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): June 05, 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 8.01 Other Events.

On June 5, 2023, Erasca, Inc. (the Company) held its previously announced virtual investor event. During the event, the Company presented the corporate slide presentation attached as Exhibit 99.1 to this report, which is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Investor Presentation, dated June 5, 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 hereunto duly authorized.

Erasca, Inc.

Date: June 5, 2023

By: /s/ Ebun Garner

Ebun Garner, General Counsel

ERASCA

Exhibit 99.1

On a Journey to Erase Cancer

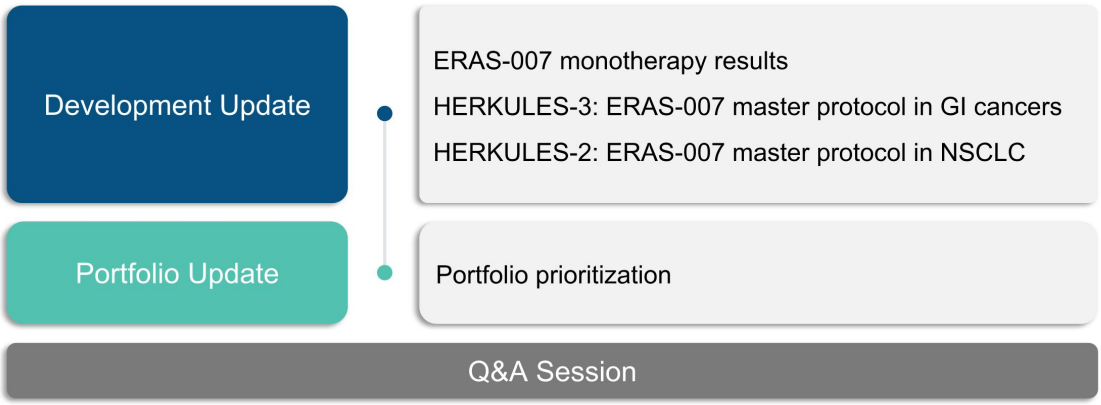
Erasca Investor Presentation

June 5, 2023

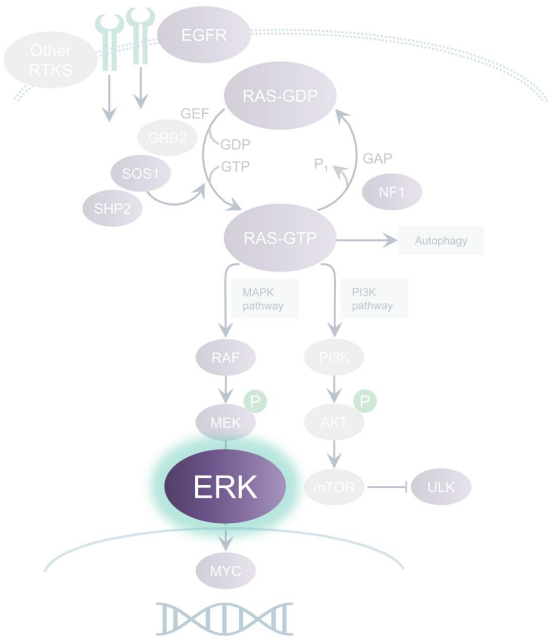
Disclaimer: Forward Looking Statements & Market Data

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 (including the timing of initiation and the timing of data readouts), costs, design and conduct of our ongoing and planned preclinical studies and clinical trials for our product candidates, the potential benefits from our current or future arrangements with third parties, the timing and likelihood of success of our plans and objectives, the planned deprioritization of certain programs, and future results of anticipated product development efforts, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. The inclusion of forward-looking statements should not be regarded as a representation by us that any of our plans will be achieved. Actual results may differ from those set forth in this presentation due to the risks and uncertainties inherent in our business, including, without limitation: our approach to the discovery and development of product candidates based on our singular focus on shutting down the RAS/MAPK pathway, a novel and unproven approach; we are early in our development efforts and have only four product candidates in clinical development and all of our other development efforts are in the preclinical or development stage; the retrospective analysis of pooled ERAS-007 data 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; we have not conducted any clinical trials of naporafenib and are reliant on data generated by Novartis in prior clinical trials conducted by it; our planned SEACRAFT trials may not support the registration of naporafenib; preliminary results of clinical trials are not necessarily indicative of final results and one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data and more patient data become available, including the risk that an uPR to treatment may not ultimately result in a cPR to treatment after follow-up evaluations; potential delays in the commencement, enrollment, and completion of clinical trials and preclinical studies; our dependence on third parties in connection with manufacturing, research, and preclinical and clinical testing; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval, and/or commercialization, or may result in recalls or product liability claims; unfavorable results from preclinical studies or clinical trials; results from preclinical studies or early clinical trials not necessarily being predictive of future results; the inability to realize any benefits from our current licenses, acquisitions, or collaborations, and any future licenses, acquisitions, or collaborations, and our ability to fulfill our obligations under such arrangements; our assumptions around which programs may have a higher probability of success may not be accurate, and we may expend our limited resources to pursue a particular product candidate and/or indication and fail to capitalize on product candidates or indications with greater development or commercial potential; regulatory developments in the United States and foreign countries; 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, 2022, 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 Investor Presentation Agenda



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



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

ERASCA

ERAS-007 monotherapy data support combinations across tumor types

Preclinical Data Highlights

Most potent ERK inhibitor in development[1]	Showed single digit nanomolar potency in biochemical and cell-based assays
Uniquely long target residence time	• Over 30x longer than when compared to other ERK inhibitors[2] • May allow for longer intervals between doses in patients
Robust in vitro and in vivo data	Showed tumor growth inhibition across multiple assays and models

Clinical Data Highlights

Multiple monotherapy responses[3]	• BRAF V600E thyroid CA (uPR) • BRAF K601E NSCLC (uPR) • HRAS salivary gland CA (cPR) • BRAF rearranged melanoma (uPR) • KRAS G12V pancreatic cancer (uPR)
Well tolerated	Likely recommended dose between 50-100mg BID-QW for combinations has been generally well tolerated
Achieved targeted PK characteristics	High target coverage ($C>IC_{90}$) for activity, followed by lower PK coverage ($C<IC_{50}$) for MAPK pathway recovery to potentially alleviate target-driven toxicity

[1] Based on ERK inhibitors of which we are aware; [2] Comparator ERKi's are ulixertinib and ravoxertinib; [3] Across ASN007-101 and HERKULES-1 studies at doses from 120-250mg QW and 125mg BID-QW
Note: uPR = unconfirmed partial response; cPR = confirmed partial response; PK = pharmacokinetics

