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): December 9, 2022

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** **(Address of Principal Executive Offices)**	**92121** **(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 1.01 Entry into a Material Definitive Agreement.

On December 9, 2022, Erasca, Inc. (the Company) entered into an exclusive license agreement (the License Agreement) with Novartis Pharma AG (Novartis) under which the Company was granted an exclusive, worldwide, royalty-bearing license to certain patent and other intellectual property rights owned or controlled by Novartis to develop, manufacture, use, and commercialize naporafenib in all fields of use. The Company has the right to sublicense (through multiple tiers) its rights under the License Agreement, subject to certain limitations and conditions, and is required to use commercially reasonable efforts to commercialize licensed products in certain geographical markets.

The license granted under the License Agreement is subject to Novartis' reserved right to: (i) develop, manufacture, use, and commercialize compounds unrelated to naporafenib under the licensed patent rights and know-how, (ii) use the licensed patent rights and know-how for non-clinical research purposes, and (iii) use the licensed patent rights and know-how to the extent necessary to perform ongoing clinical trials and its obligations under existing contracts and under the License Agreement.

Under the License Agreement, the Company will make an upfront cash payment to Novartis of $20 million, and issued to Novartis shares of common stock of the Company having an aggregate value of approximately $80 million (the Shares). The Shares were issued in a private placement in reliance on Section 4(a)(2) of the Securities Act of 1933, as amended, for transactions by an issuer not involving any public offering. The Company relied upon this exemption from registration based in part on representations made by Novartis in a stock issuance agreement entered into between the Company and Novartis, dated December 9, 2022. During the six-month period following the date of the stock issuance agreement, Novartis agreed not to sell or otherwise transfer, subject to certain exceptions, the Shares, and for the period until one year following the date of issuance, to certain volume restriction on any sales of Shares.

The Company is obligated to make future regulatory milestone payments of up to $80 million and sales milestone payments of up to $200 million. The Company is also obligated to pay royalties on net sales of all licensed products, in the low-single digit percentages, subject to certain reductions.

The License Agreement will expire upon the last to expire royalty term, which is determined on a licensed product-by-licensed product and country-by-country basis, and is the later of: (i) ten years from the date of first commercial sale for the licensed product in such country, (ii) the last to expire valid claim within the licensed patent rights covering such licensed product, or (iii) the expiration of all regulatory exclusivity for the licensed product in such country. Upon expiration of the License Agreement, on a licensed product-by-licensed product and country-by-country basis, the Company will have a fully paid-up, perpetual, and irrevocable license to develop, manufacture, use, and commercialize the licensed products.

The License Agreement may be terminated in its entirety by either party in the event of an uncured material breach by the other party. Novartis may terminate the License Agreement upon written notice in the event the Company becomes subject to specified bankruptcy, insolvency, or similar circumstances. The Company may terminate the License Agreement in its entirety at any time upon the provision of prior written notice to Novartis.

Upon termination of the License Agreement for any reason, all rights and licenses granted to the Company will terminate. In addition, upon termination of the License Agreement for any reason other than its natural expiration, Novartis has an option to negotiate a license under any patent rights, know-how, or other intellectual property rights relating to the licensed products that are owned or controlled by the Company for the purpose of developing, manufacturing and commercializing the licensed products on terms to be negotiated between the parties.

The foregoing description of the License Agreement is not complete and is qualified in its entirety by reference to the full text of the License Agreement, a copy of which will be filed as an exhibit to the Company's Annual Report on Form 10-K to be filed with respect to the fiscal year ending December 31, 2022.

Item 3.02 Unregistered Sales of Equity Securities.

The disclosure set forth in Item 1.01 above with respect to the issuance of the Shares is incorporated in this Item 3.02 by reference.

Item 8.01 Other Events.

An updated Company presentation, including an overview of naporafenib, is attached as Exhibit 99.1 to this report and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Erasca, Inc. Corporate Presentation, dated December 2022
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: December 9, 2022

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

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Exhibit 99.1

On a Journey to Erase Cancer

Erasca Corporate Presentation

December 2022

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 the anticipated naporafenib licensing transaction and when and whether such transaction will close, 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, including without limitation the anticipated naporafenib license agreement, 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 three product candidates in early 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.

Erasca is accelerating its leadership in the RAS/MAPK pathway through in-licensing of exclusive worldwide rights to naporafenib[1] (LXH254; pan-RAFi)

Bolsters pipeline with late-stage asset	• **Naporafenib is a Phase 2, pivotal-ready pan-RAF inhibitor with a potential first-in-class and best-in-class profile in NRASm melanoma & other RAS/MAPK-driven tumors** • **500+ patients treated** with naporafenib **establishing safety, tolerability and preliminary POC** in both monotherapy and combinations
Expands addressable patients	• Broad development strategy for naporafenib could **address up to ~3.5m patients WW**, significantly **expanding Erasca's total addressable patient population** • Opportunities for **multiple combination approaches (esp. with MEKi or ERKi)** in many tumor types and **populations with poor prognosis and high unmet medical need (e.g., NRASm melanoma)**
Complements Erasca's portfolio	• Naporafenib targets **BRAF and CRAF node critical to driving downstream RAS/MAPK pathway signaling** in a broad range of RAS mutant cancers • Synergistic with Erasca's **industry leading portfolio shutting down every node of the RAS/MAPK pathway**
Accelerates path to market	• Erasca's **planned SEACRAFT trials** are enabled by naporafenib's broad development opportunities **in combination with other targeted therapies** • Prioritizing rapid development for naporafenib + trametinib in RAS Q61X tissue agnostic tumors (Phase 2 **SEACRAFT-1**) and NRASm melanoma (Phase 3 **SEACRAFT-2**) • **Commercial process and formulation** have been developed and successfully manufactured at scale

[1]For commercial and portfolio prioritization reasons, Novartis is out-licensing this program and ran a competitive process with multiple bidders for a worldwide license

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Pro forma with naporafenib

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-3490, CNS-penetrant KRAS G12Ci** with best-in-class potential in NSCLC
- **ERAS-801, CNS-penetrant EGFRi** with first-in-class potential for EGFR-driven rGBM

Strong financial position with high quality investor base and industry visibility

- **~$365M in cash, cash equivalents, and short-term marketable securities[2]**
- 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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Relevant RASm's recut for naporafenib

~5.5m lives at stake annually worldwide with RAS/MAPK pathway alterations

Naporafenib's broad development strategy significantly expands our addressable patient populations

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
N/H/KRAS Q61X	**0.4**	**23**	**35**	**80**	**69**	**32**	**155**	**4.1**	**51**	**106**	**242**	**399**
H/N/KRAS G13R	**-**	**9.4**	**5.9**	**5.5**	**2.1**	**-**	**14**	**0.5**	**3.6**	**8.1**	**26**	**37**
Other K/N/HRAS	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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Erasca's SEACRAFT trials to address naporafenib's Blue Ocean opportunities

*In any nautical journey, seacraft are needed to traverse the vast blue ocean not just in their capacity as seagoing ships, but also for their important second meaning: skill in navigation. Erasca is navigating the "blue ocean" of unmet medical needs using next generation sequencing and other techniques to identify RAS/MAPK pathway-altered tumors that can be treated with naporafenib, a potent, selective, orally bioavailable pan-**RAF** inhibitor, in combination with other targeted therapies.*

1. SEACRAFT-1

Strategy: Signal-seeking trial designed to generate data in the near term to inform development, including potential tissue agnostic indication

Design: Expected to be a single-arm phase 2 trial assessing naporafenib + trametinib for the treatment of pan-RAS Q61X tissue agnostic solid tumors

2. SEACRAFT-2

Strategy: Pivotal study to support global approval in the lead indication, NRASm melanoma

Design: Expected to be a randomized phase 3 pivotal trial assessing naporafenib + trametinib for the treatment of NRASm melanoma

3. SEACRAFT-3

Strategy: Expand development of naporafenib with other RAS/MAPK targeting agents

Design: Expected to be a Phase 1/2 in patients with solid tumors driven by NF1 LOF, pan-RAS G13R, KRAS G12C, and BRAF Class 2 and 3 alterations

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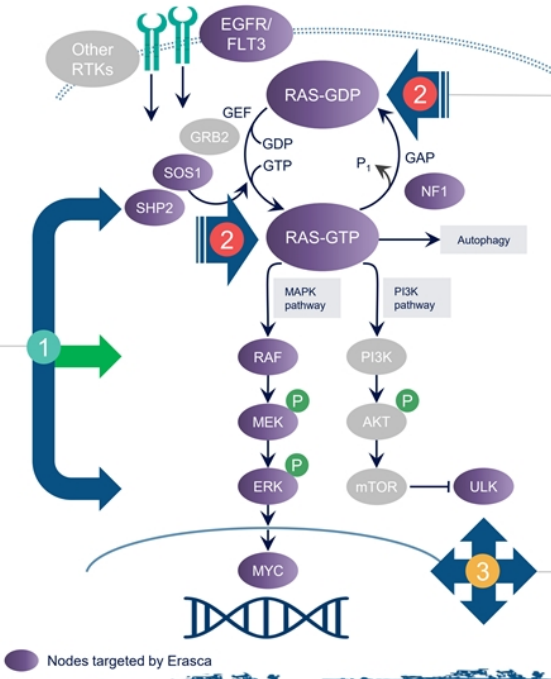
Pro forma with naporafenib

Our singular focus is on the RAS/MAPK pathway

Naporafenib targets BRAF/CRAF node critical to driving signaling in a broad range of RASm cancers

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

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Pro forma with naporafenib

Naporafenib complements and significantly advances 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

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

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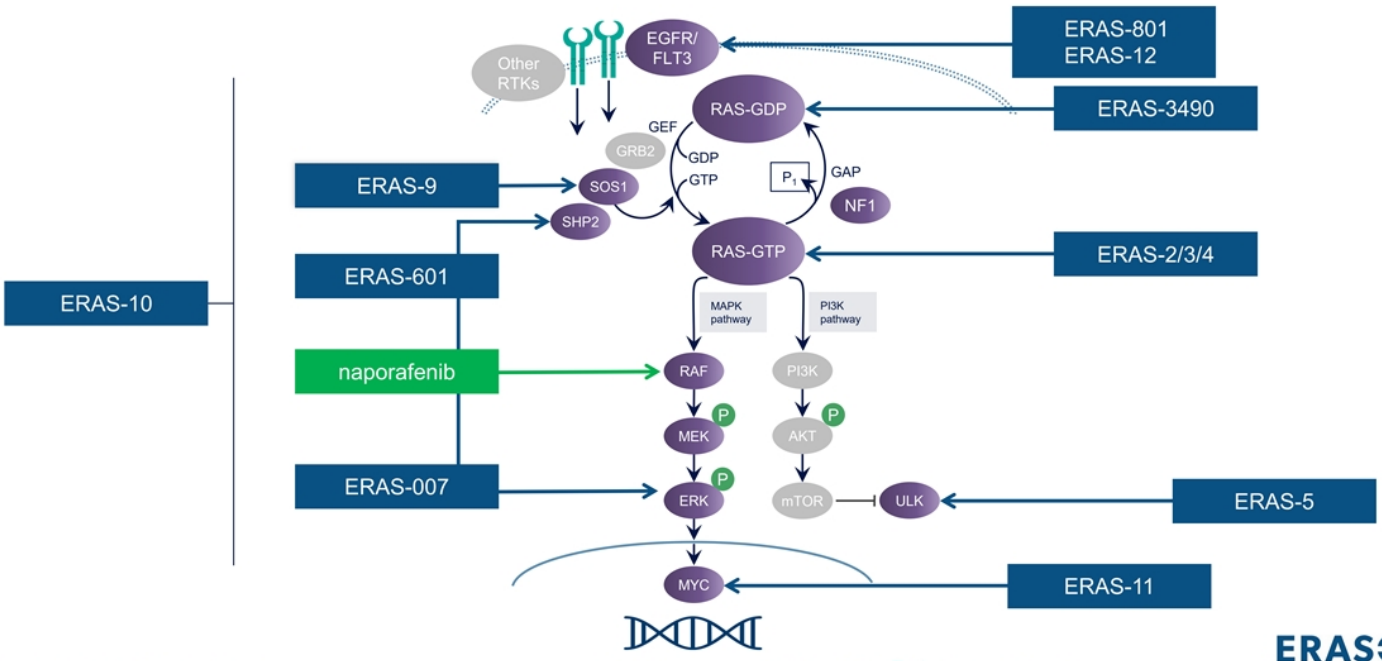
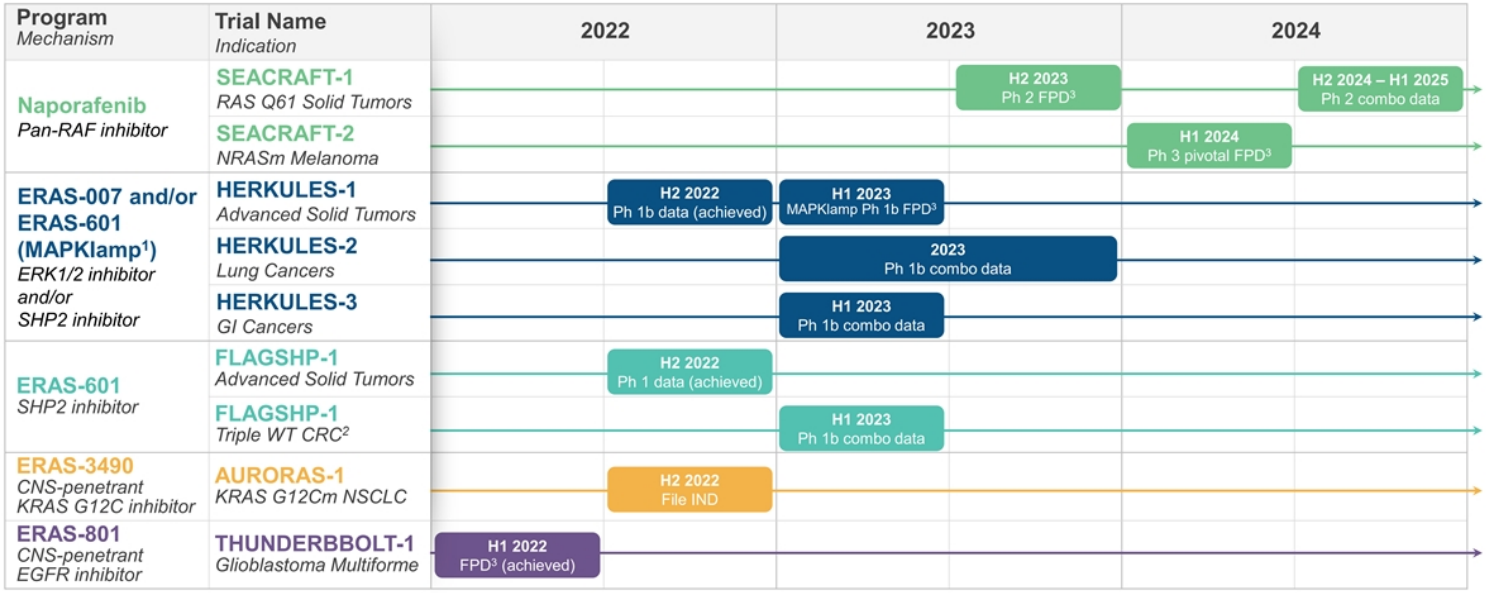
Naporafenib is synergistic with Erasca's industry-leading pipeline shutting down every node of the RAS/MAPK pathway

