ACTUATE THERAPEUTICS

Corporate Overview

November 2026



Forward-Looking Statements

This presentation contains forward-looking statements about us, including our clinical trials and development plans, and our industry, that are based on management's beliefs and assumptions and on information currently available to our management. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "ongoing," "plan," "potential," "predict," "project," "should," "target," "will," "would," or the negative of these terms or other comparable terminology are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. All statements, other than statements related to present facts or current conditions or of historical facts, contained in this presentation are forward-looking statements. Accordingly, these statements involve estimates, assumptions, substantial risks and uncertainties which could cause actual results to differ materially from those expressed in them, including but not limited to that we have incurred significant operating losses, and we expect that we will incur significant operating losses for the foreseeable future; that our financial condition raises substantial doubt as to our ability to continue as a going concern and we require additional capital to finance our operations beyond the third quarter of fiscal year 2026, and a failure to obtain this necessary capital in the near term on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our development programs, commercialization efforts or other operations; that we have a high risk of never generating revenue or becoming profitable or, if we achieve profitability, we may not be able to sustain it; that clinical and preclinical drug development involves a lengthy and expensive process with uncertain timelines and outcomes, and results of prior preclinical studies and early clinical trials are not necessarily predictive of future results, and elraglusib may not achieve favorable results in clinical trials or preclinical studies, and we may not be able to make regulatory submissions or receive regulatory approval on a timely basis, if at all; that we may not successfully enroll additional patients or establish or advance plans for Phase 1/2 or other development, including through conversations with the FDA or EMA and the standards such bodies may impose for such development; that regulatory approval processes may involve delays, unfavorable determinations or other challenges due to various factors, including government funding, staffing and political uncertainties; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities and within the medical community; that elraglusib could be associated with side effects, adverse events or other properties or safety risks, which could delay or preclude regulatory approval, cause us to suspend or discontinue clinical trials or result in other negative consequences; that this presentation includes preliminary and unpublished data which may be subject to change following the availability of more data or following a more comprehensive review of the data and should not be relied upon as a final analysis; that we do not have, and may never have, any approved products on the market and our business is highly dependent upon receiving approvals from various U.S. and international governmental agencies and will be severely harmed if we are not granted approval to manufacture and sell our product candidates; our reliance on third parties to conduct our non-clinical studies and our clinical trials; our reliance on third-party licensors and ability to preserve and protect our intellectual property rights; that we currently depend entirely on the success of elraglusib, which is our only product candidate, and if we are unable to advance elraglusib in clinical development, obtain regulatory approval and ultimately commercialize elraglusib, or experience significant delays in doing so, our business will be materially harmed; that we face significant competition from other biotechnology and pharmaceutical companies; that we may not be successful in our efforts to investigate elraglusib in additional indications and we may expend our limited resources to pursue a new product candidate or a particular indication for elraglusib and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success; that the termination of third-party licenses could adversely affect our rights to important compounds or technologies; and our ability to fund development activities, including because our financial condition raises substantial doubt as to our ability to continue as a going concern and we require additional capital to finance our operations beyond October 2027, and a failure to obtain this necessary capital in the near term on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our development programs, commercialization efforts or other operations. 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. In addition, any forward-looking statements are qualified in their entirety by reference to the factors discussed under the heading "Risk Factors" in our Annual Report on Form 10-K filed with the SEC on March 26, 2026, our Quarterly Reports on Form 10-Q, and other filings with the SEC. This presentation also contains estimates and other statistical data that we obtained from industry publications and research and studies conducted by third parties relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates.

