-101, 11JUL2022 for ERAS-601-01, 16May2022 for ERAS-007-01.

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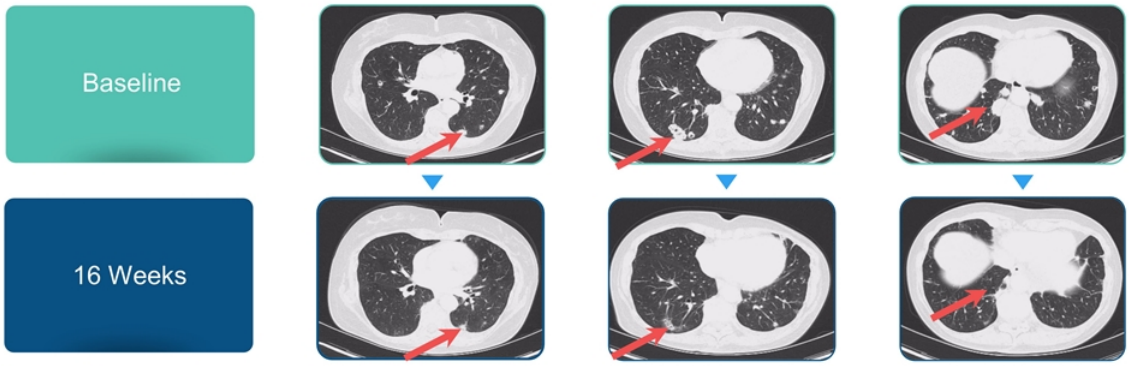
HERKULES-1 Case Study: Single agent ERAS-007 response
70-year-old female (Patient 0033) with KRAS G12V metastatic pancreatic cancer

Diagnosis	Stage II pancreatic cancer, metastatic disease, KRAS G12V, initially diagnosed in January 2018
Sites of Metastases	Lung, lymph nodes
Prior Therapy	Surgery, adjuvant radiation, gemcitabine/ capecitabine (#1); 5FU/oxaliplatin/irinotecan (#2); gemcitabine/abraxane (#3); 5FU/liposomal irinotecan (#4); alomfilimab (ICOS-targeted antibody)/atezolizumab (#5); MVT-5873 (anti-CA 19-9 antibody) (#6)
Dosing	ERAS-007 125 mg BID-QW



31% reduction
in tumor size

Per RECIST 1.1: ≥30% = objective response

Patient progressed with new lesion at subsequent assessment

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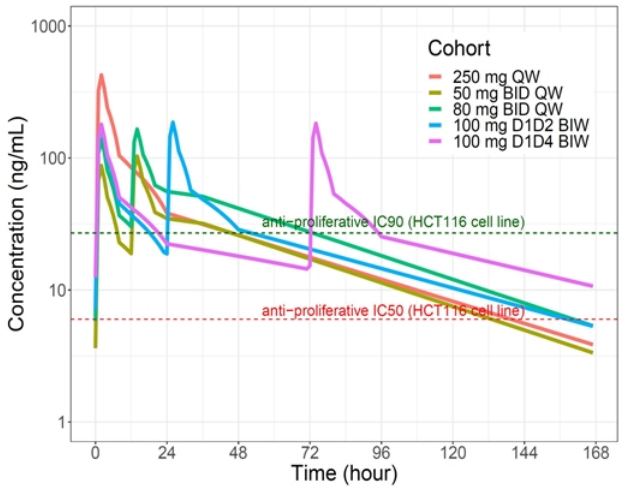
Phase 1 PK data showed QW is preferable to QD dosing; Simulations suggest BID-QW dosing may improve PK/PD profiles and combinability even more



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)

ERASCA

ERAS-601: Potential best-in-class SHP2i, favorable profile for combination

Company	Program	Stage
NOVARTIS	TNO155	Ph 3 *Observed LVEF decrease may pose combo challenges*
REVOLUTION MEDICINES	RMC-4630	Ph 2 *Observed anemia does not improve with intermittent dosing*
abbvie / Jacobio	JAB-3312	Ph 2
ERASCA	**ERAS-601**	**Ph 1b**
Genentech	RG6433	Ph 1 *In-licensed from Relay Therapeutics*
Bristol Myers Squibb	BBP398	Ph 1 *In-licensed from BridgeBio*
Pfizer	PF-07284892	Ph 1
MERCK	TAS-ASTC	Ph 1