Pro forma with naporafenib



Naporafenib milestones and clinical trial readouts complement Erasca's existing portfolio[4] and potentially accelerate path to market

Pro forma with naporafenib



[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 dosed
[4] Guidance on milestones and clinical trial readouts for rest of pipeline to be provided in 2023

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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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Leadership team has global experience and drive to make a difference

Jonathan Lim, MD
Chairman, CEO, and Co-Founder

Mike Varney, PhD
Chairman of R&D, SAB Member, and Board Director

David Chacko, MD
Chief Financial Officer

Ebun Garner, JD
General Counsel

Wei Lin, MD
Chief Medical Officer

Lisa Tesvich-Bonora, PhD
Chief People Officer

Brian Baker, CPA
SVP of Finance

Les Brail, PhD
VP of Clinical Development

Rachel Cervantes, PhD
VP of Business Development

Nik Chetwyn, PhD
SVP of Operations

Tim Grammer, PhD
VP of Portfolio, Program & Alliance Management

Amy Grekowicz Parker, MPH
VP Clinical Operations

Chandra Lovejoy, MS
SVP of Regulatory Affairs

Shannon Morris, MD PhD
SVP of Clinical Development

Robert Shoemaker, PhD
SVP of Research

Jean-Michel Vernier, PhD
VP of Chemistry

Minli Xie, PhD
VP of CMC

Dawei Xuan, PhD
VP of Clinical Pharmacology

Jing Yi, PhD
VP of Data Science

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Product Development Team leadership with deep collective experience and track record of successfully obtaining approvals

Complex / Novel CDP and Study Designs	HA Negotiations, Study Implementation, Overall Development	Global Marketing Application Content & Strategy	Commercialization, ROW Submissions, Payer Plans
✓ **Successful study designs** for Phase 2 approvals, use of novel endpoints, and companion diagnostics	✓ **Successful health authority negotiations**: US/ EU/ Japan/ China	✓ **Successful Marketing Application Development:** Strategies to support AA/CMA and Full Approval	✓ **Successful Global Marketing Application Submissions:** US/EU/China/Japan
✓ **Master protocol experience**: designing and implementing complex trials	✓ **Complex trial implementation** across multiple geographies	✓ **ROW Strategy & Planning**	✓ **Life Cycle Management planning** (label expansion)
	✓ **Successful overall development plans** to include Pediatric Strategies, Rare Diseases and Biomarkers;	✓ **Successful regulatory inspections (US/EU):** establishing quality systems for rapid Phase 2 initial approvals	✓ **HTA/Payer Experience** to support reimbursement and price negotiation
	✓ **Creativity and Drive:** Success in short timelines and in small companies		✓ Continued **process verification and product serialization** to support global demands
	✓ **Regulatory Designations:** BTD, PRIME, Sakigake, Orphan, EU SME		

*Examples from previous companies where **drive and creativity** led to efficient and novel initial global approvals*

Tumor agnostic and CDx approval	Novel indication on Ph 2 Data	Novel drug/Dx on Ph 2 Data	Early CDP/BLA on Ph 2 Data	Novel ROW Filing	Fast Filing Initiative
ROZLYTREK entrectinib	COSELA trilaciclib	ALECENSA alectinib	IMFINZI durvalumab	TECENTRIQ atezolizumab	TECENTRIQ atezolizumab
Ignyta/Roche	*G1 Therapeutics*	*Roche/Genentech*	*MedImmune*	*Roche/Genentech*	*Roche/Genentech*

CDP: clinical development plan

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Key license terms for naporafenib (LXH254) pan-RAFi: Potential first-to-market molecule for melanoma, tissue agnostic, and more

- **License scope:** Exclusive license to patent rights, know-how, and regulatory documentation covering naporafenib and all backups
- **Field:** All fields of use
- **Territory:** Worldwide
- **Drug supply:** Novartis will transfer existing inventory of naporafenib and provide access to trametinib

Expected financial terms	**Amount** ($M unless otherwise indicated)
Total upfront *– Cash* *– Equity*[1]	**$100** *$20* *$80*
Total development milestones – cash	$0
Total regulatory milestones – cash[2]	Up to $80 *(incl. up to $30 for 2nd indication)*
Total commercial milestones – cash *– First commercial sale* *– Sales-based milestones*	Up to $200 *– $0* *– Up to $200*
Total deal value before royalties *(excluding equity)*	**Up to $300**
Royalties	**Low single digit percentage**

Erasca and Novartis are currently negotiating the definitive agreement[3] and are targeting deal signing and announcement during the week of December 5, 2022

[1] Equity to be issued at an agreed upon price
[2] Covers two indications in US, EU, and JP
[3] Deal terms subject to change until the definitive agreement is executed

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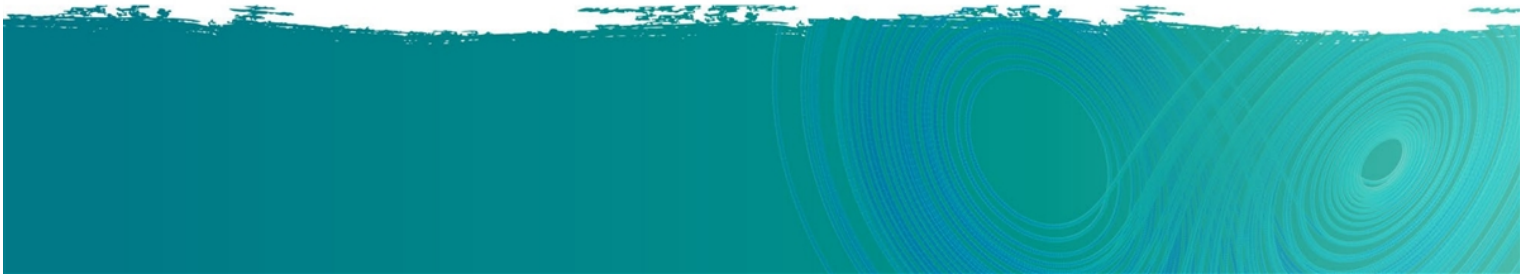
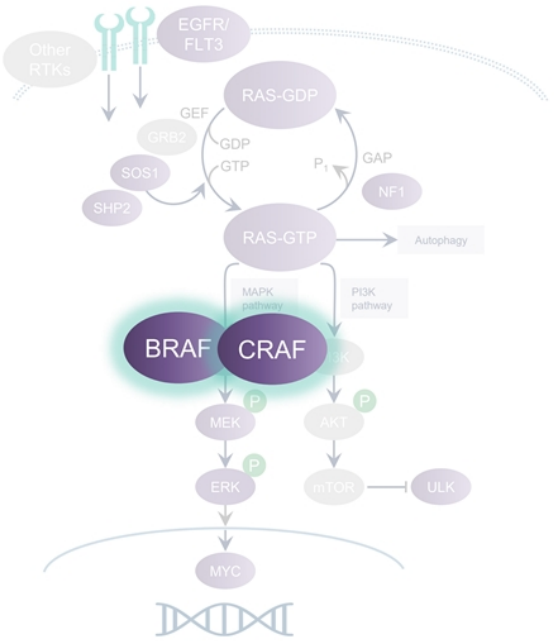
Naporafenib Overview



BRAF/CRAF is a critical node of the RAS/MAPK pathway



- **BRAF and CRAF drive downstream RAS/MAPK pathway signaling** in RAS mutant cancers
- **NRASm melanoma and RAS Q61X solid tumors** are exquisitely dependent on BRAF and CRAF
- RAF kinases are **activated through dimerization** with the same or other members of the RAF family
- Opportunities exist for **multiple combination approaches**, especially with inhibitors of downstream nodes, MEK and/or ERK

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

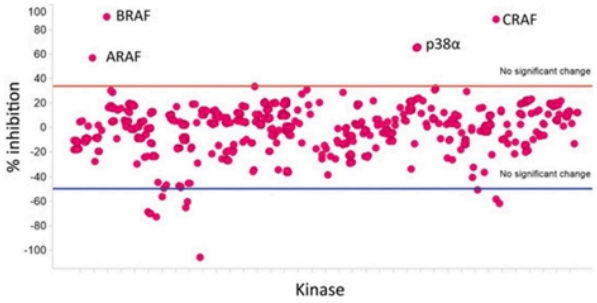
Biochemical activity of naporafenib against RAF kinase family

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

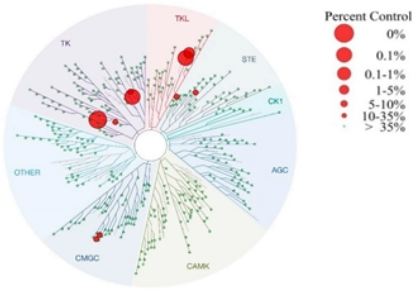
Kinases inhibited >80% by naporafenib at 1 µM out of 456 kinases, per KINOMEscan (kinases are WT unless marked otherwise)

Kinase	% Inhibition at 1 µM
PDGFRB	99.9%
DDR1	99.7%
BRAF V600E	99.7%
BRAF	99.6%
CRAF	98.8%
DDR2	84.0%

Biochemical kinome profiling of LXH254 in HCT116 cell lysates



Biochemical activity of naporafenib across 456 kinases (KINOMEscan)

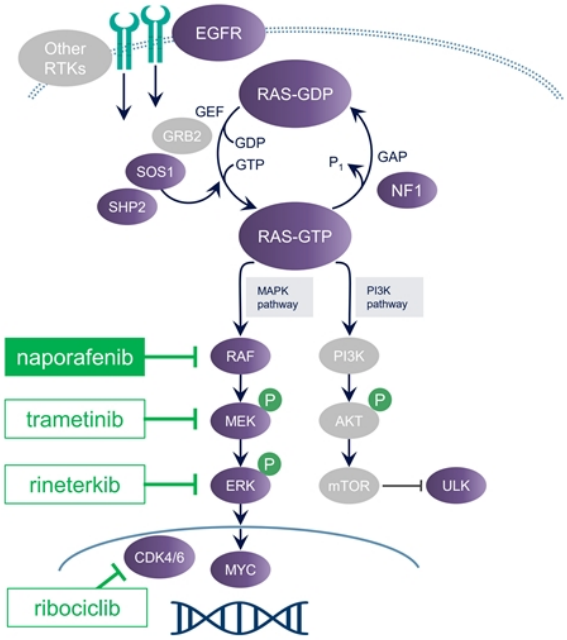


ERASCA

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 clinical development to date in more than 500 patients

Wealth of early phase data has established safety, tolerability and preliminary POC

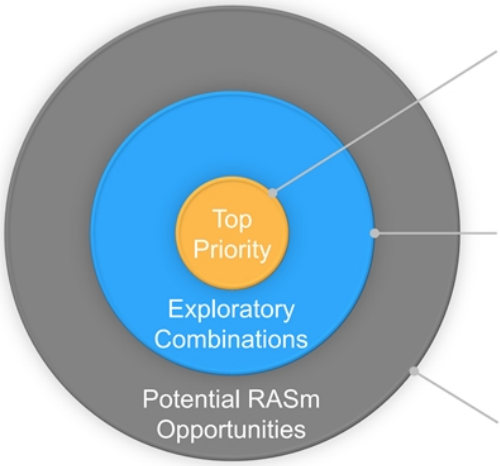


- **Trial LXH254X2101 (n=142)**: naporafenib FIH dose escalation study conducted in patients with RAS/MAPK-driven solid tumors
- **Trial LXH254X2102 (n=241):** dose finding study of naporafenib combinations (+rineterkib [ERKi] [n=101], trametinib [MEKi] [n=115], or ribociclib [CDK4/6i] [n=25]) in patients with NRASm melanoma, KRASm or BRAFm NSCLC
- **Trial LXH254C12201 (n=134)**: Phase 2 study of naporafenib combinations (+rineterkib [n=59], trametinib [n=53], or ribociclib [n=22]) in patients with NRASm or BRAF V600X melanoma
- **Trial ADPT01C12101 (n=7)**: platform study exploring the triplet combination of naporafenib + dabrafenib + rineterkib (n=7) in BRAF V600X CRC
- ***Total size of safety database > 500 patients (includes monotherapy and combinations)***

Source: Novartis Non-Confidential Materials

ERASCA

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 doublet, and possibly triplet, combination(s) in NF1 LOF, RAS G13R, KRAS G12C, and BRAF Class 2 and 3 altered solid tumors (SEACRAFT-3)

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

ERASCA

~5.5m lives at stake annually worldwide with RAS/MAPK pathway alterations

Prioritized development plan for naporafenib potentially addresses ~3.5m (over 63%) of these

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
N/H/KRAS Q61X	0.4	23	35	80	69	32	155	4.1	51	106	242	399
H/N/KRAS G13R	-	9.4	5.9	5.5	2.1	-	14	0.5	3.6	8.1	26	37
Other K/N/HRAS	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
									542			
										1,285		
											3,696	
												5,522

Top priority addresses ~395,000 patients worldwide

Exploratory combos address ~1.2m patients worldwide

Potential RASm opportunities address ~1.9m patients worldwide

Blue ocean opportunities Red ocean opportunities

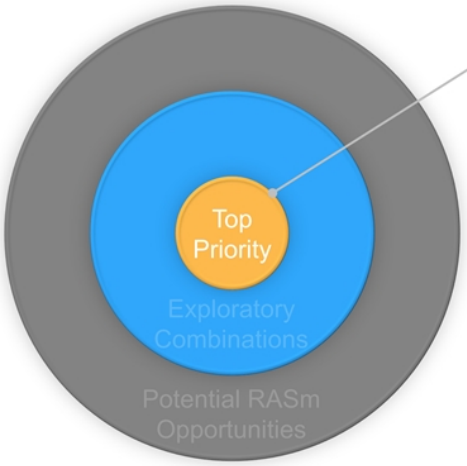
* Post-Osimertinib resistant population shown for EGFRm NSCLC except for SCLC transformation