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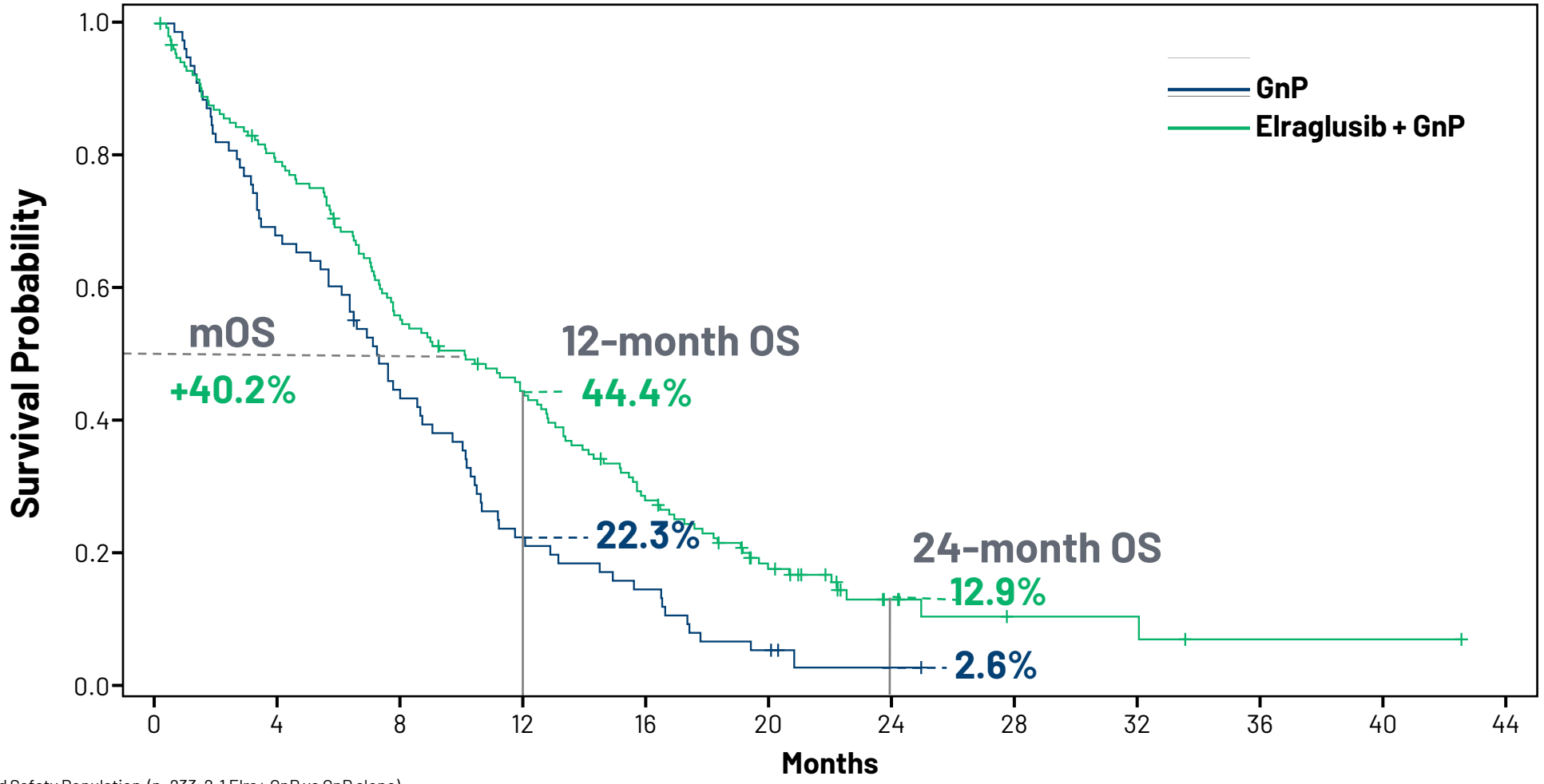
Elraglusib – "Pipeline in a Molecule"

Therapeutic Potential Across a Broad Range of Cancers

- Elraglusib is a class-leading GSK-3β inhibitor with a novel, multimodal MOA
- Clinical trials in 500+ patients resulted in significant increases in survival and complete responses in multiple difficult-to-treat cancers
- Demonstrated synergy with multiple SOCs, and potential synergy with RAS/RAF/MEK inhibitors
- Oral tablet with high bioavailability is ready to enter clinical trials
- IP provides exclusivity to 2038 before PTE in all major markets