Strong potency, favorable ADME/PK

- Strong *in vivo* potency relative to other SHP2i's in development
- Good exposure above IC50 for sustained target coverage

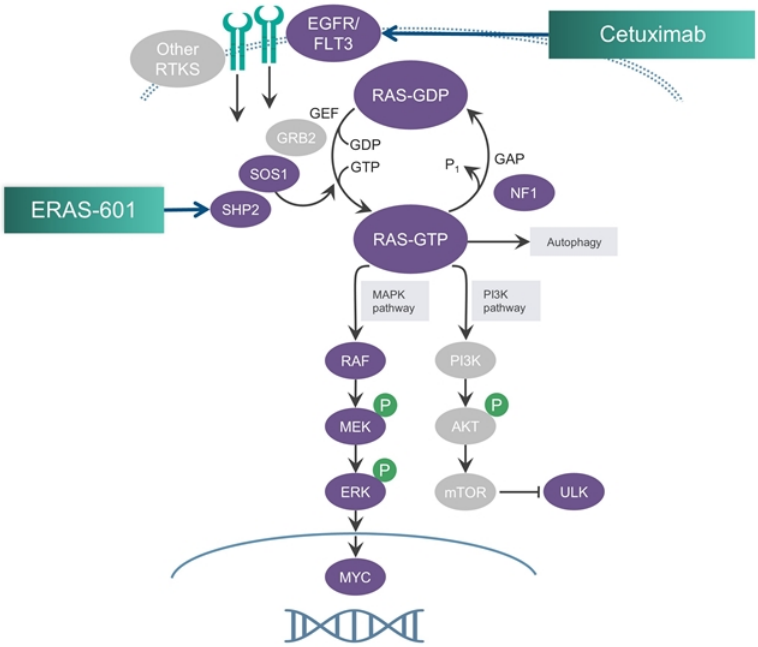
Safety and tolerability profile

- Clinical data to-date suggests ERAS-601 is generally safe and tolerable with reversible AEs
- Favorable for combinations

Encouraging signs of efficacy

- Although SHP2i expected to have its greatest impact in combination, ERAS-601 achieved monotherapy cPR (BRAF Class III endometrial)

Scientific rationale: Dual inhibition of EGFR and SHP2 in triple wildtype CRC and HPV-negative head and neck squamous cell carcinoma (HNSCC)



- EGFR-driven CRC and HPV-negative HNSCC are **highly dependent on RAS/MAPK pathway signaling**
- Dual blockade of EGFR and SHP2 could potentially **broaden and deepen responses compared to EGFR inhibition alone,** including in:
  - Triple wildtype (KRASwt, NRASwt, BRAFwt) CRC, representing nearly 50% of all patients with CRC
  - HPV-negative HNSCC, representing 70-75% of all patients with HNSCC

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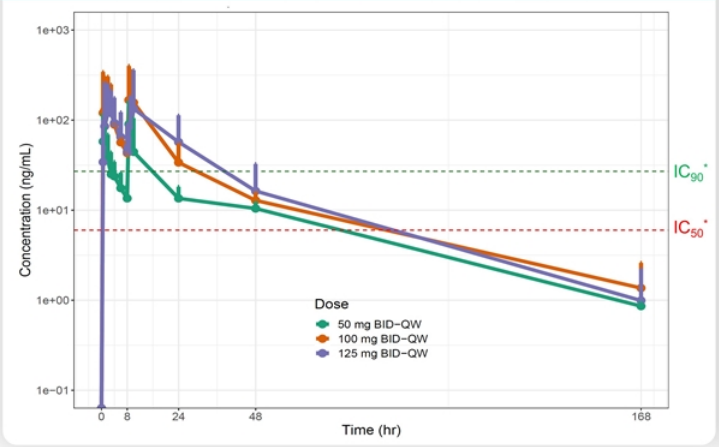
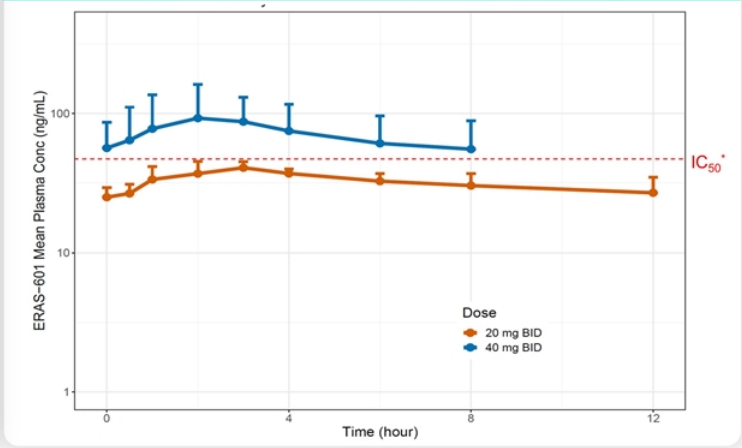
ERAS-007 and ERAS-601 use different target coverage strategies that seek to achieve optimal efficacy and safety