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

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

ERASCA

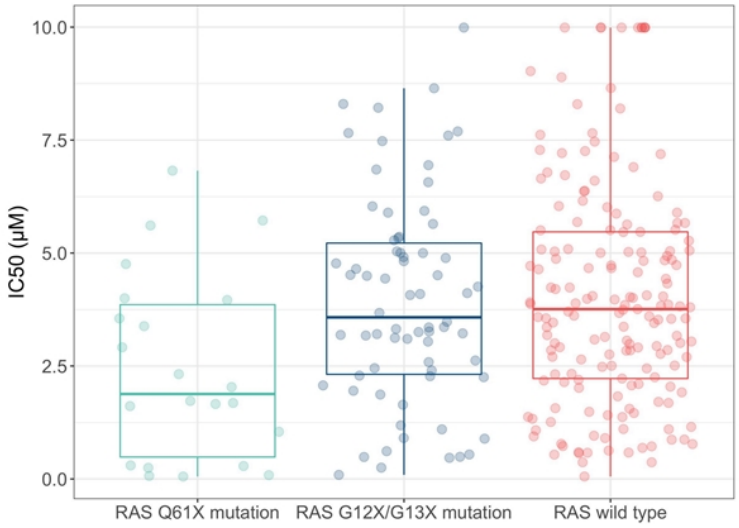
Focused development plan in Q61X tissue agnostic solid tumors (SEACRAFT-1)



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

Structural and cell line screening data suggest that differences exist across different RAS mutants in vitro; e.g., Q61X mutant tumors likely to be CRAF addicted

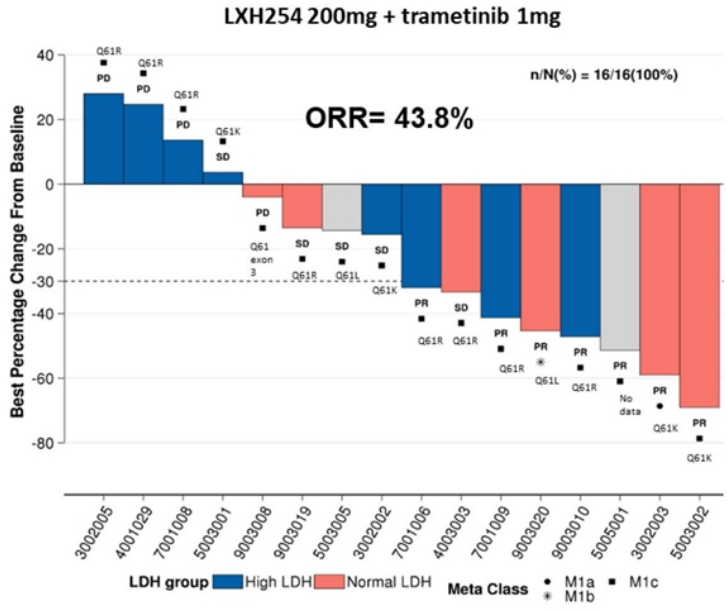
Cellular activity of naporafenib across 265 cell lines, separated by RAS mutation type



ERASCA

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

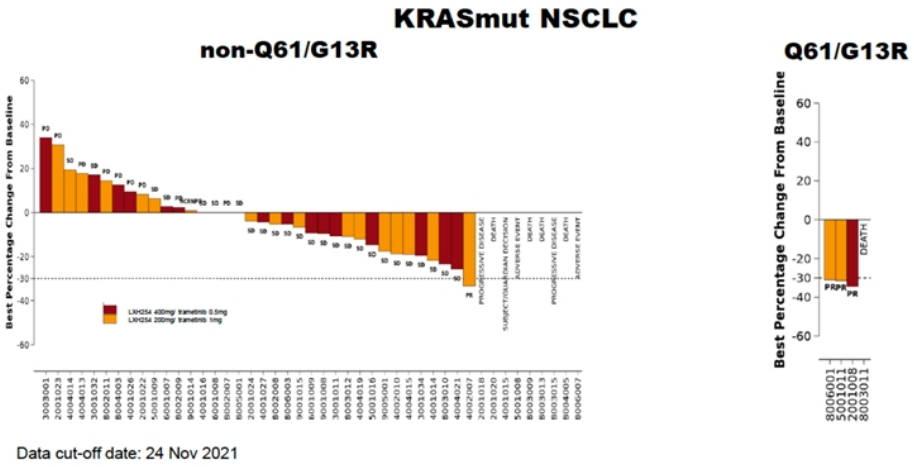
Strong activity of naporafenib + trametinib observed in NRASm melanoma in LXH254X2102 Phase 1 may also be driven by natural enrichment of Q61X mutations



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

Source: Novartis Non-Confidential Materials

Strong activity of naporafenib + trametinib also observed in KRASm NSCLC (N=49) in LXH254X2102 Phase 1, showing 34x higher ORR in Q61X/G13R mutated group



Data cut-off date: 24 Nov 2021

- ***ORR in mutated group is 34x more than the ORR in the non-mutated group***
  - ORR in mutated group (n=4): 75% (95% CI: 19.4% - 99.4%) (variability is high and sample size is low in the mutated group)
  - ORR in non-mutated group (n=45): 2.2% (95% CI: 0.1% - 11.8%)
  - Confirmed/unconfirmed RECIST responses shown

Source: Novartis Non-Confidential Materials

ERASCA

Naporafenib + trametinib combination has a compelling opportunity to address unmet needs in the Q61X tissue agnostic solid tumor indication

Clinical Unmet Need

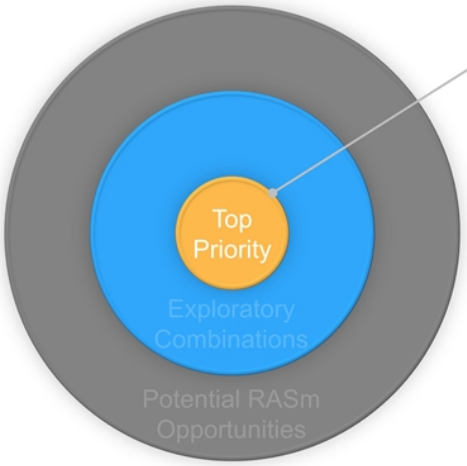
- The targeted patient population has exhausted all treatment options
- In these types of advanced patients without any SOC options, preventing progression is important since progression frequently leads to mortality; i.e., there are not any approved therapies they can receive once they progress

Naporafenib and trametinib

- Strong scientific rationale for targeting RAS Q61X mutations with naporafenib; trametinib adds synergistic activity
- Clinical POC for Q61X already achieved for melanoma and NSCLC
- Trametinib is already an established SOC component which is predicted to facilitate physician comfort with this combination

SOC = standard of care

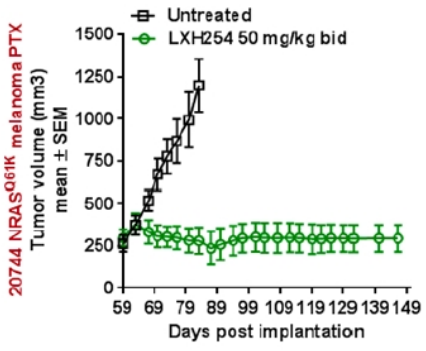
Focused development plan in NRASm melanoma (SEACRAFT-2)



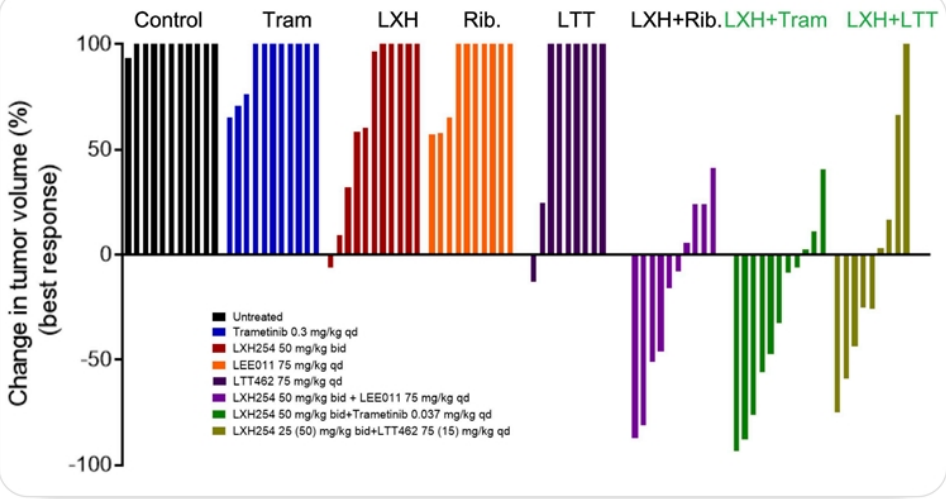
Focus on securing regulatory approval for naporafenib + trametinib in RAS Q61X tissue agnostic solid tumors (SEACRAFT-1) and/or NRASm melanoma (SEACRAFT-2) as soon as possible

NRAS mutant in vivo models exhibited sensitivity to naporafenib both as a single agent and in anchored combinations

NRASm model treated with LXH254 single agent



NRASm melanoma PDX models treated with LXH254 anchored combinations



Note: LEE011 or Rib. (ribociclib) is a CDK4/6 inhibitor; Tram (trametinib) is a MEK inhibitor; and LTT (LTT462) is an ERK inhibitor
Source: Novartis Non-Confidential Materials

ERASCA

Current Standard of Care for metastatic melanoma with NRAS mutation

Poor SOC in post-IO setting highlights a high unmet need indication

Frontline therapy is IO mono or combo

Immunotherapy

Nivolumab
Pembrolizumab
Nivolumab + Ipilimumab
Nivolumab + Relatlimab

Post-IO therapy is predominantly chemo

Chemotherapy

Dacarbazine
Temozolomide
Paclitaxel
Nab-paclitaxel
Carboplatin + paclitaxel
Cisplatin + vinblastine + dacarbazine

MEKi (not approved)

Binimetinib (recommended by US NCCN but not by EU guidelines)

SOC *	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

* NEMO trial (*Lancet Oncol* (2017) 18: 435-445.)

ERASCA

The observed clinical activity of naporafenib + trametinib in NRASm melanoma was reproducible across Phase 1 and Phase 2 studies at two RDEs

Study/Indication	Data Cutoff	LXH254 (200 mg BID) + trametinib (1.0 mg QD)			LXH254 (400 mg BID) + trametinib (0.5 mg QD)			Source
		ORR	DCR	DOR	ORR	DCR	DOR	
LXH254X2102* NRASm melanoma	9 Dec 2021	7/15 (46.7%)	12/15 (80.0%)	3.75 mo	2/15 (13.3%)	10/15 (66.7%)	3.75 mo	AACR 2022
LXH254C12201# NRASm melanoma	4 July 2022	6/24 (25%)	17/24 (70.8%)	NA	5/17 (29%)	12/17 (70.6%)	NA	ESMO 2022

Total of 13/39 responses
33.3% ORR

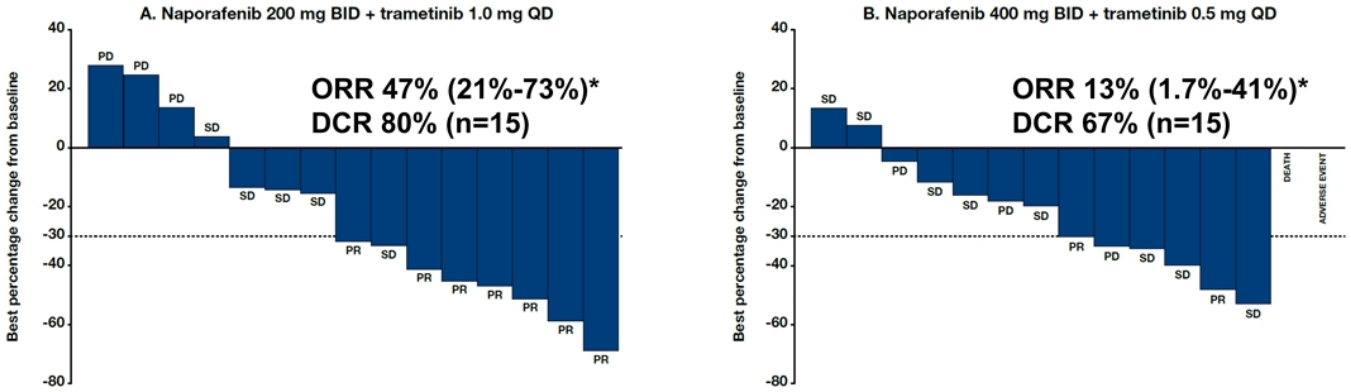
Total of 7/32 responses
21.9% ORR

RDE = recommended dose expansion
*De Braud et al AACR 2022
Lebbe et al ESMO 2022

ERASCA

Naporafenib + trametinib exhibited anti-tumor activity in NRASm melanoma

Addition of naporafenib to MEKi improves the historical MEKi mono activity



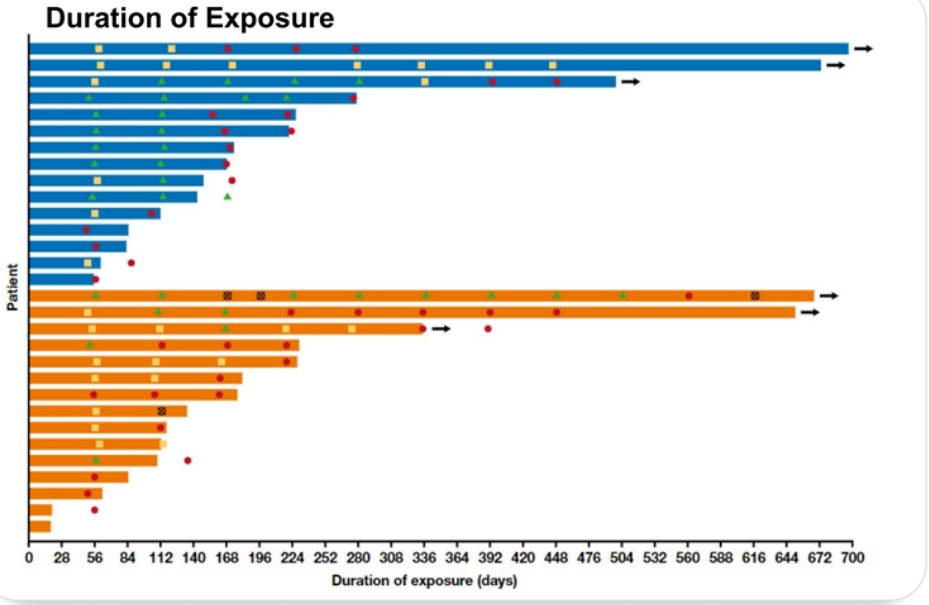
BID, twice daily; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease.