ERAS-007 CDP enables efficient evaluation of three key biological hypotheses

Preventing in-pathway resistance

HERKULES-3

Regimen	Indication
ERAS-007 + EC	EC-naïve BRAF V600E-mutant CRC

Reversing in-pathway resistance

HERKULES-3

Regimen	Indication
ERAS-007 + EC	EC-treated BRAF V600E-mutant CRC

HERKULES-2

Regimen	Indication
ERAS-007 + osimertinib	Post-osimertinib EGFR-mutant NSCLC

Targeting adjacent pathways

HERKULES-3

Regimen	Indication
ERAS-007 + palbociclib	KRAS- or NRAS-mutant CRC; KRAS-mutant PDAC

Note: CDP = clinical development plan; EC = encorafenib and cetuximab; BRAF V600E CRC is also referred to as BRAFm CRC in this presentation

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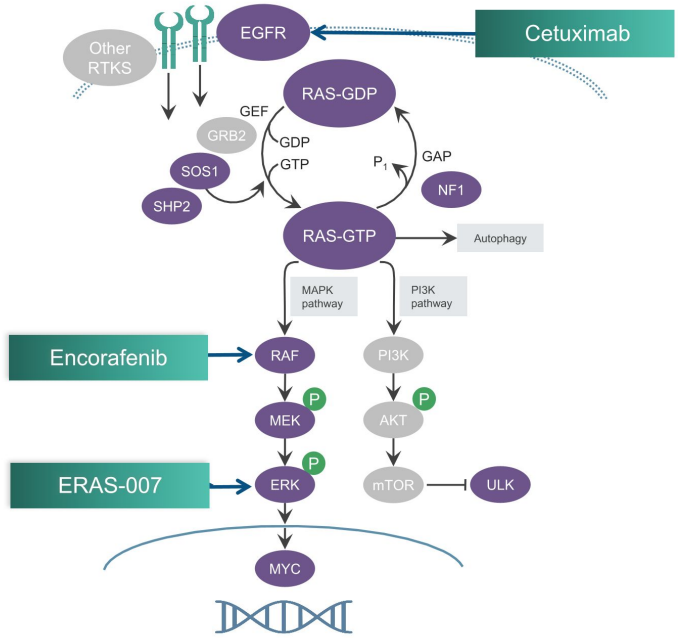
Opportunity to improve SoC in patients with 2L+ BRAFm CRC (10% of all CRC)

Patient Population	2/3L BRAFm CRC (EC-naïve)	3L+ BRAFm CRC (EC-treated)
Standard of Care	encorafenib + cetuximab	TAS-102 + bevacizumab
Benchmark	ORR 20% mDOR 6.1m mPFS 4.2m	ORR 6% mDOR N/A mPFS 5.6m

SoC: standard of care; ORR: overall response rate; mDOR: median duration of response; mPFS: median progression free survival
2/3L BRAFm CRC Benchmark = BEACON trial from encorafenib prescribing information
3L+ BRAFm CRC Benchmark = SUNLIGHT trial; Tabernero et al. 2023 ASCO GI Annual Meeting

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



- Combined blockade of ERK plus BRAF/EGFR via treatment with ERAS-007 + encorafenib + cetuximab (EC) could:
  - More effectively inhibit the RAS/MAPK pathway and prevent resistance in **EC-naïve BRAFm CRC patients** than BRAF/EGFR inhibition alone
  - Overcome treatment-induced resistance to BRAF/EGFR inhibition in **EC-treated BRAFm CRC patients**

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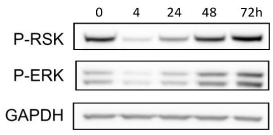
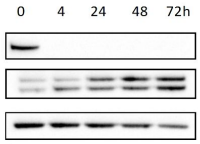
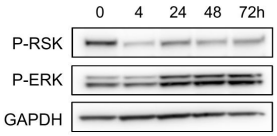
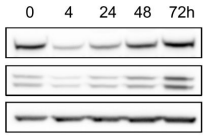
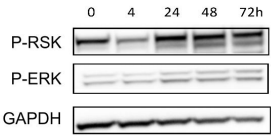
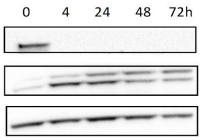
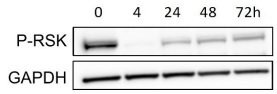
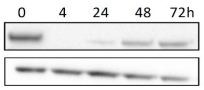
ERAS-007 blocked the MAPK feedback reactivation observed with MEK or other ERK plus BRAF inhibitor combinations

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

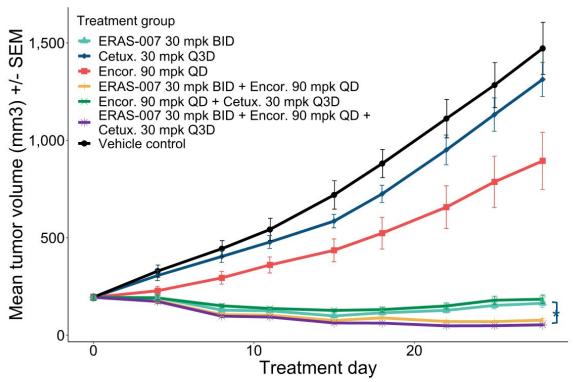
Source: Unpublished data

ERAS-007 + EC in BRAFm CRC:

Robust in vivo combination activity in BRAF V600E CRC

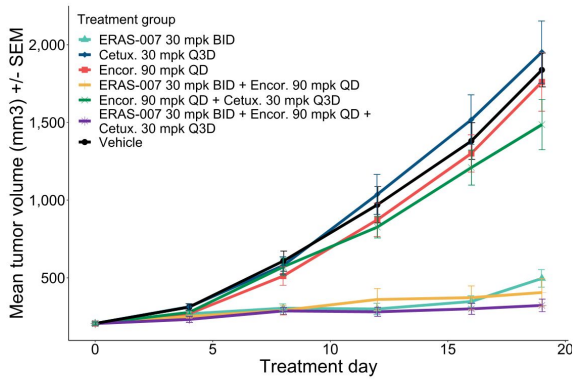
TGI in WiDr (BRAF V600E CRC)

EC-sensitive CDX Model



TGI in RKO (BRAF V600E CRC)