Elraglusib Significantly Improves OS in a Most Difficult to Treat Cancer

Doubled percentage of 1L mPDAC patients alive at one year in international Phase 2 RCT



Predefined Safety Population (n=233, 2:1 Elra+ GnP vs GnP alone)
Data cut as of Nov 22, 2025

mPDAC: metastatic pancreatic ductal adenocarcinoma; GnP: Gemcitabine + Nab-paclitaxel; OS: Overall survival

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Elraglusib Development Strategy

Expand Pipeline Potential with Elraglusib Oral Tablet

Initiate clinical trials to expand into additional high value / blockbuster indications

Advance Pathway to be a SOC Backbone in PDAC

Complete nonclinical research assessing potential synergy for combination use of elraglusib and RAS / MEK inhibitors

Advance Pediatric Indications in Neuroblastoma (NBL) and Ewing Sarcoma

Pursuing non-dilutive support for clinical trials in two rare disease indications

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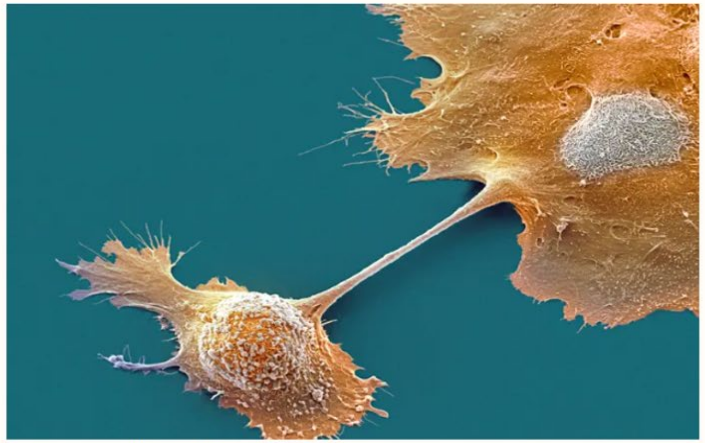
HEALTH CANCER

Two New Drugs Offer Hope for Pancreatic Cancer

ADD TIME ON GOOGLE

by Alice Park
SENIOR CORRESPONDENT

APR 14, 2026 11:23 AM CT



Pancreatic cancer cells *Steve Gschmeissner, Science Photo Library—Getty Images*

Pancreatic cancer is one of the most challenging diseases to treat, and while survival rates have improved since the 1970s, they have plateaued in recent years. But two promising drugs in the pipeline each seem to double survival.