ERAS-007 Mean Cycle 1 PK Profile



ERAS-601 Mean Steady State PK Profile



ERAS-007: 50-125mg BID-QW dosing provided high target coverage ($C>IC_{90}$) for maximum activity, followed by lower PK coverage ($C<IC_{50}$) for MAPK pathway recovery to alleviate target driven toxicity

ERAS-601: 40mg BID dosing provided sustained target coverage ($C>IC_{50}$) throughout the dosing interval

*HCT 116 anti-proliferation assay for ERAS-007; pERK in NCI-358 for ERAS-601

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TRAEs of ERAS-601 and ERAS-007 have been largely non-overlapping

ERAS-601 and ERAS-007 by common SHP2i TRAEs

Treatment-related AEs in Preferred Terms	ERAS-601 20 and 40 mg BID (N=13)		ERAS-007 50-125mg BID-QW (N=23)	
	All Grade	Gr ≥ 3	All Grade	Gr ≥ 3
HEMATOLOGIC				
Thrombocytopenia*	3 (23.1%)	2 (15.4%)	0	0
Anemia	3 (23.1%)	1 (7.7%)	1 (4.3%)	1 (4.3%)
CARDIOVASCULAR				
Hypertension	3 (23.1%)	1 (7.7%)	0	0
Hypertensive encephalopathy	1 (7.7%)	1 (7.7%)	0	0
HEPATIC				
AST increase	2 (15.4%)	1 (7.7%)	0	0
ALT increase	2 (15.4%)	0	0	0
Blood bilirubin increased	0	0	1 (4.3%)	1 (4.3%)
GENERAL				
Peripheral edema	4 (30.8%)	0	1 (4.3%)	0

Gr 4 AEs:
ERAS-601: anemia, hypertensive encephalopathy
ERAS-007: none

- Data cut off for FLAGSHP-1: 11JUL2022 & for HERKULES-1: 23May2022
- In this table is reported the number of patients who experienced the reported AE at the highest grade.
- TRAEs included in this table met at least one of the following criteria: (1) experienced by ≥ 2 patients in either the 20 and 40 mg BID treatment group for ERAS-601 **OR** the 50-125 mg BID-QW column for ERAS-007; (2) experienced by at least 1 patient and Grade ≥3.
- *includes platelets count decrease

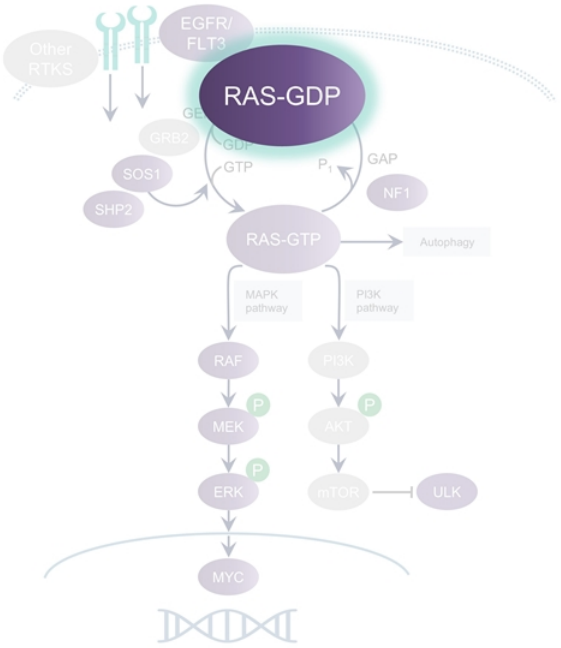
ERAS-601 and ERAS-007 by common ERKi TRAEs