Regimen (n)	Median Prior Therapy ^	ORR *	DCR
Napo + Trame (30 combined in both RDEs)	**2 (1-7)**	30% (15-49)	73%
Dacarbazine (133)	**1**	7% (3-13)	25%
Binimetinib (269)	**1**	15% (11-20)	58%

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).

ERASCA

Naporafenib + trametinib exhibited durable responses in NRASm melanoma



- Responses observed in patients with normal or high LDH
- Median DOR was 3.75 months for both doses
- ***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
- Naporafenib 400 mg BID + trametinib 0.5 mg QD

De Braud et al AACR 2022 (Trial LXH254X2102, NCT02974725)
* For both doses combined.

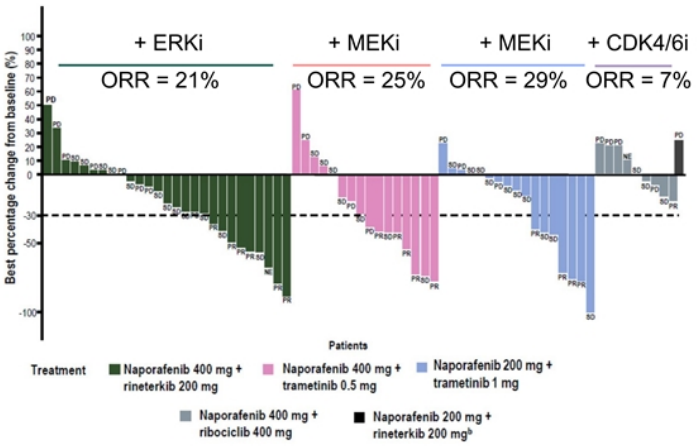
BID, twice daily; CR, complete response; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease; UNK, unknown.

ERASCA

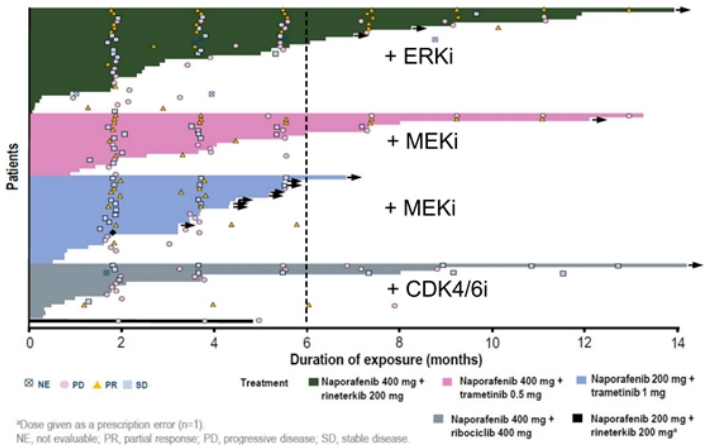
Dual MAPK blockade with naporafenib regimens was effective in NRASm melanoma

LXH254C12201 Ph 2 trial confirms encouraging activity of panRAFi + MEKi/ERKi combinations

Best Overall Responses in NRASm Melanoma (n=70)



Treatment Duration in NRASm Tumors



[a]Dose given as a prescription error (n=1).
NE, not evaluable; PR, partial response; PD, progressive disease; SD, stable disease.

Responses were ongoing in 14 patients

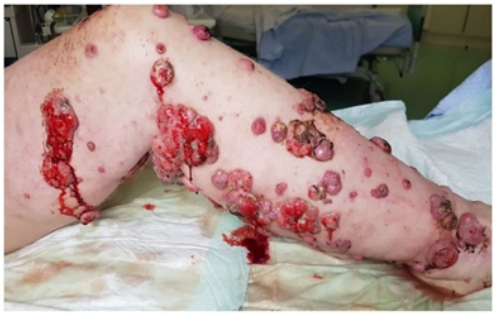
Naporafenib combination activity in NRASm melanoma was consistent across two nodes (MEK, ERK) and two doses (200mg, 400mg)

Source: Lebbe et al, ESMO 2022

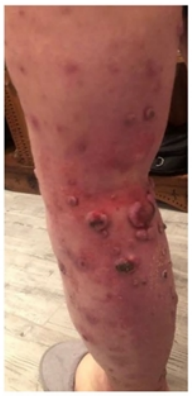
ERASCA

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

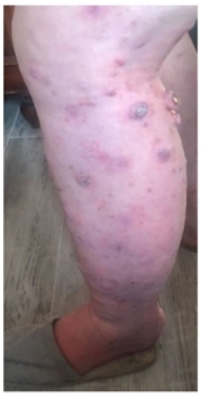
C1D1



C3D1

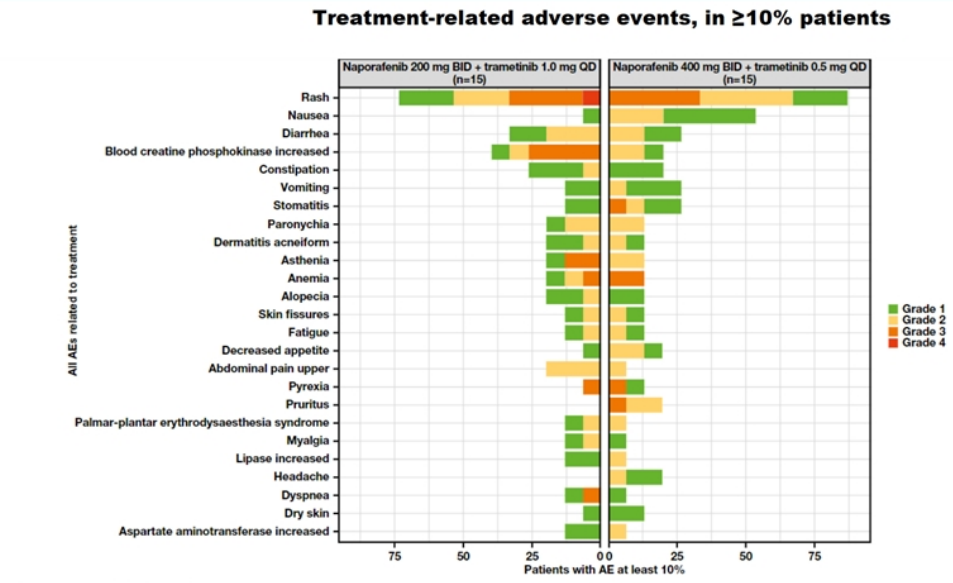


C6D1



Source: Novartis Non-Confidential Materials

Naporafenib + trametinib has a favorable safety and manageable AE profile



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

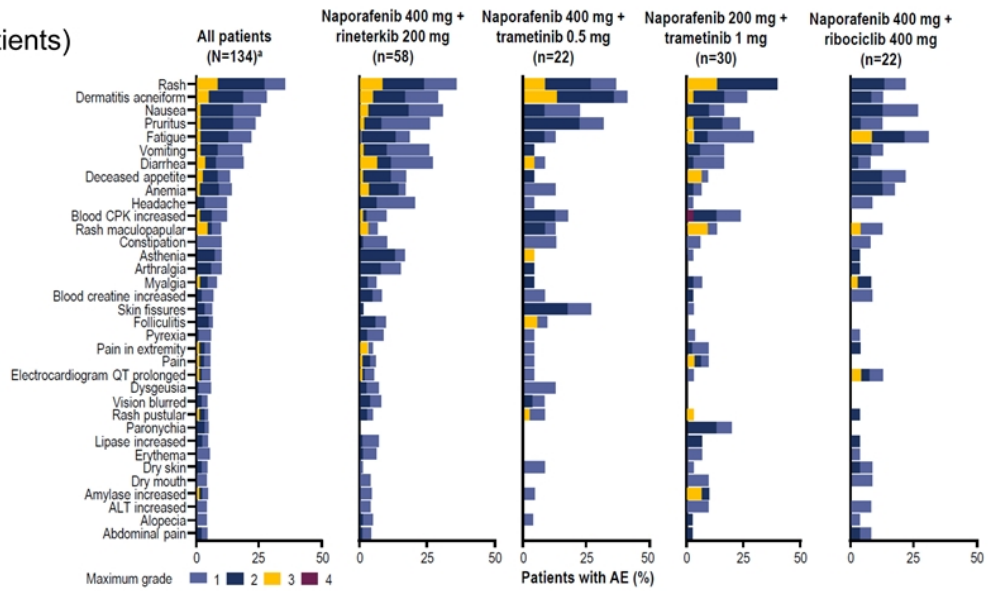
De Braud et al AACR 2022

Naporafenib demonstrates combinability with inhibitors of MAPK and other pathways

No apparent drug-drug interactions noted

Treatment-related AEs (in ≥5% of patients)

- Treatment-related AEs were generally mild to moderate across all combinations with naporafenib
- Among all patients with *BRAF V600* and *NRAS* mutations (N=134), AEs of any grade were experienced by 129 (96%) patients
- Skin toxicities were most common; rash (35%), dermatitis acneiform (28%), and rash maculopapular (10%); these were mostly Grade 1–2



[a]Includes patients receiving naporafenib 200 mg + rineterkib 200 mg (n=1) and naporafenib 400 mg + trametinib 1 mg (n=1) due to prescription errors.
AE, adverse event; ALT, alanine aminotransferase; CPK, creatine phosphokinase.

PARIS 2022 ESMO congress

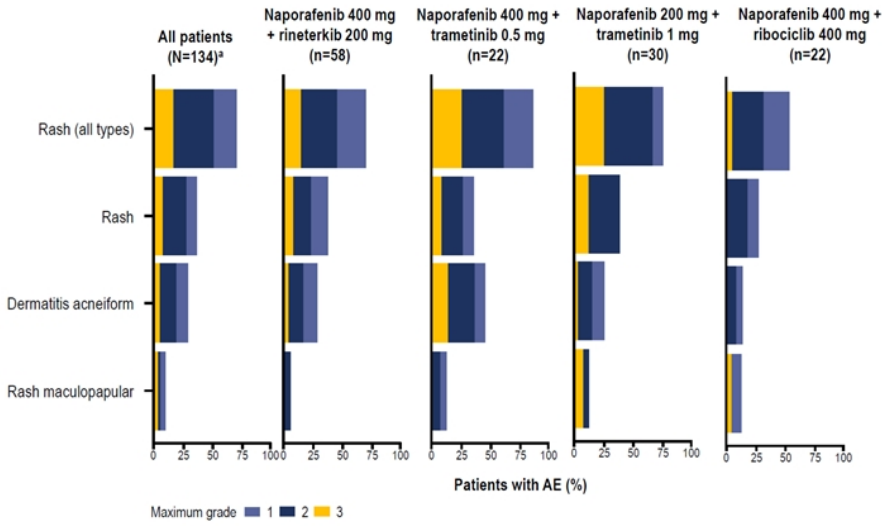
Source: Lebbe et al, ESMO 2022

Skin toxicities are the most common AEs in naporafenib combinations

AEs are manageable and expected to improve with prophylactic skin care

Treatment-related Skin AEs (in ≥5% of patients)

- The most common skin toxicities, regardless of treatment, were rash (37%), dermatitis acneiform (29%), and rash maculopapular (10%)
- Prophylactic skin care was not mandated early on and has now been introduced



[a]Includes patients receiving naporafenib 200 mg + rineterkib 200 mg (n=1) and naporafenib 400 mg + trametinib 1 mg (n=1) due to prescription errors.

PARIS 2022 ESMO congress

Source: Lebbe et al, ESMO 2022

Naporafenib + trametinib combination has a compelling opportunity to address unmet needs in NRASm melanoma

Clinical Unmet Need

- For patients with NRASm melanoma, the SOC therapies in the post-IO space are minimally active
  - Median PFS on chemotherapy is only 1.5 months
  - Median OS on chemotherapy is only 10.1 months
- In these types of advanced patients without good SOC options, preventing progression is important since progression frequently leads to mortality; i.e., there aren't any therapies they can receive once they progress

Naporafenib and trametinib

- Higher ORR and DCR than comparators (chemo or MEKi) coupled with encouraging duration of treatment in Ph 1 and Ph 2 studies are predicted to translate into prolonged PFS and/or OS compared to SOC
- Naporafenib + trametinib predicted to be more efficacious than MEKi monotherapy
- Trametinib is the established SOC in BRAF V600 melanoma and considered to be the best-in-class MEKi, which is predicted to facilitate adoption of naporafenib + trametinib combo in NRASm melanoma
- Enthusiastic KOL support

SOC = standard of care

ERASCA

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

Preliminary plan subject to global health authority feedback

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)

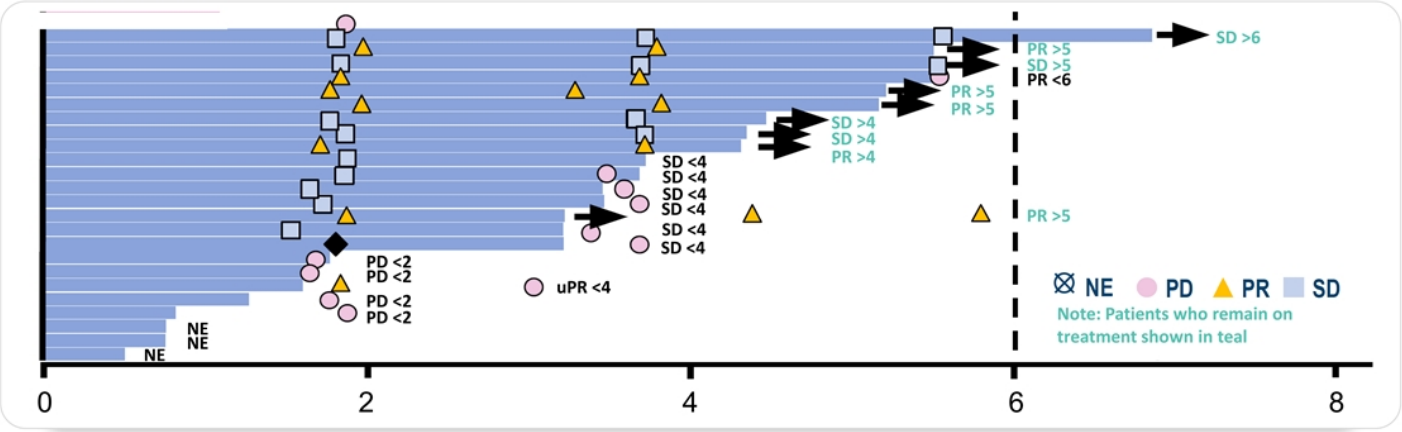
N~350 - 400

* Assumptions: CoC for naporafenib monotherapy in melanoma from FIH trial. CoC in solid tumors is not needed. AA: accelerated/conditional approval. RA: regular approval.