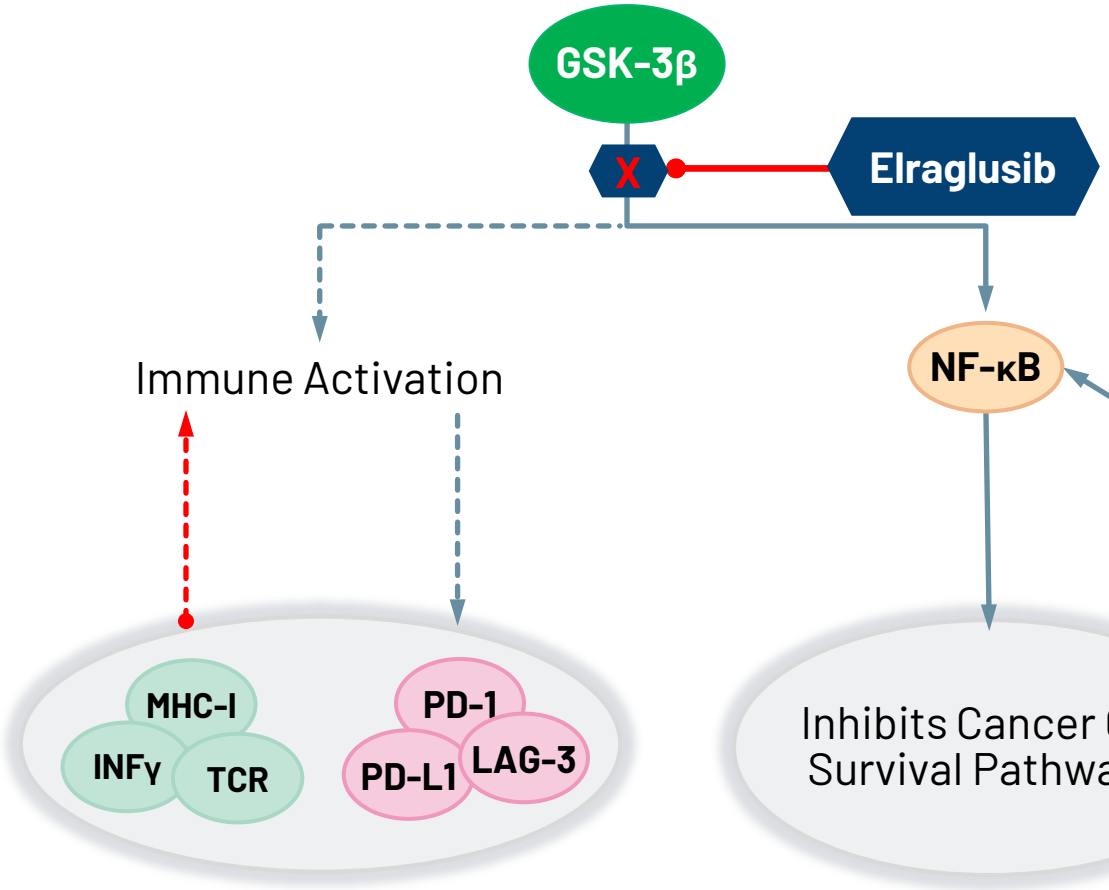
Revolution Medicines reported on April 13 that its cancer pill, daraxonrasib, helped patients survive an average of 13.2 months after starting treatment, compared to 6.7 months for those receiving standard chemotherapy. "These are dramatic results, with practice-changing outcomes," says Dr. Mark Goldsmith, CEO of Revolution Medicines, in an interview with TIME.

The following day, research supported by another company, Actuate Therapeutics, was published in *Nature Medicine* showing that the company's pancreatic cancer drug, elraglusib, also doubled one-year survival for patients taking it compared to those getting standard chemotherapy. Elraglusib is given by IV.

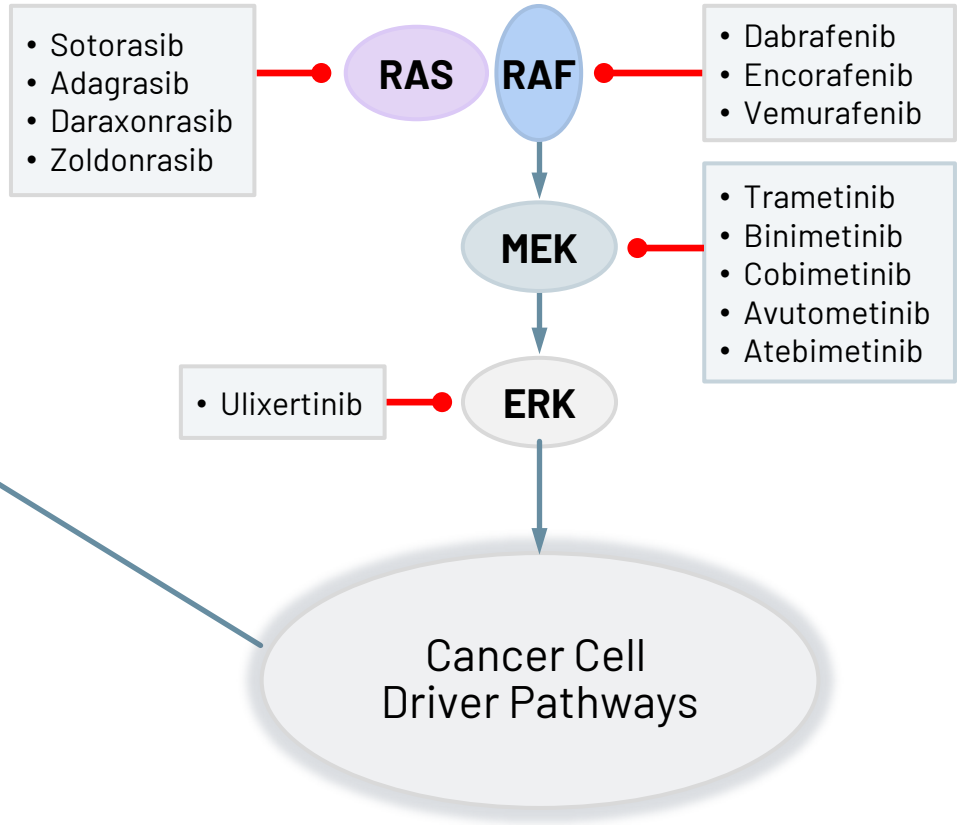
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Elraglusib Targets a Unique Pathway vs RAS/RAF/MEK