EC-resistant CDX Model

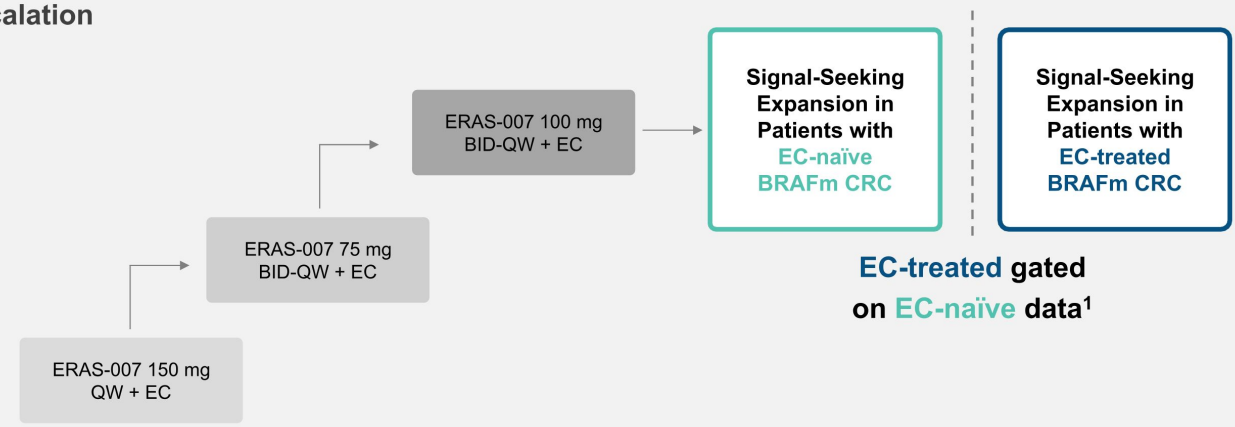


- ERAS-007 60 mpk QD dose showed similar activity to 30 mpk BID, either as a mono or combo Tx with encor. +/- cetux.
- ERAS-007 combinations were generally well tolerated across the tested models as demonstrated by the minimal percentage body weight changes observed.

*p-value < 0.01
TGI = tumor growth inhibition; Cetux. = cetuximab; Encor. = encorafenib; EC = encorafenib plus cetuximab (BEACON regimen); mpk = milligrams per kilogram; BID = twice a day; Q3D = once every 3 days; QD = once daily

HERKULES-3: Ph 1b/2 evaluating ERAS-007 + EC in BRAFm CRC

Dose escalation



Patient enrollment (efficacy evaluable population)			
EC-naïve	1	1	6
EC-treated	1	4	5

QW: oral once a week; BID-QW: oral twice a day on a single day each week; EC: encorafenib 300 mg oral daily + cetuximab 500 mg/m2 intravenous infusion once every 2 weeks
[1] EC-treated segment may be explored if efficacy data continue to be promising in the EC-naïve segment

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

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

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

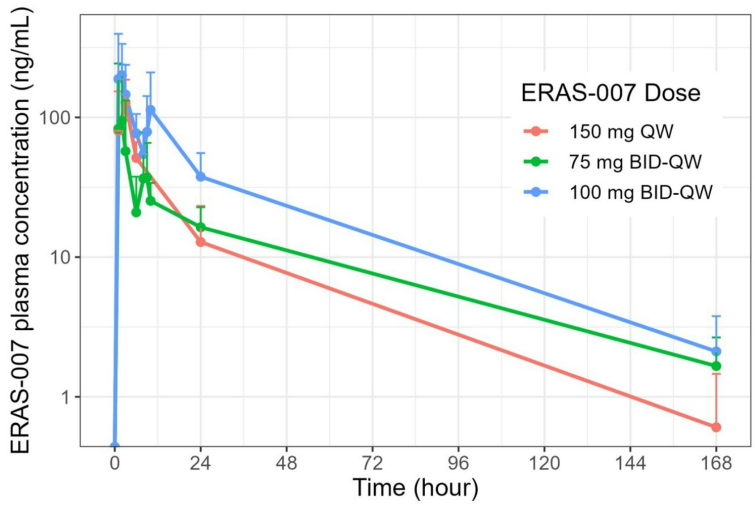
ERAS-007 Dose + EC[a]	150 mg QW[b] (n = 2)		75 mg BID-QW[c] (n = 6)		100 mg BID-QW[c] (n = 12)		ALL (n = 20)	
Preferred Term	Any Grade n (%)	Grade ≥ 3 n (%)	Any Grade n (%)	Grade ≥ 3 n (%)	Any Grade n (%)	Grade ≥ 3 n (%)	Any Grade n (%)	Grade ≥ 3 n (%)
Fatigue	1 (50)	1 (50)	3 (50)	0	3 (25)	0	7 (35)	1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

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

Data cut 23MAR2023 / * Related to ERAS-007
[a]EC: encorafenib 300 mg oral daily + cetuximab 500 mg/m2 intravenous infusion once every 2 weeks[b]ERAS-007 QW: ERAS-007 oral once a week. [c]ERAS-007 BID-QW: ERAS-007 oral twice a day on a single day each week

ERAS-007 exhibited predictable PK when in combination with EC with no apparent drug-drug interactions

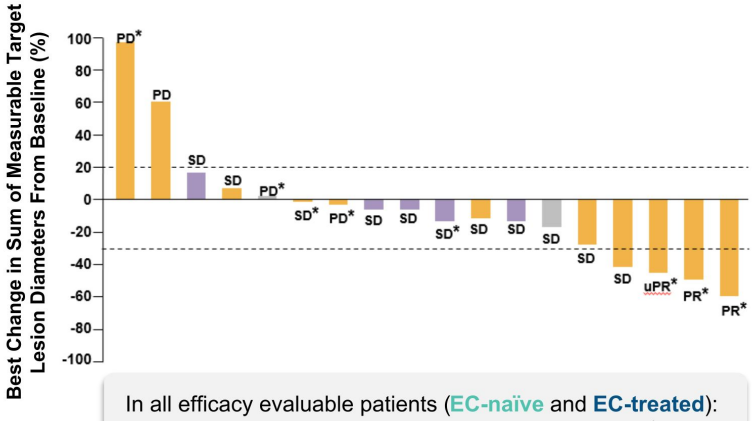
Mean ERAS-007 Concentration-Time Profiles Following the First Dose



Error bars = standard deviation
EC = encorafenib 300 mg QD + cetuximab 500 mg/m² Q2W
ERAS-007 QW: ERAS-007 oral once a week / ERAS-007 BID-QW: ERAS-007 oral twice a day on a single day each week