ERASCA

Analysis of pts with NRASm melanoma in Ph 2 who remain on treatment show potential for napo + tram to potentially demonstrate PFS benefit in SEACRAFT-2

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



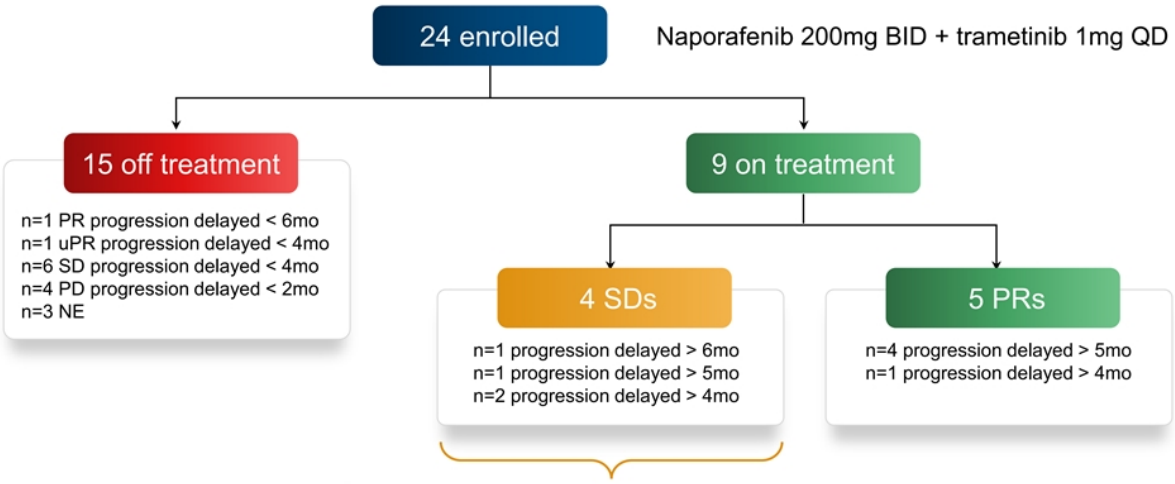
9/24 patients remain on treatment as of data cutoff

- 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 potential PFS advantage in SEACRAFT-2



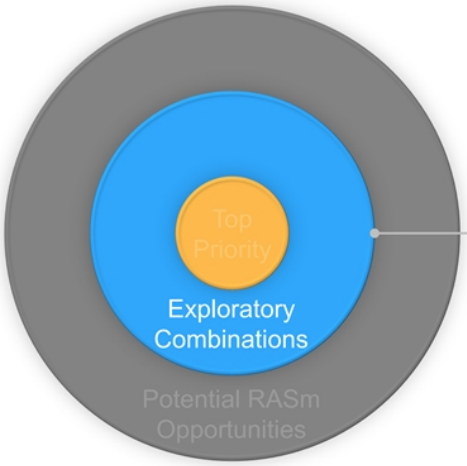
Patients with SD at, or on track, for delayed progression > 4 months could contribute to PFS benefit vs. SOC

*includes unconfirmed responses

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

ERASCA

Naporafenib's addition to Erasca's pipeline can broaden our exploration into other well-defined indications



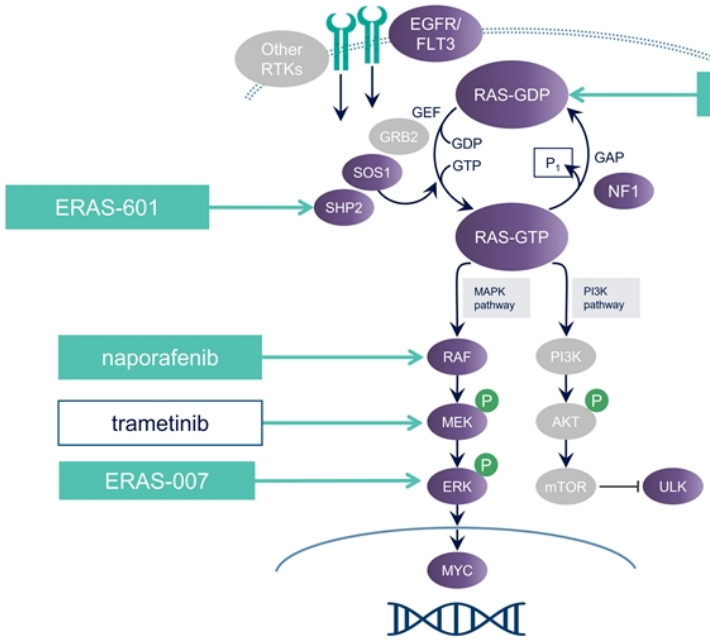
Explore novel doublet, and possibly triplet, combination(s) in NF1 LOF, RAS G13R, KRAS G12C, and BRAF Class 2 and 3 altered solid tumors (SEACRAFT-3)

- These biomarker defined tumors have shown biologically a strong addiction to the RAS/MAPK pathway and are selected as the next indications to explore.
- Combinations of naporafenib with Erasca's RAS/MAPK pathway focused pipeline may demonstrate efficacy by effecting a more complete shutdown of the pathway.

ERASCA

Pro forma with naporafenib

Our pipeline supports multiple pairwise combinations to expand the potential of naporafenib to patients with other RAS/MAPK-driven tumors and unmet clinical needs



Potential Naporafenib combos with Erasca Pipeline

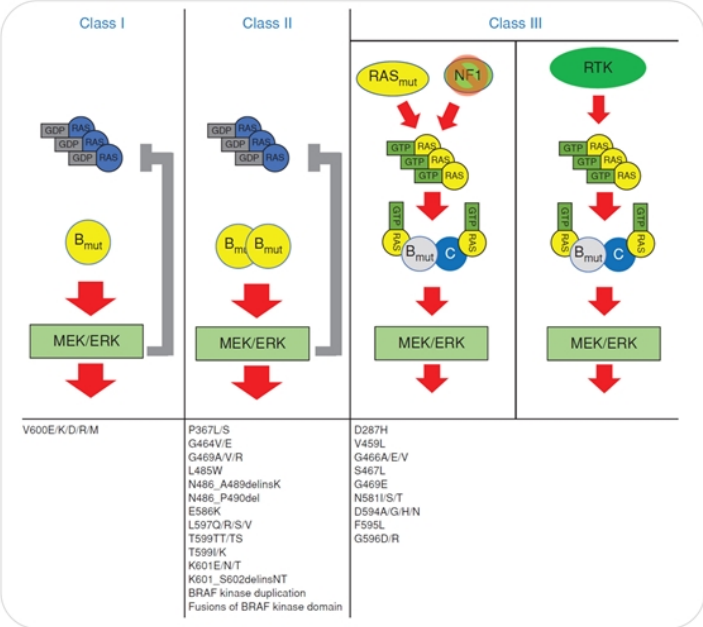
- **naporafenib + ERAS-007**
- **naporafenib + ERAS-601**
- **naporafenib + ERAS-007 + ERAS-601**
- **naporafenib + ERAS-3490**

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

ERASCA

BRAF Class 2 and Class 3 mutations represent an unmet need

Naporafenib provides us with an additional agent to target these



Potential combinations within Erasca Pipeline that could target BRAF Class 2 and 3 mutations

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

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Erasca's pipeline can expand naporafenib into other RAS-driven tumors that lack direct targeted inhibitors

- Confirmation of proof-of-concept in NRASm melanoma and RAS Q61X solid tumors, together with signals from exploration into RAS G13R, KRAS G12C, NF1 LOF, and BRAF Class 2 and 3 mutations, will help to better define the tumor types, mutations, and combinations for the potential upside opportunities such as other RASm settings.
- Erasca's deep pipeline in the RAS/MAPK pathway can maximize the central role naporafenib may play in improving the standard of care in RAS-driven tumors.

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

ERASCA

Pro forma with naporafenib

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	KRASm/ NRASm CRC	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 26%, mDOR 4.2 mos.
Regimen tested	naporafenib + trametinib	naporafenib + trametinib	ERAS-007 + ERAS-601 (our first MAPKlamp)	ERAS-007 + osimertinib	ERAS-007 or ERAS-601 + sotorasib	ERAS-007 + encorafenib + cetuximab	ERAS-007 + encorafenib + cetuximab	ERAS-007 + palbociclib	ERAS-601 + cetuximab	ERAS-601 + cetuximab	ERAS-801 monotherapy
			ERAS-007 (alternative schedules)		ERAS-3490						
			ERAS-601 (alternative schedules)								
Erasca trial(s)	SEACRAFT-1	SEACRAFT-2	HERKULES-1	HERKULES-2 Sub-study 1	HERKULES-2 Sub-study 2	HERKULES-3 Sub-study 1	HERKULES-3 Sub-study 1	HERKULES-3 Sub-study 2	FLAGSHP-1	FLAGSHP-1	THUND-ERBBOLT-1
			FLAGSHP-1		AURORAS-1 (planned)						

100% of CRC

ERASCA

Pro forma with naporafenib

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

FOUR CLINICAL STAGE COMPOUNDS
Differentiated profiles including naporafenib, a phase 2, pivotal-ready pan-RAF inhibitor for NRASm melanoma and Q61X tissue agnostic solid tumors

MULTIPLE POTENTIAL NEAR-TERM AND LONG-TERM VALUE DRIVERS
Five compounds anticipated to be in the clinic in 2023; addl. IND filings anticipated every 12-18 mos. through 2026

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Thank You!

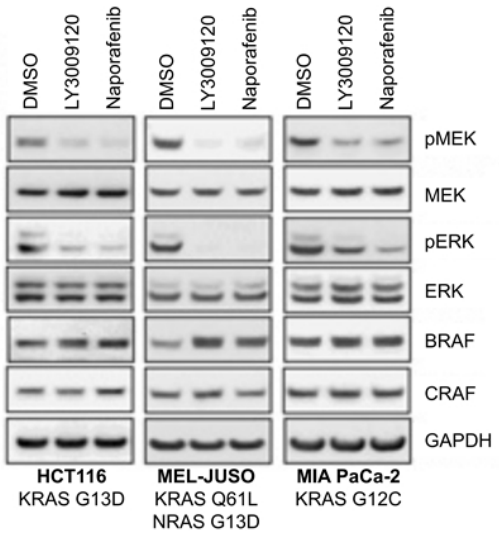
Naporafenib (LXH254): a Phase 2, pivotal-ready pan-RAF inhibitor with potential first-in-class and best-in-class profile in RAS/MAPK-altered tumors

Naporafenib

- Potent (sub-nanomolar IC50 against BRAF and CRAF), selective, orally bioavailable pan-RAF inhibitor
- Type 2, ATP-competitive inhibitor of RAF by maintaining the kinase in an inactive αc-in/DFG-out conformation
  - Generates minimal paradoxical activation (as observed with V600X targeting RAFi's)
  - Inhibits both monomeric (V600E) and dimerized RAF
  - Enables suppression of RAS/MAPK pathway signaling, including RAS-activated wild-type RAF and activated mutant RAF
- 500+ patients treated with naporafenib as a single agent or in combination
- Clinical POC or responses have been achieved in pan-RAS Q61X solid tumors (melanoma, NSCLC), NRASm melanoma, and KRAS G13R NSCLC
- Key toxicities are generally consistent with on-target effects observed with other RAF inhibitors (e.g., skin, GI, fatigue)

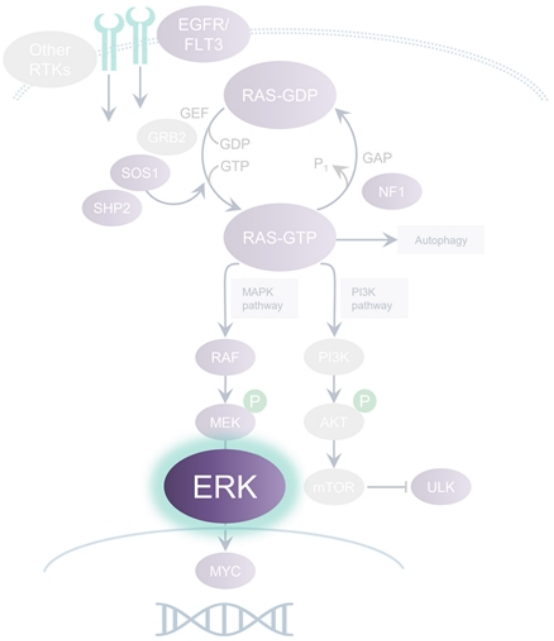
Naporafenib inhibits RAS/MAPK pathway signaling in RAS mutant cells

Cellular Assay	IC50 (nM)
pMEK (Calu-6, KRAS Q61K)	14
Cellular proliferation inhibition (Calu-6)	470



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

As the terminal node of the RAS/MAPK pathway, ERK is a critical target



- ERK is **less susceptible to pathway reactivation** compared to MEK
- ERK is **implicated in acquired resistance** to RAFi/MEKi's and other targeted therapies
- Opportunities exist for **multiple combination approaches**

ERASCA

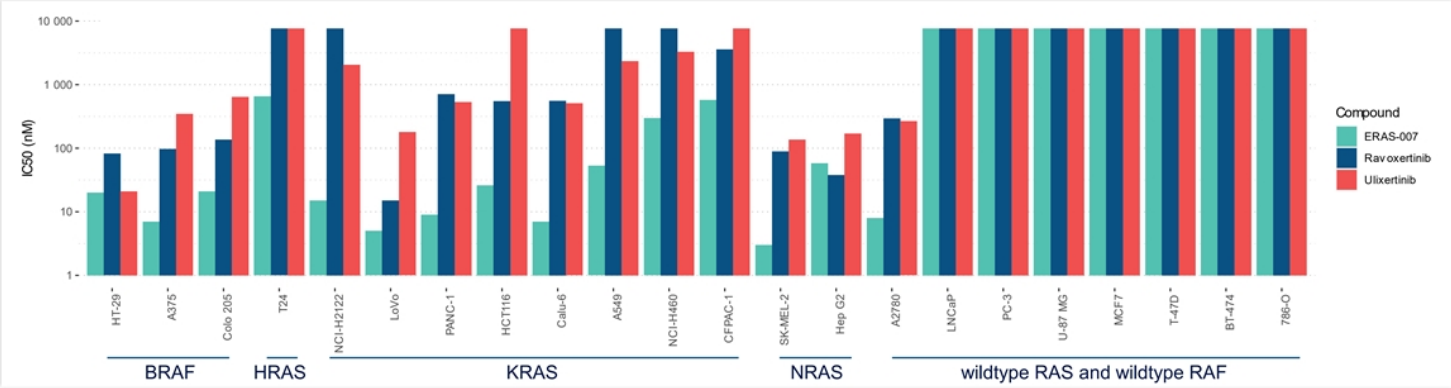
We believe ERAS-007 is the most potent ERK inhibitor in development