Elraglusib targets cancer survival pathways



RAS pathway inhibitors alone target driver mutations, with treatment escape nodes on NF-κB pathway





Ben Sasse ✓
@BenSasse

"Bad: Tests on the tumors show they were more advanced than we thought — meaning always-mutating tumors have developed some resistance tricks to our former treatment protocol (**daraxonrasib**). Bummer but that's life; and was eventually expected. Next: We're gunna change up treatment to carpet-bomb-chemo"
Source: @BenSasse on X, September 22, 2026. Link

Elraglusib Potentiates Antitumor Effects of Zoldonrasib and Daraxonrasib

Consistent greater-than-additive activity across mouse and human pancreatic cancer cell lines

Zoldonrasib + Elraglusib

KRAS G12D-selective inhibitor

20 / 20

models demonstrated synergistic or additive combination activity

✓

13 / 13 mouse KPC models • 7 / 7 human PDAC/PDX models

Including 5 FOLFIRINOX-resistant models

Daraxonrasib + Elraglusib

RAS(ON) multi-selective inhibitor

4 / 4

models demonstrated synergistic or additive combination activity

✓

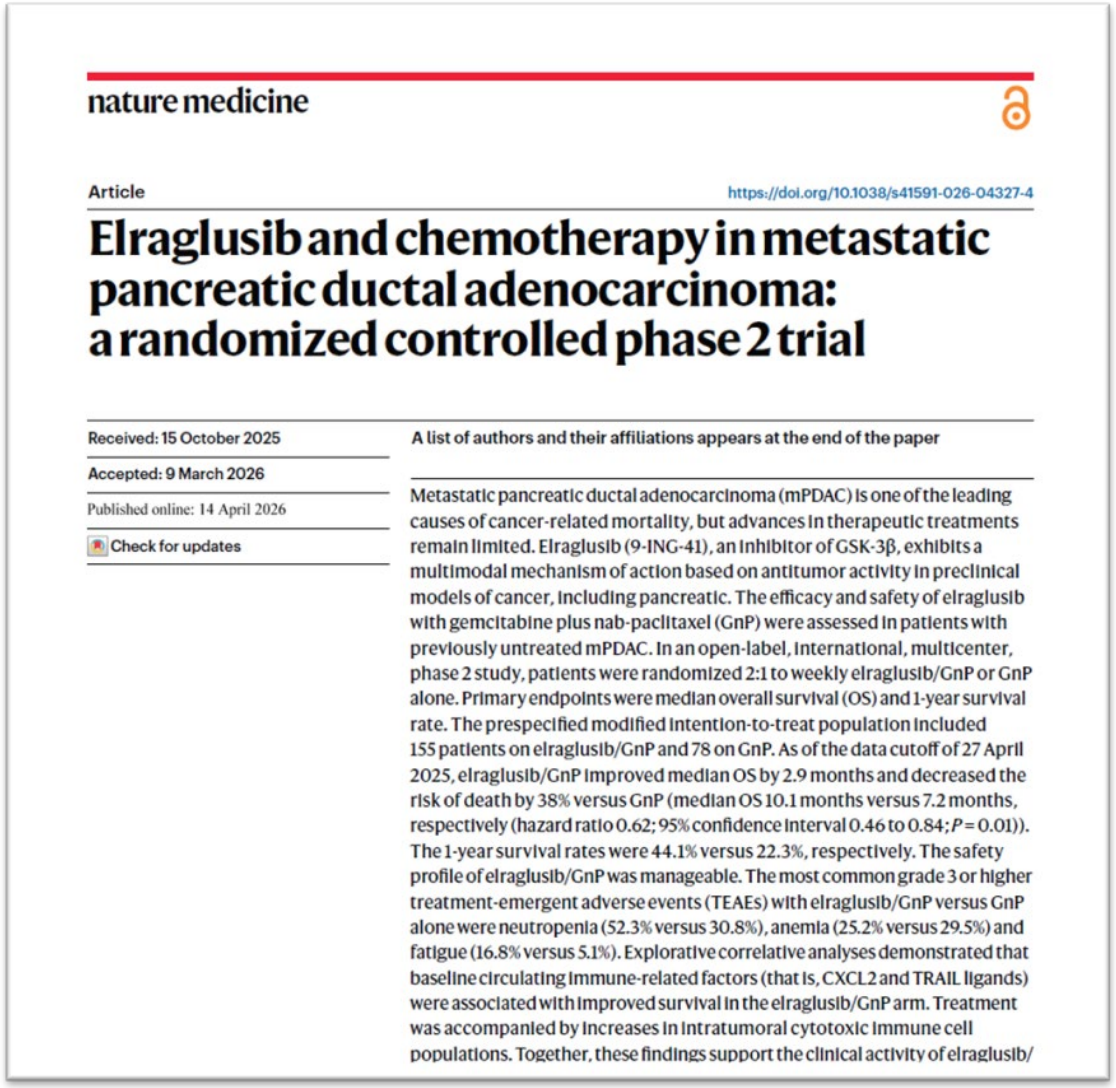
2 / 2 mouse KPC models • 2 / 2 human PDAC/PDX models

MOA and preclinical data support elraglusib as a potential combination therapy with multiple RAS inhibitors

In vitro studies - Bliss interaction analyses
Source: Mayo Clinic and Northwestern University

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Elraglusib Significantly Improves Survival with Once Weekly IV Dosing



nature medicine

Article

https://doi.org/10.1038/s41591-026-04327-4

Elraglusib and chemotherapy in metastatic pancreatic ductal adenocarcinoma: a randomized controlled phase 2 trial

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Check for updates