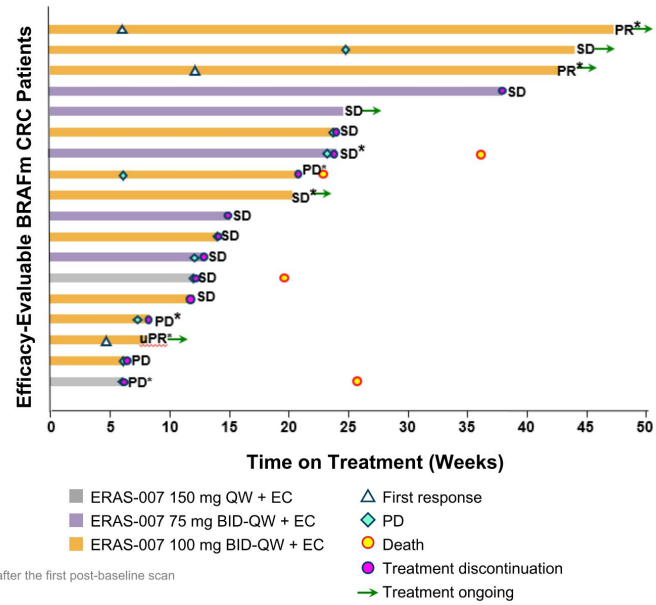
Encouraging early efficacy results observed in BRAFm CRC patients (EC-naïve and EC-treated)

Preventing resistance
Reversing resistance



In all efficacy evaluable patients (EC-naïve and EC-treated):

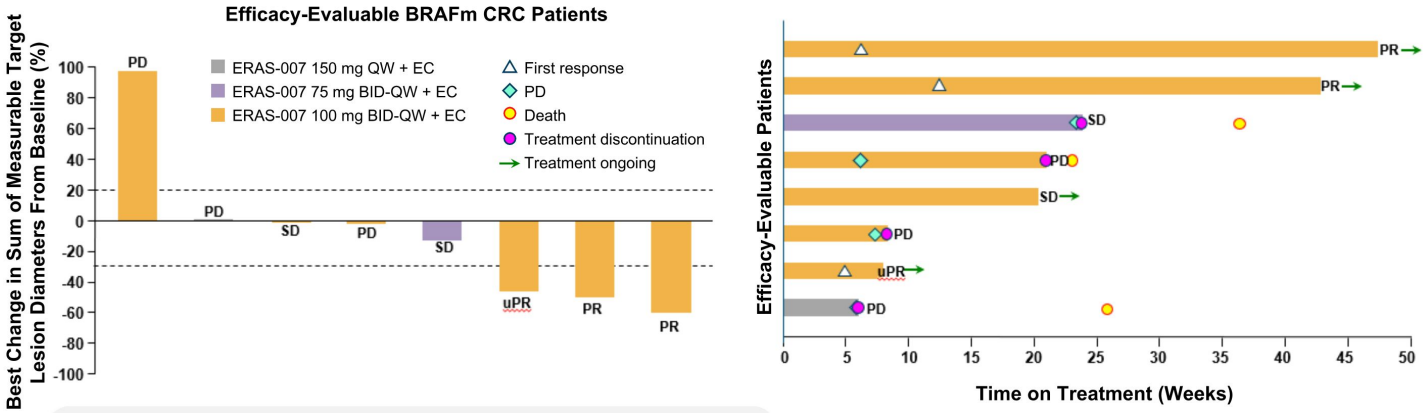
- 17% (3/18) response rate (2 confirmed PR, 1 uPR[1])
- 78% (14/18) disease control rate[2]



Data cut as of 21MAY2023
Response on the bar represents the best overall response based on investigator assessments.
* Represents EC-naïve population
[1] Per site communication, the patient with uPR was still in response at the subsequent scan (26MAY2023), which was conducted 25 days after the first post-baseline scan
[2] Disease control rate (DCR) = CR + PR + SD; uPR is included
EC: encorafenib + cetuximab; PD: progressive disease; CR: complete response; PR: confirmed partial response; uPR: unconfirmed partial response; SD: stable disease
ERAS-007 QW: ERAS-007 oral once a week / ERAS-007 BID-QW: ERAS-007 oral twice a day on a single day each week

ERASCA

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



In EC-naïve BRAFm CRC patients at the highest dose tested (100 mg BID-QW):

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

In EC-naïve BRAFm CRC patients across all dose levels:

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

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

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

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

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

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

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

ERASCA

ERAS-007 CDP enables efficient evaluation of three key biological hypotheses

Preventing in-pathway resistance

HERKULES-3

Regimen	Indication
ERAS-007 + EC	EC-naïve BRAF V600E-mutant CRC

Reversing in-pathway resistance

HERKULES-3

Regimen	Indication
ERAS-007 + EC	EC-treated BRAF V600E-mutant CRC

HERKULES-2

Regimen	Indication
ERAS-007 + osimertinib	Post-osimertinib EGFR-mutant NSCLC

Targeting adjacent pathways

HERKULES-3

Regimen	Indication
ERAS-007 + palbociclib	KRAS- or NRAS-mutant CRC; KRAS-mutant PDAC

Note: CDP = clinical development plan; EC = encorafenib and cetuximab; BRAF V600E CRC is also referred to as BRAFm CRC in this presentation

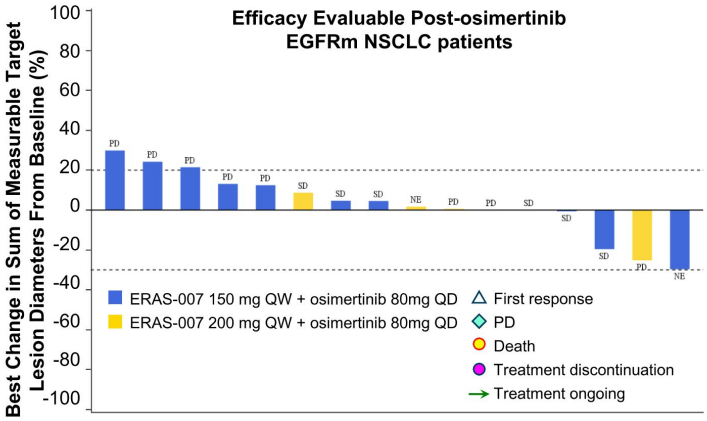
HERKULES-2: ERAS-007 + osimertinib had acceptable and manageable AEs with no apparent DDI observed in patients with EGFRm NSCLC