ERAS-007

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 exhibited **potent anti-proliferative activity** in cell lines with mutations in the RAS/MAPK pathway compared to other ERKi's



ERAS-007's uniquely long target residence time may enable dosing flexibility

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

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

HERKULES 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		

Ongoing sub-study

Future sub-study

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®)

Note: CTCSA = clinical trial collaboration and supply agreement

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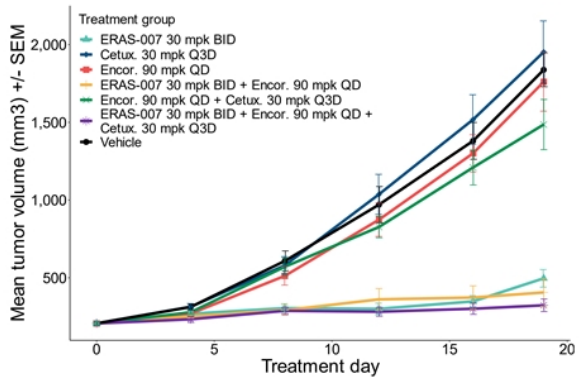
ERAS-007 showed strong in vivo combination activity in BRAF V600E CRC

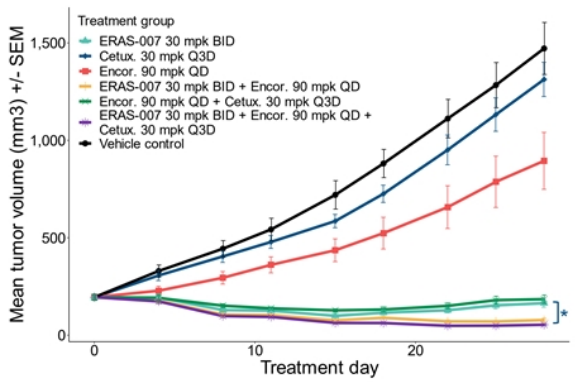
TGI in RKO (BRAF V600E CRC)

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)

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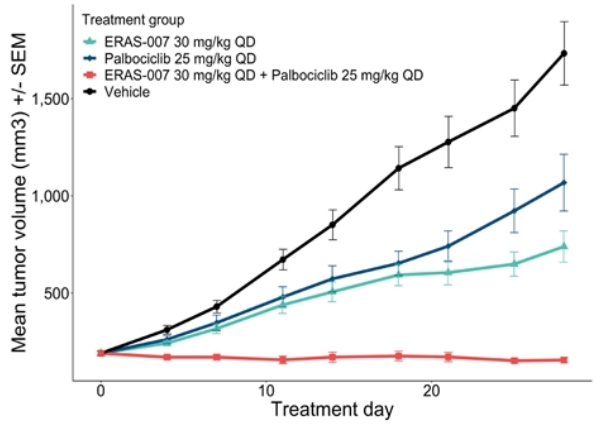
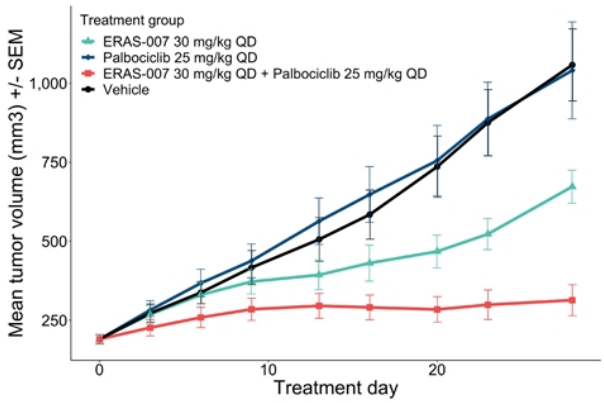
ERAS-007 + palbociclib enhanced tumor growth inhibition (TGI) in KRASm CRC and PDAC models

TGI in KRAS G13D CRC CDX LoVo



TGI in KRAS G12D PDAC PDX PAN026

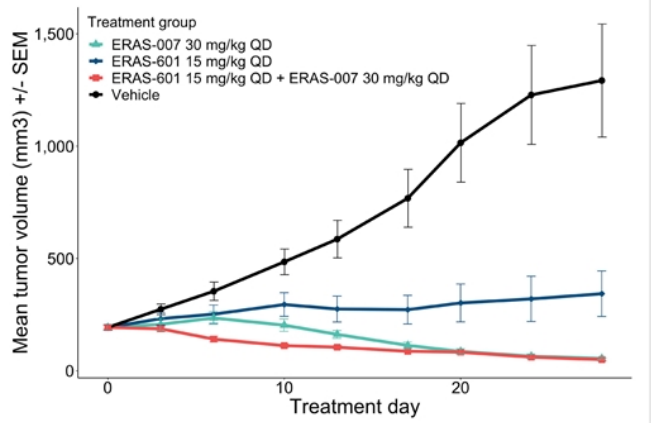


- Combination was tolerated in mice (e.g., no dose holidays, deaths, or euthanizations)
- ERAS-007 and palbociclib were dosed orally and continuously

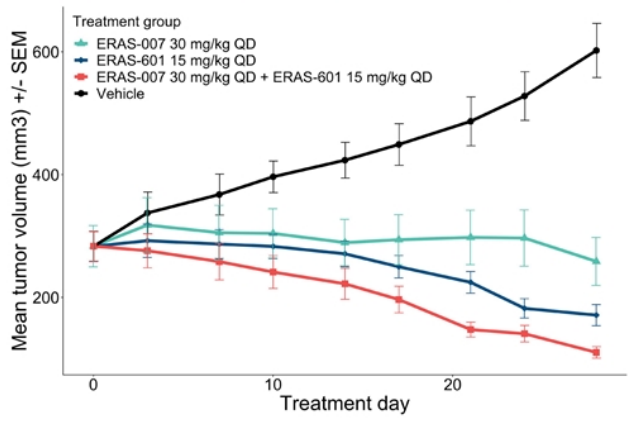
ERASCA

ERAS-007 + ERAS-601 MAPKlamp showed consistent combination activity in BRAF class 3 and NF1 loss of function (LoF) models

TGI in BRAF Class 3 NSCLC PDX LUN023



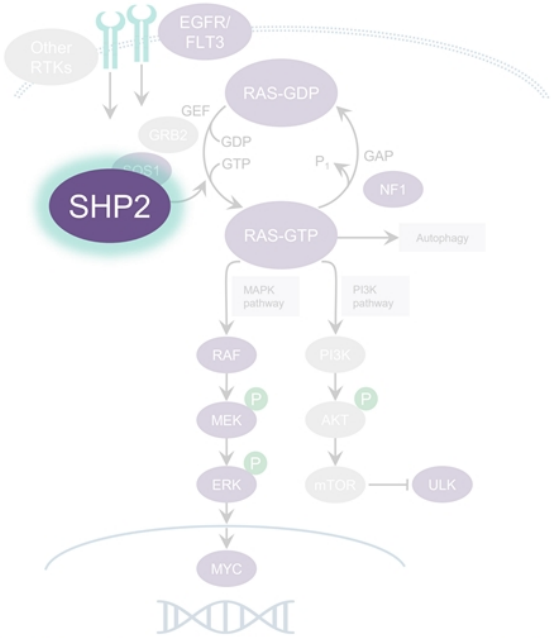
TGI in NF1 LoF NSCLC NCI-H1838



- 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

ERASCA

SHP2 is a critical “on/off switch” that activates GTP-bound KRAS signaling



- SHP2 is a **convergent node for upstream RTK signaling**
- A SHP2i can block dephosphorylation to maintain GTP-bound KRAS in a “dark state” and thereby **reduce RAS signaling**
- SHP2 inhibition is emerging as a **backbone of combination therapy**

ERASCA

ERAS-601 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-601: favorable physicochemical, ADME, and PK properties well suited for combination therapy

Assay	ERAS-601
cLogP/PSA	<1/<130
MW	<600
PBS solubility (µM)	>300
Caco2 permeability at 10 µM, Papp (AB/BA) (10^{-6}, cm/s)	2.57/27.5
Plasma protein binding, Free fraction % M/R/D/H	26/11/35/33
Stability in liver microsomes, M/R/D/H	Low Clearance
Inhibition of CYP 3A4, 2C9, 2D6, IC50 (µM)	>100
CYP3A4 TDI	No flag
hERG Q-patch IC50 (µM)	>30
GLP hERG IC50 (µM)	12

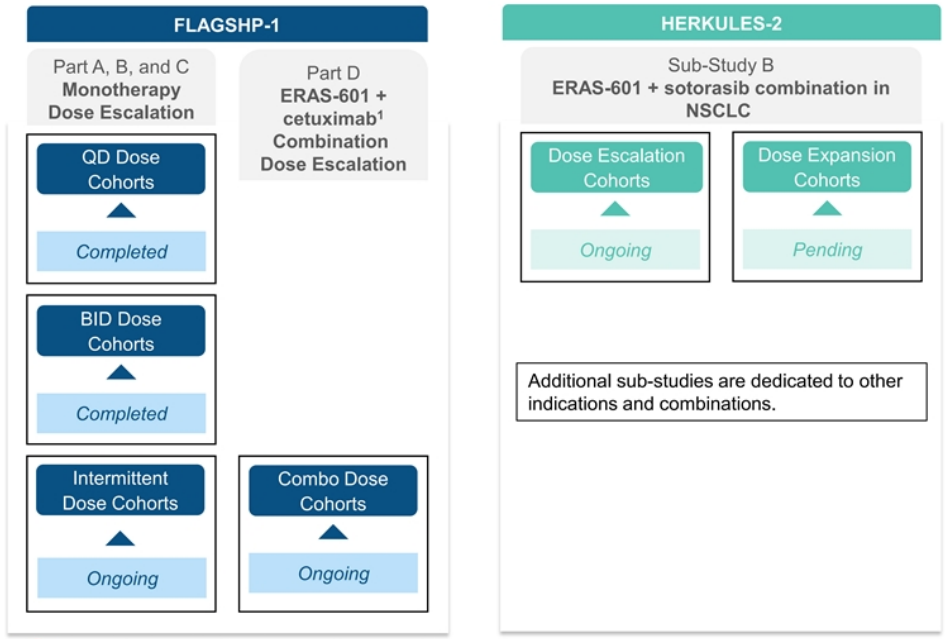
Route of Administration	PK Parameter (Unit)	ERAS-601		
		Mouse (CD-1)	Rat (SD)	Dog (Beagle)
IV	Cl (mL/min/kg)	13	9.9	9.8
PO	%F	63	48-83	75-107

Key takeaways:

- Low DDI risk and no CYP flags make ERAS-601 well suited for combination therapy
- Low in vivo Cl and high bioavailability in multiple species suggest favorable human PK profile

ERASCA

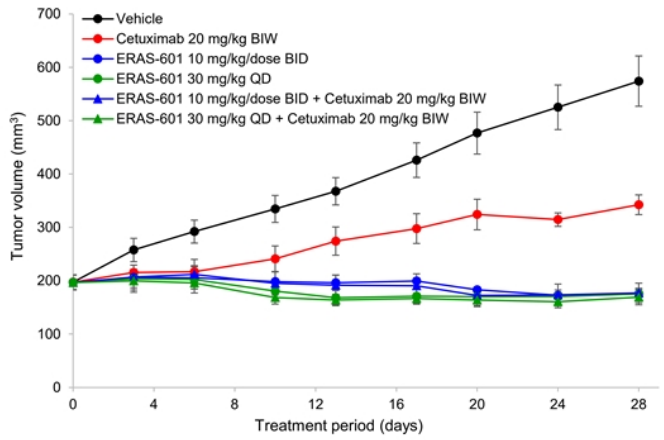
ERAS-601 in FLAGSHP-1 clinical trial and HERKULES master protocol



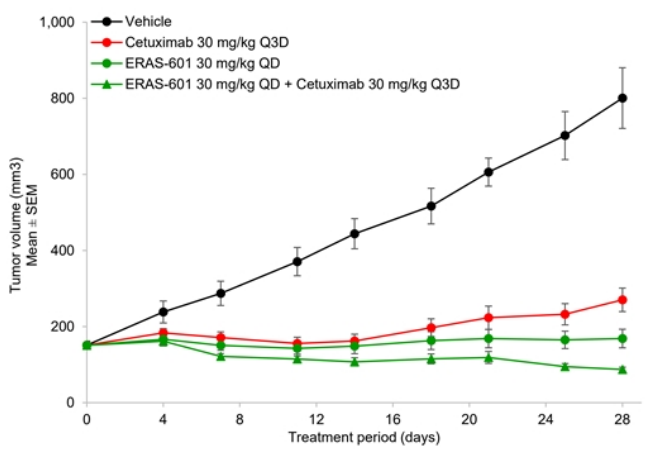
[1] Jul 2022: Clinical trial collaboration and supply agreement with Lilly for cetuximab (Erbitux®) executed

ERAS-601 + cetuximab demonstrated significantly greater tumor inhibition vs. cetuximab alone in triple wildtype CRC and HPV-negative HNSCC models

TGI in Triple WT CRC PDX model CRC1021



TGI in HPV-negative HNSCC PDX HN3411

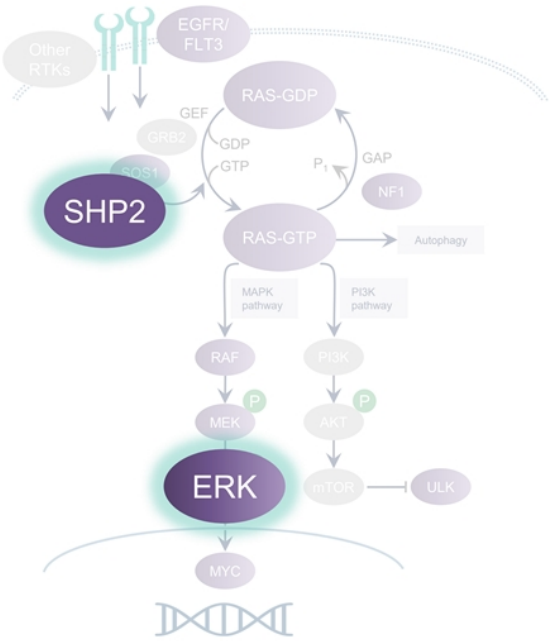


- Combination was tolerated in mice (e.g., no dose holidays, deaths, or euthanizations)
- ERAS-007 and palbociclib were dosed orally and continuously