A list of authors and their affiliations appears at the end of the paper

Metastatic pancreatic ductal adenocarcinoma (mPDAC) is one of the leading causes of cancer-related mortality, but advances in therapeutic treatments remain limited. Elraglusib (9-ING-41), an inhibitor of GSK-3β, exhibits a multimodal mechanism of action based on antitumor activity in preclinical models of cancer, including pancreatic. The efficacy and safety of elraglusib with gemcitabine plus nab-paclitaxel (GnP) were assessed in patients with previously untreated mPDAC. In an open-label, international, multicenter, phase 2 study, patients were randomized 2:1 to weekly elraglusib/GnP or GnP alone. Primary endpoints were median overall survival (OS) and 1-year survival rate. The prespecified modified intention-to-treat population included 155 patients on elraglusib/GnP and 78 on GnP. As of the data cutoff of 27 April 2025, elraglusib/GnP improved median OS by 2.9 months and decreased the risk of death by 38% versus GnP (median OS 10.1 months versus 7.2 months, respectively (hazard ratio 0.62; 95% confidence interval 0.46 to 0.84; $P = 0.01$)). The 1-year survival rates were 44.1% versus 22.3%, respectively. The safety profile of elraglusib/GnP was manageable. The most common grade 3 or higher treatment-emergent adverse events (TEAEs) with elraglusib/GnP versus GnP alone were neutropenia (52.3% versus 30.8%), anemia (25.2% versus 29.5%) and fatigue (16.8% versus 5.1%). Exploratory correlative analyses demonstrated that baseline circulating immune-related factors (that is, CXCL2 and TRAIL ligands) were associated with improved survival in the elraglusib/GnP arm. Treatment was accompanied by increases in intratumoral cytotoxic immune cell populations. Together, these findings support the clinical activity of elraglusib/