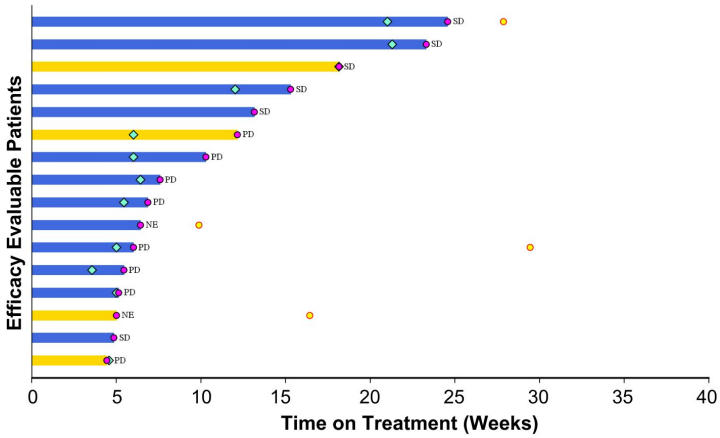
- ERAS-007 150 mg QW + osimertinib 80mg QD **identified as the MTD/RD**
- Combination had **acceptable and manageable AEs**
  - AEs similar to monotherapy ERAS-007
  - Most frequent (≥ 20%) TRAEs were diarrhea (50%), nausea (40%), rash (35%), vision blurred (35%) and vomiting (25%)[1]
- **No apparent drug-drug interactions** (DDI) were observed
  - ERAS-007 PK and osimertinib PK results were comparable to historical PK results observed in monotherapy trials

[1] Data cut-off 23SEP22
MTD: maximum tolerated dose; RD: recommended dose

Efficacy data do not support continued evaluation of ERAS-007 + osimertinib

Best response of ERAS-007 + osimertinib in limited sample size (N=16) was SD





Data Cutoff 23SEP2022
PD: progressive disease; SD: stable disease; NE: not evaluable

ERAS-007 CDP enables efficient evaluation of three key biological hypotheses

Preventing in-pathway resistance

HERKULES-3

Regimen	Indication
ERAS-007 + EC	EC-naïve BRAF V600E-mutant CRC

Reversing in-pathway resistance

HERKULES-3

Regimen	Indication
ERAS-007 + EC	EC-treated BRAF V600E-mutant CRC

HERKULES-2

Regimen	Indication
ERAS-007 + osimertinib	Post-osimertinib EGFR-mutant NSCLC

Targeting adjacent pathways

HERKULES-3

Regimen	Indication
ERAS-007 + palbociclib	KRAS- or NRAS-mutant CRC; KRAS-mutant PDAC

Note: CDP = clinical development plan; EC = encorafenib and cetuximab; BRAF V600E CRC is also referred to as BRAFm CRC in this presentation

ERAS-007 + palbociclib: acceptable safety and tolerability with reversible and manageable TRAEs

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

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

ERAS-007 BID-QW Palbo QD n	75 mg 75 mg 7		75 mg 100 mg 2		100 mg 100 mg 7		75 mg 125 mg 14		100 mg 125 mg 15		125 mg 125 mg 1		All 46	
Preferred Term	**Any Gr n (%)**	**Gr ≥ 3 n (%)**	**Any Gr n (%)**	**Gr ≥ 3 n (%)**	**Any Gr n (%)**	**Gr ≥ 3 n (%)**	**Any Gr n (%)**	**Gr ≥ 3 n (%)**	**Any Gr n (%)**	**Gr ≥ 3 n (%)**	**Any Gr n (%)**	**Gr ≥ 3 n (%)**	**Any Gr n (%)**	**Gr ≥ 3 n (%)**
Diarrhea	2 (28.6)	0	2 (100)	0	4 (57.1)	1 (14.3)	6 (42.9)	0	6 (40.0)	1 (6.7)	0	0	20 (43.5)	2 (4.3)
Nausea	2 (28.6)	0	2 (100)	0	3 (42.9)	0	2 (14.3)	0	9 (60.0)	0	0	0	18 (39.1)	0
Vision blurred	3 (42.9)	0	0	0	2 (28.6)	0	4 (28.6)	0	4 (26.7)	0	0	0	13 (28.3)	0
Vomiting	1 (14.3)	0	2 (100)	0	2 (28.6)	0	4 (28.6)	0	3 (20.0)	0	1 (100)	0	13 (28.3)	0
Fatigue	0	0	2 (100)	0	1 (14.3)	0	2 (14.3)	0	5 (33.3)	0	1 (100)	0	11 (23.9)	0
Dermatitis acneiform	0	0	1 (50)	0	1 (14.3)	1 (14.3)	3 (21.4)	0	5 (33.3)	0	0	0	10 (21.7)	1 (2.2)

- Overall data suggest that TRAEs were reversible and manageable
- Two Grade 5 treatment-emergent adverse events were reported:
  - Hemorrhage intracranial (unrelated to ERAS-007 75 mg BID-QW and palbo 75 mg QD)
  - Bacteremia (related to ERAS-007 75 mg BID-QW and palbo 125 mg QD)

Bacteremia (Gr5) deemed related by investigator, but confounded by:

- Underlying cancer involved bone, compromising bone marrow function
- Palbo black box warning of neutropenia, which increases infection risk
- ERAS-007 monotherapy has not been associated with neutropenia
- Patient decision to focus on comfort care while hospitalized