ERASCA

SHP2 and ERK are critical nodes of the RAS/MAPK pathway

- SHP2 is a **convergent node for upstream RTK signaling**
- A SHP2i can block dephosphorylation to maintain GTP-bound KRAS in a “dark state” and thereby **reduce RAS signaling**
- SHP2 inhibition is emerging as a **backbone of combination therapy**

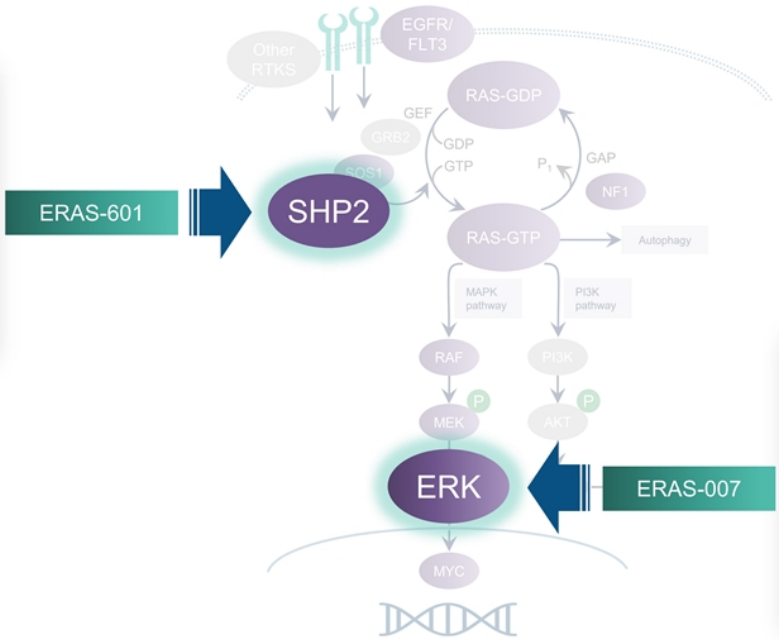


- As the terminal node, ERK is **less susceptible to pathway reactivation** compared to MEK
- ERK is **implicated in acquired resistance** to RAFi/MEKi’s and other targeted therapies
- Opportunities exist for **multiple combination approaches**

ERASCA

ERAS-601 and ERAS-007 target SHP2 and ERK, respectively

Potent, selective, orally bioavailable SHP2 inhibitor in clinical development in FLAGSHP-1 and HERKULES-2



Potent, selective, orally bioavailable ERK inhibitor in clinical development in HERKULES-1, -2, -3 and SU2C

ERASCA

Sept. 2022 R&D Day and ENA 2022 highlights

Efficacy

- ERAS-007 and ERAS-601 are active drugs – monotherapy responses
- 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 can be managed with prophylaxis or supportive care

PK

- 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

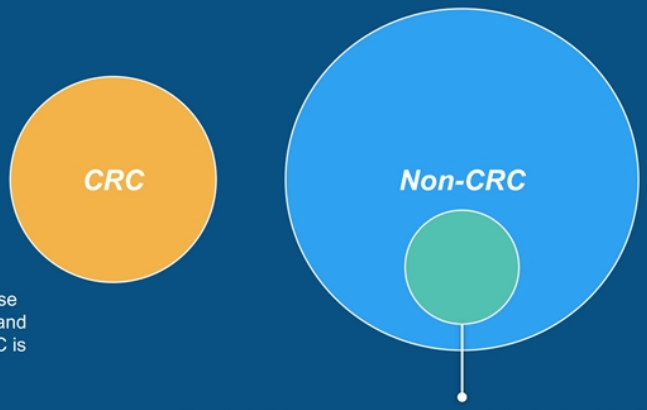
Note: PK = pharmacokinetics; u/cPR = unconfirmed/confirmed partial response; PDAC = pancreatic ductal adenocarcinoma; BID-QW = two doses on one day each week

Segmentation framework to identify more responsive subsets within the Blue Ocean for prioritized combination development

"Blue Ocean indications" of solid tumors with RAS/MAPK alterations and no approved targeted therapies

Less sensitive to monotherapy inhibition due to more RAS/MAPK reactivation and bypass pathway activation

Evaluation of combinations addressing these mechanisms is ongoing in HERKULES-3 (and combination addressing triple wildtype CRC is ongoing in FLAGSHP-1)



Phase 1/1b monotherapy responses used to inform prioritized combination development

Targetable, more responsive subset of patients prioritized for combination development

ERASCA

Methodology for retrospective pooled efficacy analysis for ERAS-007 and ERAS-601 in solid tumors with RAS/MAPK pathway alterations*

Retrospective Pooled Analysis	All trials assessing ERAS-007 or ERAS-601 as monotherapies: ASN007-101, HERKULES-1, FLAGSHP-1
Dosing Regimens	Biologically relevant regimens above the efficacious dose and at or below the maximum tolerated dose (MTD) for ERAS-007 and at or below the maximum administered dose (MAD) for ERAS-601 ERAS-007: weekly dose intensity between 120mg and 250mg, ERAS-601: daily dose intensity of 40mg
RAS/MAPK Alterations in Solid Tumors	**CRC:** Less sensitive to monotherapy inhibition due to more RAS/MAPK reactivation and bypass pathway activation **Non-CRC:** Less RAS/MAPK reactivation and no targeted therapies with full approval
Efficacy Evaluable Patients	Evaluable tumor assessment at baseline and at least one post dose tumor assessment Evaluated as per RECIST v1.1 by investigator

* 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.

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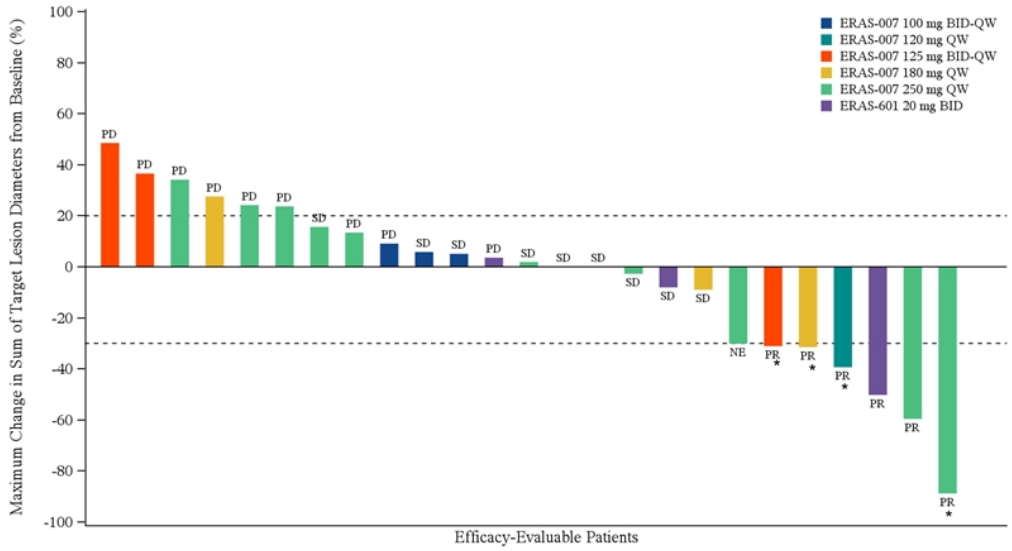
Best overall response with ERAS-007 or ERAS-601 in 15 RAS/MAPK-altered Blue Ocean Indications across lines of therapy

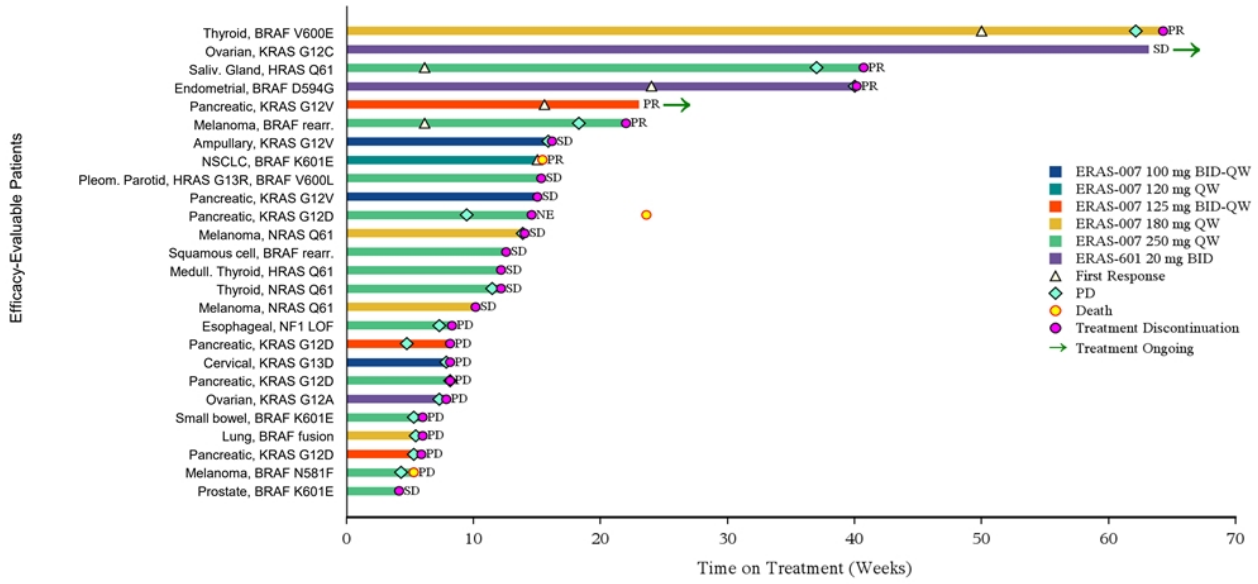


23% (6 out of 26) of patients responded (confirmed and unconfirmed PR) to single agent ERAS-007 or ERAS-601

* 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

ERASCA

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

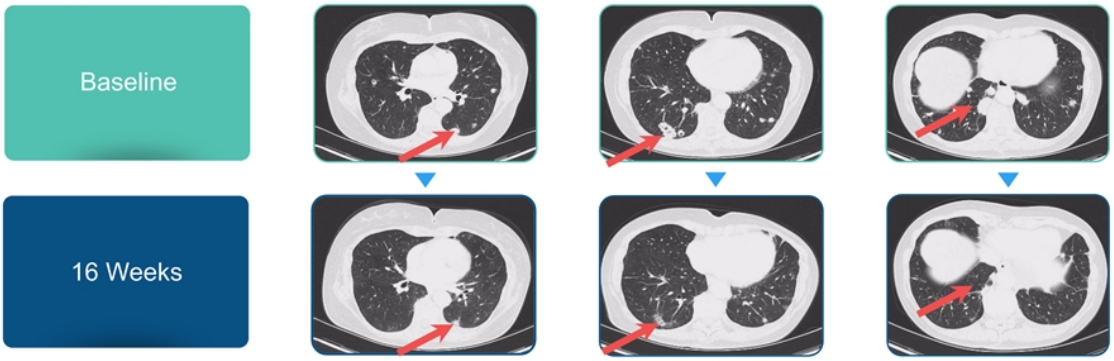


NOTE: Blue Ocean Indications defined as populations of unmet need with relevant tumor types and RAS/MAPK alterations where no targeted therapies are approved; Biologically relevant dose defined as weekly monotherapy dose intensity between 120mg and 250mg for ERAS-007 and daily monotherapy dose intensity 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.

ERASCA

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

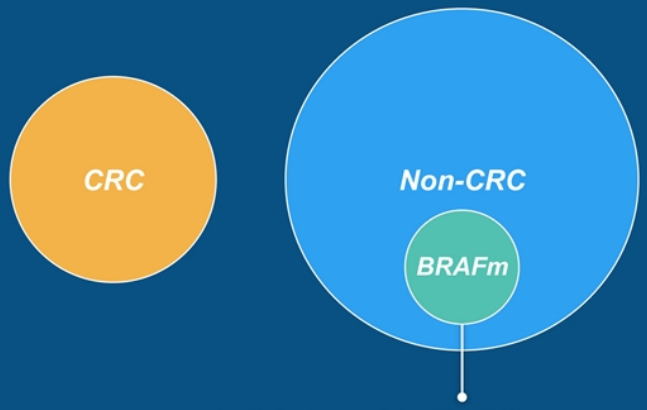
Per RECIST 1.1: ≥30% = objective response

Patient progressed with new lesion at subsequent assessment

ERASCA

Targetable, more responsive subset of patients with RAS/MAPK alterations

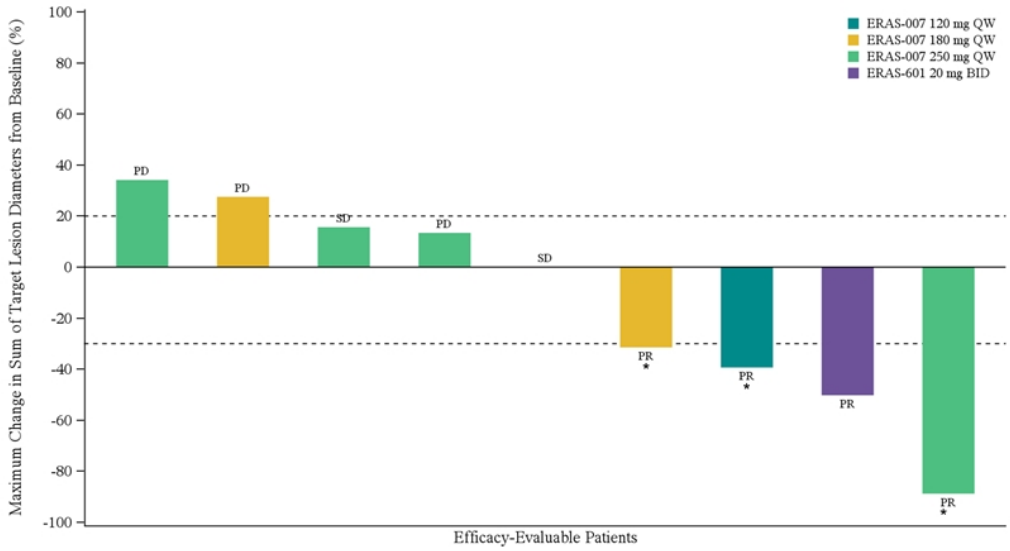
"Blue Ocean indications" of solid tumors with RAS/MAPK alterations and no approved targeted therapies