- Elraglusib + GnP doubled 1-year OS vs. GnP alone (p=0.0004)
- 2.5x increase in 1-year OS in patients with liver metastases (p=0.0003)
- Elraglusib + SOC (GnP) improved median OS by 40% (**HR: 0.62**; p=0.02)
- Greater benefit seen in patients receiving at least one full cycle (4 weeks) of treatment (**HR:0.58**; p=0.035)
- Excellent safety profile with TEAEs/SAEs and discontinuations balanced between treatment groups

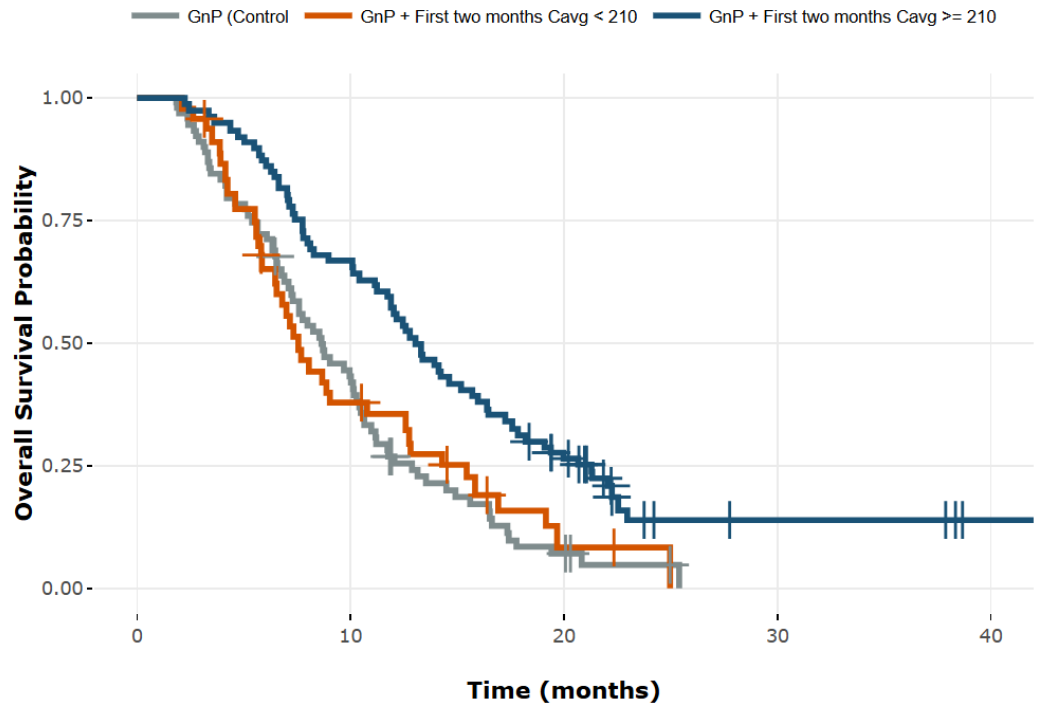
Randomized Phase 2 trial met primary endpoint

SOC: Standard of Care

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Greater Elraglusib Exposure Drives Improved OS Outcomes

Target Therapeutic IV Dose Identified



Multivariable Cox Proportional Hazards Analysis

Term	Hazard Ratio (95% CI)	Coefficient (beta)	Standard Error	z-statistic	p value
First two months Cavg <210 ng/mL relative to GnP alone	0.869 (95% CI: 0.584; 1.29)	-0.141	0.202	-0.695	0.487
First two months Cavg >210 ng/mL relative to GnP alone	0.477 (95% CI: 0.341; 0.668)	-0.740	0.172	-4.30	< 0.001