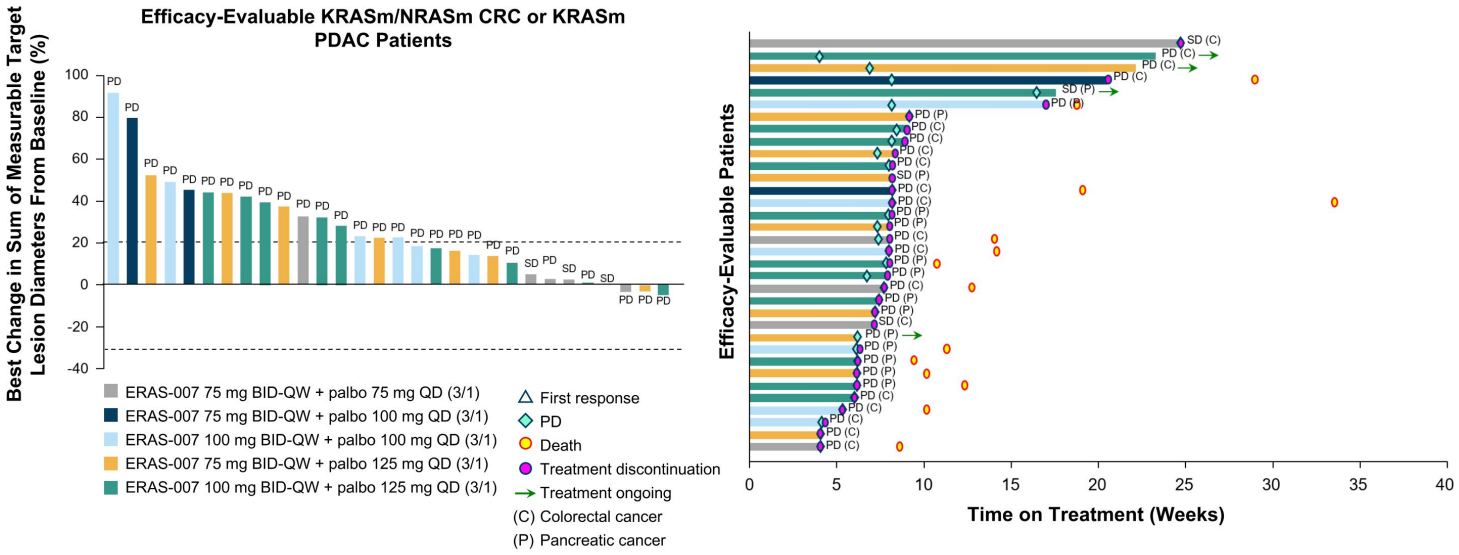
Data Cut-off 23MAR2023; Gr: Grade

Four patients experienced 6 dose-limiting toxicities: ERAS-007 75 mg + palbo 125 mg (Gr 3 bacteremia, N=1), ERAS-007 75 mg + palbo 125 mg (Gr 3 rash maculopapular, N=1), ERAS-007 100 mg + palbo 100 mg (Gr 3 dermatitis acneiform neutropenia and anemia, N=1), ERAS-007 100 mg + palbo 125 mg (Gr 3 thrombocytopenia, N=1)

* Related to ERAS-007

Efficacy data do not support continued evaluation of ERAS-007 + palbociclib

Best response of ERAS-007 + palbociclib in limited sample size (N=34) was SD



Data cut 23MAR2023

Response on the bar represents the best overall response based on investigator assessments

PD: progressive disease; SD: stable disease.

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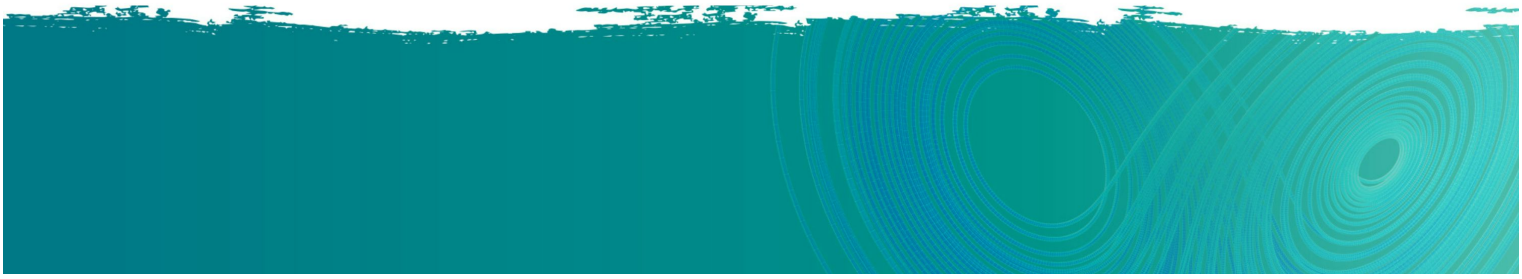
Other ERAS-007 Clinical Update / Wrap-up

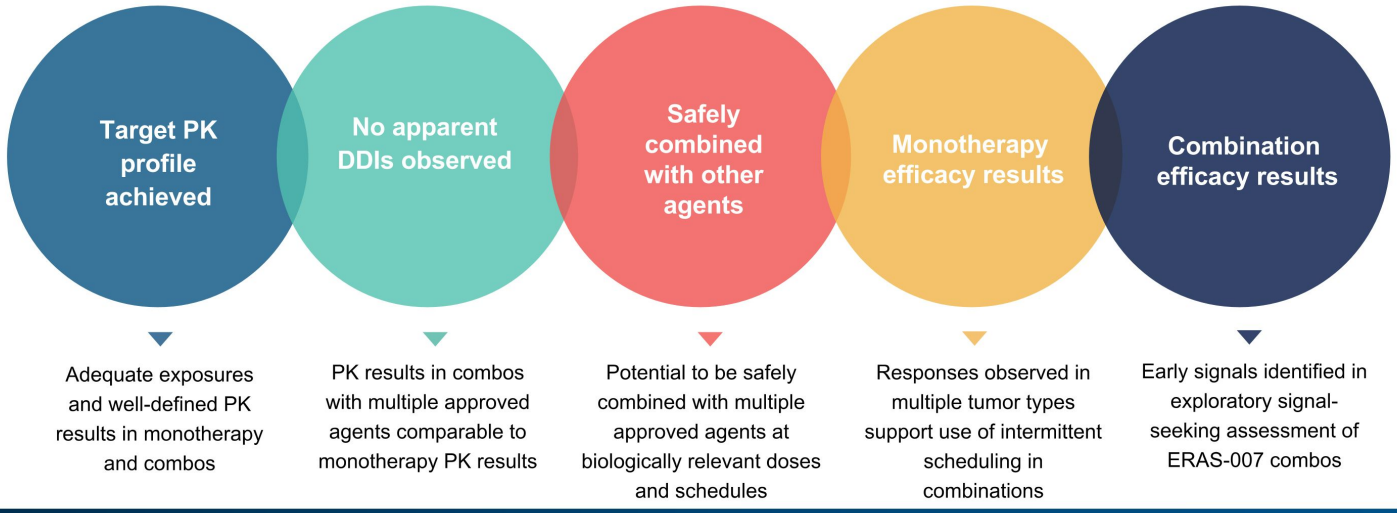


HERKULES-1: ERAS-601 + ERAS-007 combination safety data do not support continued evaluation of regimen tested

- **Dosing Regimen Tested**: ERAS-601 40 mg BID (3 weeks on/1 week off) + ERAS-007 50 mg BID-QW
  - Rationale: ERAS-601 was positioned at its MTD as backbone therapy with dose escalation of ERAS-007
- 2 DLTs were reported in 6 DLT-evaluable patients enrolled in the first dosing cohort
  - Grade 3 elevated AST
  - Grade 3 neutropenia

Data as reported by investigators on 25MAY2023 investigator call and subsequent follow up
BID: twice a day; BID-QW: oral twice a day on a single day each week; MTD: maximum tolerated dose; DLT: dose limiting toxicity