- N = 9 (subset of the N = 26)
- Higher rate of single agent responses to either agent was observed

ERASCA

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



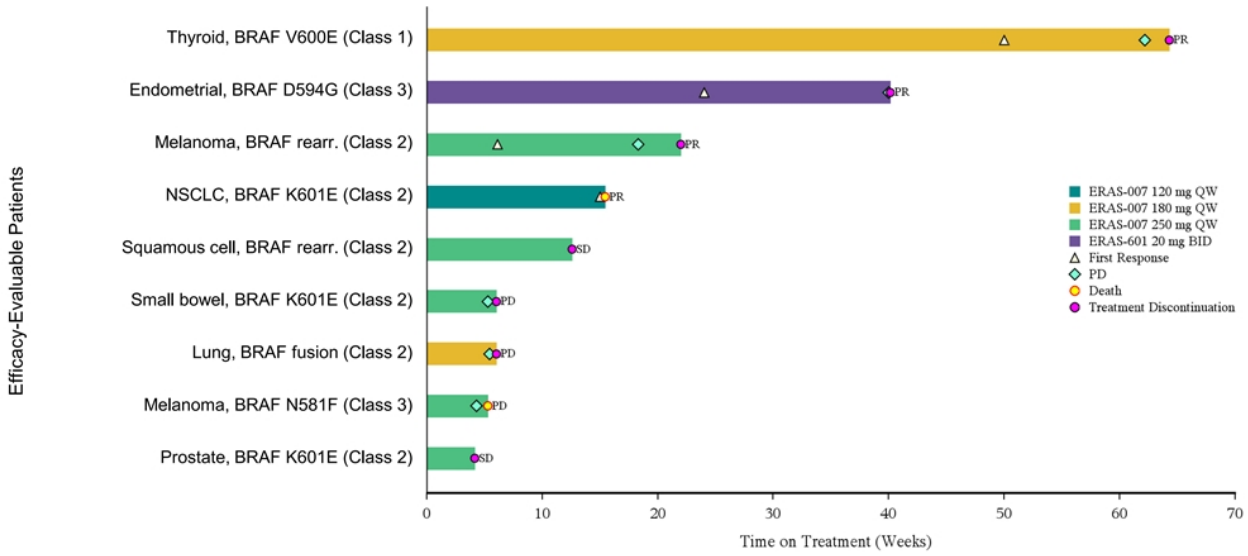
44% (4 out of 9) of patients responded (confirmed and unconfirmed PR) to single agent ERAS-007 or ERAS-601

* 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

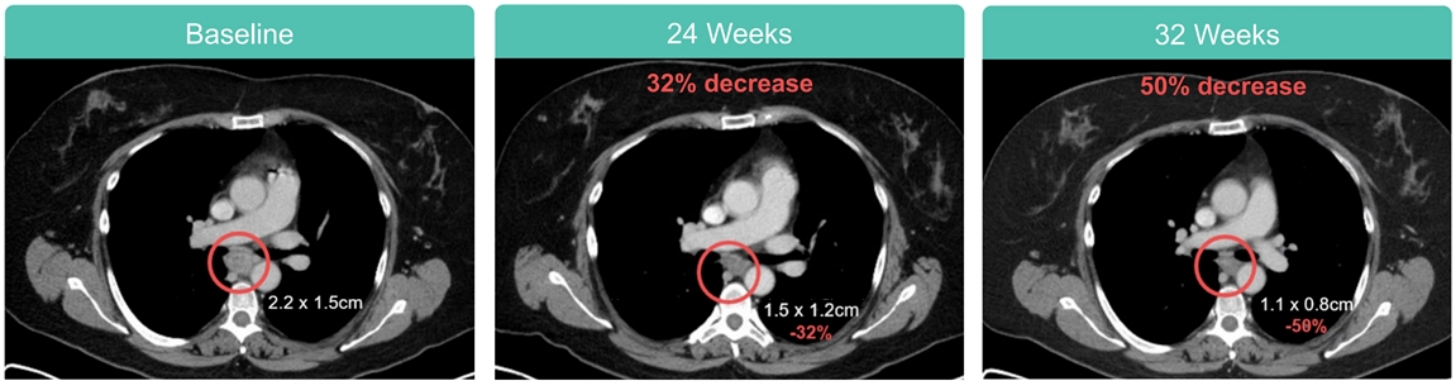


NOTE: Blue Ocean Indications defined as populations of unmet need with relevant tumor types and RAS/MAPK alterations where no targeted therapies are approved; Biologically relevant dose defined as weekly monotherapy dose intensity between 120mg and 250mg for ERAS-007 and daily monotherapy dose intensity 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



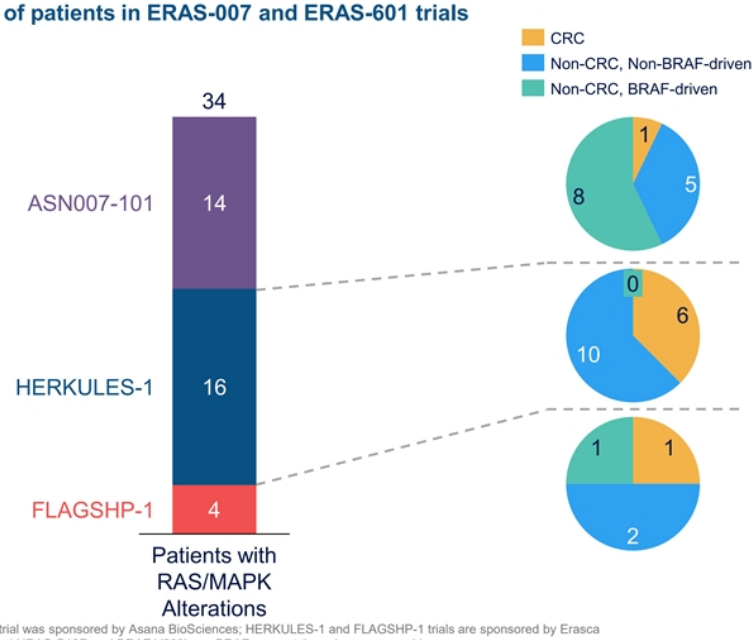
Per RECIST 1.1: ≥30% = objective response

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

Breakdown of tumor types and molecular drivers by trial

Number of patients in ERAS-007 and ERAS-601 trials



ASN007-101 trial[1]:

- ~93% of patients had non-CRC tumors
- Of these, ~62% were BRAF-driven

HERKULES-1 trial[1]:

- ~63% of patients had non-CRC tumors
- Of these, none were solely BRAF-driven[2]

FLAGSHP-1 trial[1]:

- 75% of patients had non-CRC tumors
- Of these, ~33% were BRAF-driven

1 ASN007-101 trial was sponsored by Asana BioSciences; HERKULES-1 and FLAGSHP-1 trials are sponsored by Erasca
2 One patient had HRAS G13R and BRAF V600L, so BRAF was not the sole oncogene driver

ERASCA

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

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%)

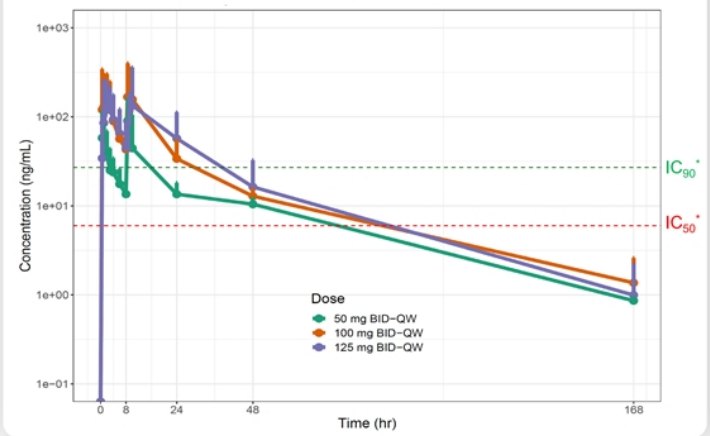
Likely recommended dose between 50 – 100mg BID-QW for combinations was well tolerated

*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

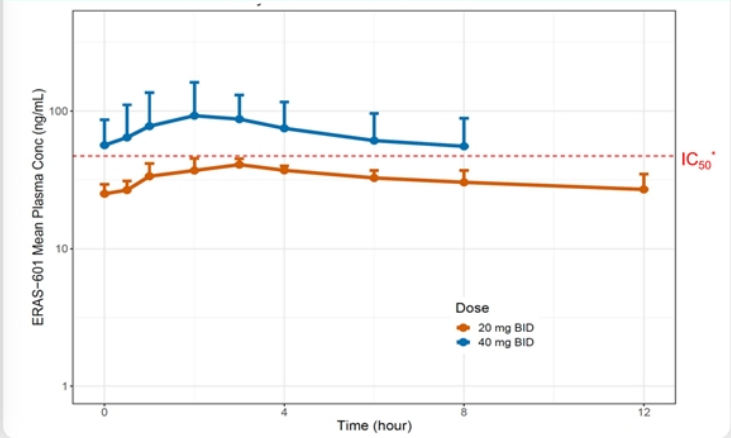
ERASCA

ERAS-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



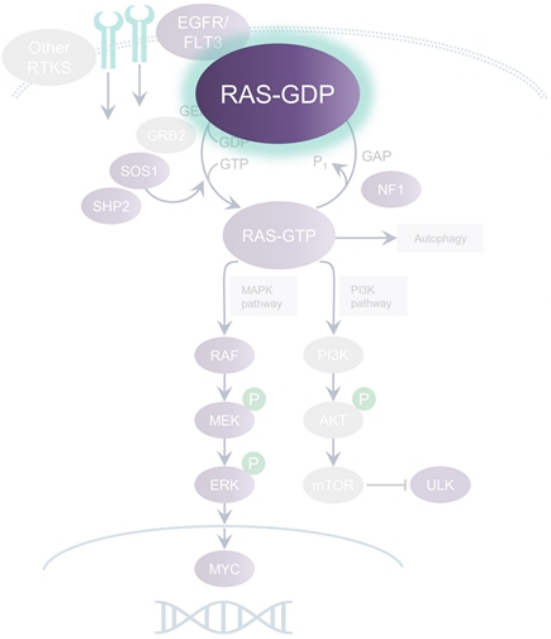
ERAS-007: 50-125mg BID-QW dosing provided high target coverage ($C>IC_{90}$) for maximum activity, followed by lower PK coverage ($C<IC_{50}$) for MAPK pathway recovery to alleviate target driven toxicity

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

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

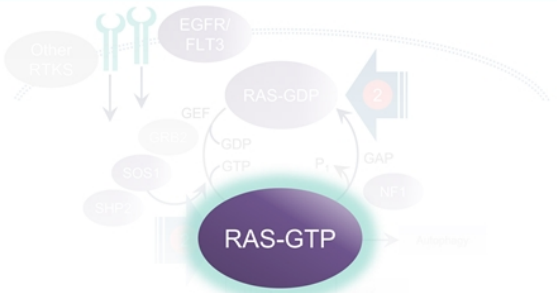
We have discovered promising CNS-penetrant KRAS G12Ci pre-candidates

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.

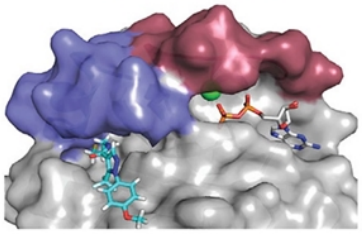
ERASCA

Beyond G12C: Targeting KRAS G12D and other RAS-GTP mutations

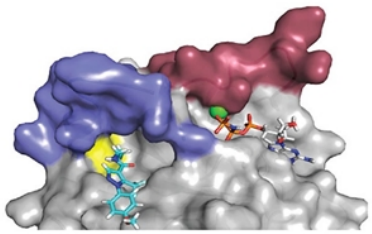


- Targeting KRAS G12D and other RAS-GTP mutations is more challenging, as they are more commonly found in the active GTP state
- **ERAS-4** KRAS G12D program leverages expertise from ERAS-3490 and ERAS-2/3 discovery; molecules in lead op have demonstrated ***low nM IC50 potency*** in RAS-RAF binding assay
- **ERAS-2/3** RAS-GTP inhibitor program based on Kevan Shokat's identification of a new binding site called S-IIG that is present in both RAS-GTP and RAS-GDP states
  - Discovery opens possibility to selectively target other RAS mutations in active state
  - Erasca has exclusive WW license from UCSF related to work performed by Shokat in this field

RAS-GDP State



RAS-GTP State

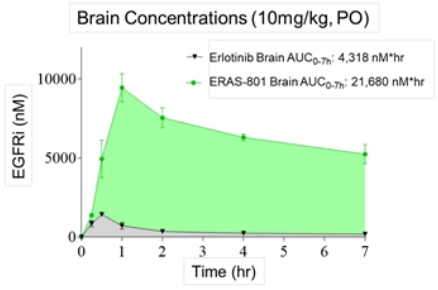


Source: Gentile DR, et al., Cell Chem Biol. 2017 Dec 21;24(12):1455-1466.e14

ERASCA

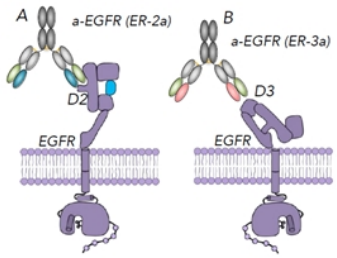
Our EGFR franchise programs are highly differentiated

ERAS-801:
CNS-penetrant EGFRvIII/wt inhibitor



- High BBB penetration and good oral bioavailability
- Oral inhibitor with high CNS exposure (3.7:1 brain:plasma)
- $K_{p,uu}$[1] over 4x higher than approved EGFRi's
- Potently/selectively inhibited EGFR alterations (e.g., vIII, amps., polysomy)
- High unmet monotherapy opportunity in recurrent GBM

ERAS-12:
EGFR D2/D3 bispecific for CRC and other tumors



- Next generation EGFR bispecific antibody discovered by Drs. Dev Sidhu, Sekar Seshagiri & Jagath Reddy Junutula; former Genentech
- Approved EGFR mAbs target D3, not D2
- EGFR D2 targeting antibodies expected to be more effective when EGF is overexpressed (like pertuzumab blocking receptor dimerization in HER2)

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

ERASCA