Treatment-related AEs in Preferred Terms	ERAS-601 20 and 40 mg BID (N=13)		ERAS-007 50-125mg BID-QW (N=23)	
	All Grade	Gr ≥ 3	All Grade	Gr ≥ 3
SKIN				
Maculopapular rash	0	0	2 (8.7%)	0
Dermatitis acneiform	2 (15.4%)	0	8 (34.8%)	0
EYE DISORDERS				
Blurred vision	2 (15.4%)	0	5 (21.7%)	1 (4.3%)
Retinopathy	0	0	6 (26.1%)	0
Retinal Detachment	0	0	1 (4.3%)	1 (4.3%)
Vision Impairment	0	0	1 (4.3%)	1 (4.3%)
GASTROINTESTINAL				
Nausea	0	0	12 (52.2%)	0
Vomiting	0	0	7 (30.4%)	0
Diarrhea	5 (38.5%)	1 (7.7%)	5 (21.7%)	0
Constipation	0	0	2 (8.7%)	0
Dyspepsia			2 (8.7%)	0
GENERAL				
Fatigue	1 (7.7%)	0	9 (39.1%)	2 (8.7%)
Dehydration	0	0	4 (17.4%)	0
Dizziness	0	0	2 (8.7%)	0

Potential overlapping tox; can be managed proactively

ERASCA

Dr. Kevan Shokat at UCSF turned KRAS from undruggable to druggable



- Shokat identified a G12C-specific inhibitor that locks KRAS in inactive state, spurring multiple companies to develop KRAS G12C inhibitors
- High unmet need remains for patients with NSCLC (**CNS metastases occur in up to 40% of patients**)
- Focus of our discovery efforts has been on developing KRAS G12C inhibitors with **high CNS penetration**

Source: Ostrem J., et al. K-Ras(G12C) inhibitors allosterically control GTP affinity and effector interactions. Nature, 2013. PMID: 24256730

We have discovered promising CNS-penetrant KRAS G12Ci pre-candidates

Parameter	3490[1]	3691	3599	3537	3788	Reference compounds[2]
Mouse AUC_{po}/D (hr*kg*ng/mL/mg)	↑ 693	↔ 597	↑ 1,333	↔ 535	↔ 326	102 - 637
Rat $brain_{total}$ / $plasma_{total}$ (%)	↑ 52%	↑ 13%	↑ 66%	↑ 68%	↑ 11%	1 - 6%
Rat brain concentration (ng / g)	↑ 156	↔ 32	↑ 176	↑ 290	↑ 91	6 - 36
P-gp substrate ratio[3]	↑ 1.5	↑ 4.1	↑ 2.7	↑ 8.3	↑ 4.0	30.9[4]
Human LM metabolic stability (CL normalized to hepatic blood flow)	↔ 0.7	↑ 0.5	↔ 0.6	↑ 0.4	↑ 0.5	0.7 - 0.8
Mouse LM metabolic stability (CL normalized to hepatic blood flow)	↔ 0.8	↔ 0.6	↔ 0.7	↔ 0.7	↑ 0.4	0.4 - 0.9
In vitro potency (4 hr pERK IC50, nM / RAS Initiative KRAS G12C 3D 5-day viability IC50, nM)	↔ 13 / 4	↘ 58 / 9	↘ 37 / 15	↔ 21 / 9	↔ 12 / 2	17 - 31 / 1 - 4

[1] ERAS-3490 has been selected as the KRAS G12C inhibitor development candidate
[2] The reference compounds are sotorasib and adagrasib
[3] P-gp substrate ratios were characterized in a P-gp expressing MDCK cell line. Per compound, a P-gp substrate ratio was calculated by dividing its efflux ratio in absence of a P-gp inhibitor by its efflux ratio in presence of a P-gp inhibitor. Compounds with lower P-gp substrate ratios are less likely to be P-gp substrates
[4] The P-gp substrate ratio was characterized for a single reference compound.

ERASCA