Early clinical data reinforce potential combinability of ERAS-007 as a backbone to treat patients with GI cancers including BRAFm CRC



Further evaluation of **ERAS-007 + encorafenib and cetuximab (EC)** in patients with **EC-naïve BRAFm CRC** is ongoing in HERKULES-3

Note: PK = pharmacokinetics; DDI = drug-drug interaction; Approved agents evaluated in clinic are osimertinib, encorafenib, cetuximab, and palbociclib

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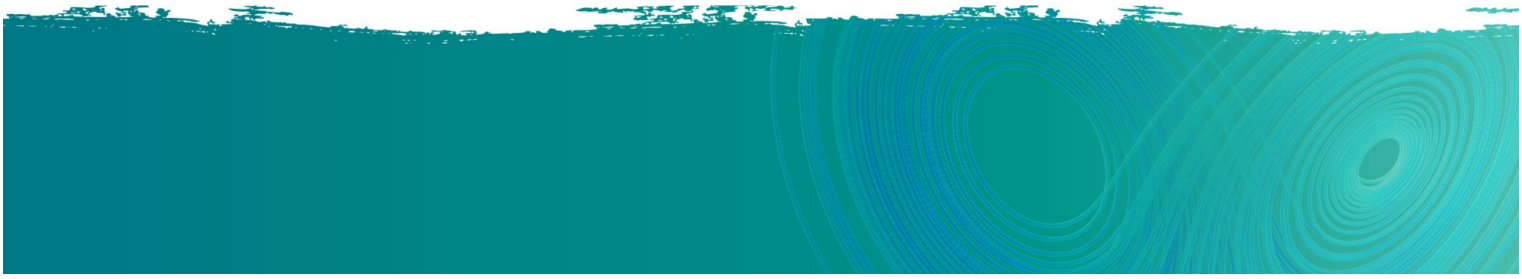
Portfolio Update



Data-driven prioritization focuses resources on opportunities with the highest probability of success for patients

Development Programs	Action	Rationale
HERKULES-3: ERAS-007 + EC in **EC-naïve CRC** segment	**Expanding**	Encouraging early efficacy data in EC-naïve patients
HERKULES-3: ERAS-007 + EC in **EC-treated CRC** segment	**Gated on EC-naïve data**[1]	More challenging to show treatment benefit in EC-treated segment than in EC-naïve segment
HERKULES-2: **ERAS-007 + osimertinib**	**Deprioritized**	Clinical efficacy data do not support continued evaluation
HERKULES-3: **ERAS-007 + palbociclib**	**Deprioritized**	Clinical efficacy data do not support continued evaluation
HERKULES-1: **ERAS-007 + ERAS-601**	**Deprioritized**	Dose escalation safety data do not support continued evaluation of regimen tested
AURORAS-1: **ERAS-3490**	**Deprioritized**	Despite program's differentiation, G12C inhibitor landscape is increasingly competitive for SMID cap biopharma
Research Programs	**Action**	**Rationale**
ERAS-9 SOS1	**Deprioritized**	Focusing on SHP2 as key upstream RAS/MAPK pathway node due to promise of ERAS-601 compound
ERAS-11 MYC	**Deprioritized**	Preclinical characterization does not support continued work
ERAS-2/3 RAS Switch-II Groove targeting	**Deprioritized**	Pursuing other promising Research approaches to target RAS mutations beyond G12C

EC: encorafenib and cetuximab; [1] EC-treated segment may be explored if efficacy data continue to be promising in the EC-naïve segment

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, BRAF Class 2/3 solid tumors			SEACRAFT-3 (planned)			1	ERASCA
ERAS-007[1]	ERK1/2		BRAF V600E CRC			HERKULES-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-4	KRAS G12D		KRAS G12D solid tumors						2	ERASCA
ERAS-5	ULK		RAS/MAPK altered tumors						3	ERASCA
ERAS-10	RAS/MAPK		RAS/MAPK altered tumors						1 2 3	ERASCA
ERAS-12	EGFR D2/D3		EGFR & RAS/MAPK altered 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

[1] Also being evaluated in combo w/ G12Ci in KRAS G12C NSCLC and GI Tumors under Stand Up to Cancer grant

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Anticipated key milestones and clinical trial readouts

Program *Mechanism*	Trial Name *Indication* *(Combo partner if applicable)*	Upcoming Milestone(s)
Naporafenib *Pan-RAF inhibitor*	**SEACRAFT-1** *RAS Q61X Solid Tumors* *(+ trametinib)*	• **H2 2023:** Ph 1b FPD • **Q2 2024 – Q4 2024:** Ph 1b combo signal-seeking efficacy data in relevant tumor types
	SEACRAFT-2 *NRASm Melanoma* *(+ trametinib)*	• **H1 2024:** Ph 3 pivotal FPD
ERAS-007 *ERK1/2 inhibitor*	**HERKULES-3** *EC-naïve BRAFm CRC* *(+ encorafenib and cetuximab)*	• **H2 2023 – H1 2024:** Ph 1b combo dose expansion data in EC-naïve BRAFm CRC
ERAS-601 *SHP2 inhibitor*	**FLAGSHP-1** *Advanced Solid Tumors* *(+ cetuximab)*	• **H1 2024:** Ph 1b combo dose expansion data in relevant patient populations, including HPV-neg HNSCC
ERAS-801 *CNS-penetrant EGFR inhibitor*	**THUNDERBBOLT-1** *Glioblastoma*	• **H2 2023:** Ph 1 monotherapy dose escalation data in GBM; preliminary safety and PK

FPD = first patient dose; PK = pharmacokinetics

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Thank You!

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

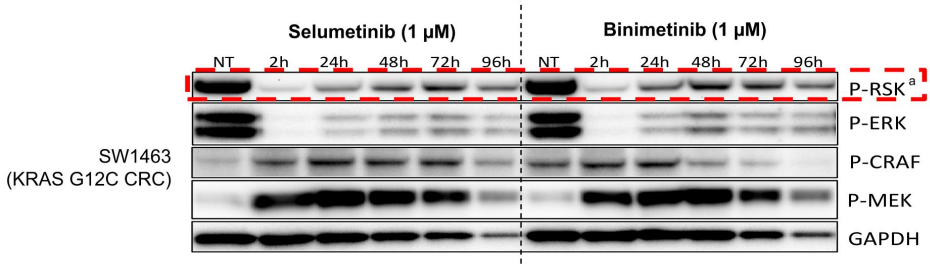
ERAS-007 was designed to be a **potent**, **selective,** reversible, oral inhibitor of ERK1/2

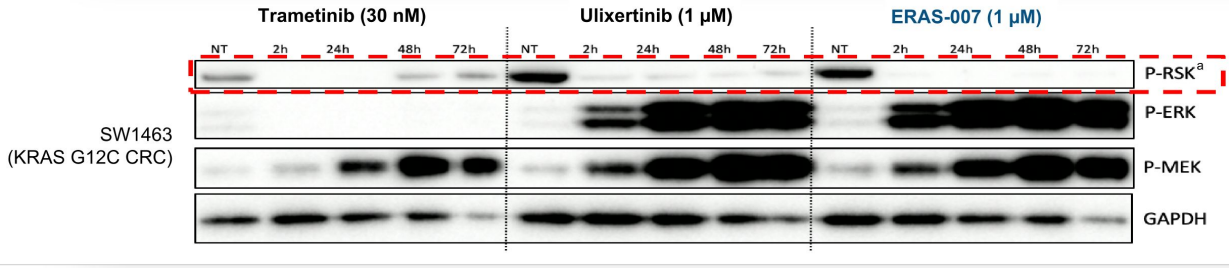
Assay Type	Assay	ERAS-007 IC50 (nM)
Biochemical	ERK1	2
	ERK2	2
Cell-based mechanistic (HT-29)	pRSK	7

ERAS-007 has shown a longer target residence time when compared to 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

ATP-competitive ERK inhibitors were more robust than MEK inhibitors in shutting down MAPK pathway reactivation; ERAS-007 was most robust in vitro





[a] *ERK directly phosphorylates the p90 ribosomal S6 kinase protein (RSK) so RSK phosphorylation (P-RSK) serves as a biomarker of ERK and ultimately RAS/MAPK pathway activity*
Source: Unpublished data

Likely recommended dose of ERAS-007 for combinations has been generally well tolerated

Treatment-related Adverse Events Occurring in ≥ 20% and ≥ 2 Patients in Any Dose
(arranged by descending frequency in the 125 mg BID-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)	
	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%)
Eye Disorders*	1 (25.0%)	0	6 (54.5%)	1 (9.1%)	5 (62.5%)	2 (25.0%)
Nausea	2 (50.0%)	0	5 (45.5%)	0	5 (62.5%)	0
Fatigue	1 (25.0%)	1 (25.0%)	4 (36.4%)	0	4 (50.0%)	1 (12.5%)
Diarrhea	0	0	2 (18.2%)	0	3 (37.5%)	0
Vomiting	1 (25.0%)	0	3 (27.3%)	0	3 (37.5%)	0
Dermatitis acneiform	1 (25.0%)	0	4 (36.4%)	0	3 (37.5%)	0
Dehydration	2 (50.0%)	0	1 (9.1%)	0	1 (12.5%)	0

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

*includes uniocular 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

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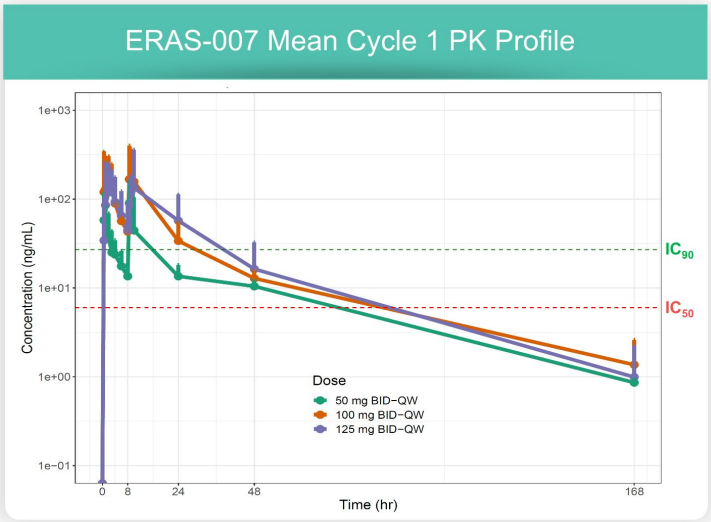
ERAS-007 BID-QW (monotherapy) enhances time above IC_{90} to drive tumor cell killing while extending time below IC_{50} to allow normal cell recovery



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

*HCT 116 anti-proliferation assay for ERAS-007
Error bars = Standard deviation

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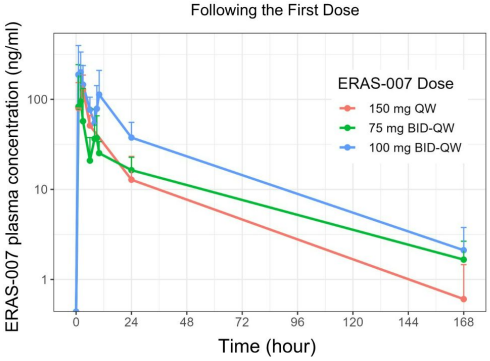
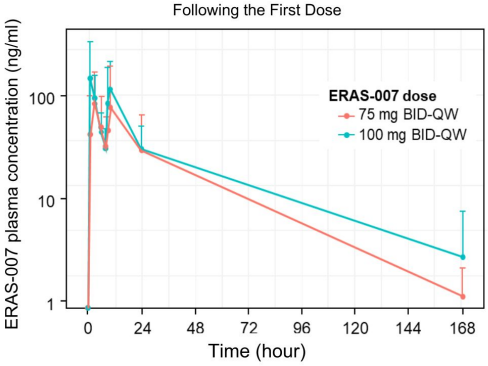
ERAS-007 PK when administered in combination (+ EC, + palbociclib, and + osimertinib) was comparable to monotherapy PK, suggesting no apparent DDI

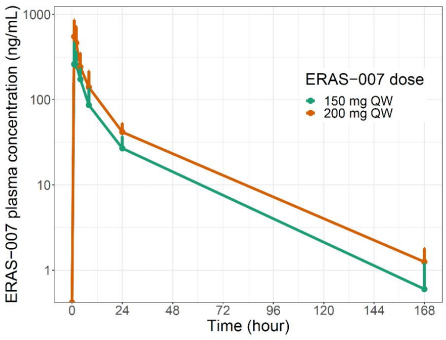
ERAS-007 + encorafenib and cetuximab
Mean ERAS-007 Concentration-Time Profiles
Following the First Dose



ERAS-007 + palbociclib
Mean ERAS-007 Concentration-Time Profiles
Following the First Dose



ERAS-007 + osimertinib
Mean ERAS-007 Concentration-Time Profiles
Following the First Dose



Error bars = Standard deviation
PK: pharmacokinetics; EC: encorafenib + cetuximab; DDI: drug-drug interaction