- PK analyses showed patients exceeding exposure C_{avg} of 210 ng/ml with significantly better outcomes **(HR= 0.48)**
- ~ 60% of Elra QW patients achieve target exposure

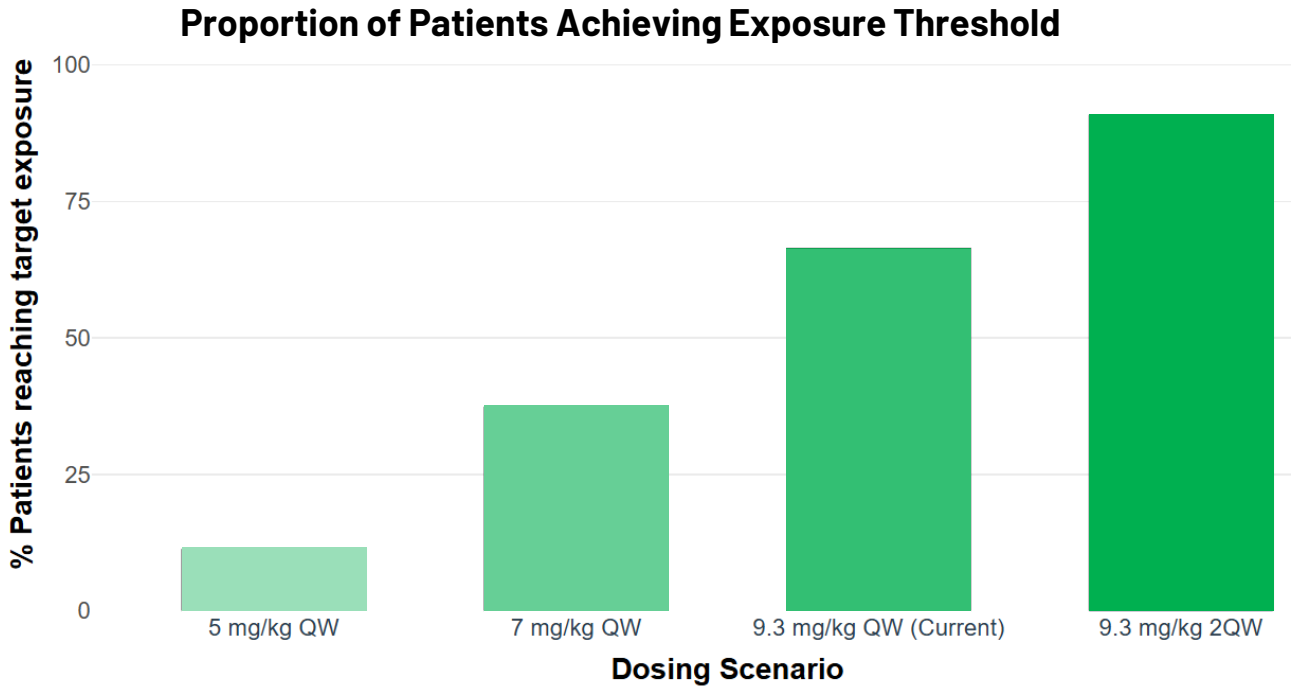
Increased frequency of dosing could further improve OS benefit

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Oral Tablet Provides Expedited Pathway to High Dose Exposure

Increased frequency of dosing could further improve OS benefit

- Analysis demonstrates 9.3 mpk QW as Minimally Effective Dose (MED).
- ~85% of elraglusib 2QW patients vs ~60% QW patients achieve target exposure
- Oral dosing in models suggest 210 ng/ml target achievable with ~1 – 2 (250 mg) tablets per day in adults.



Oral elraglusib daily dosing may achieve exposures to further improve OS

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Elraglusib Tablet to Expand Portfolio of Blockbuster Indications

- Oral tablets could replace and improve treatment vs IV infusion
- Increase overall exposure with daily dosing
- IND clearance received from FDA to initiate Ph1/2 study



Potential first clinical candidate indications include:

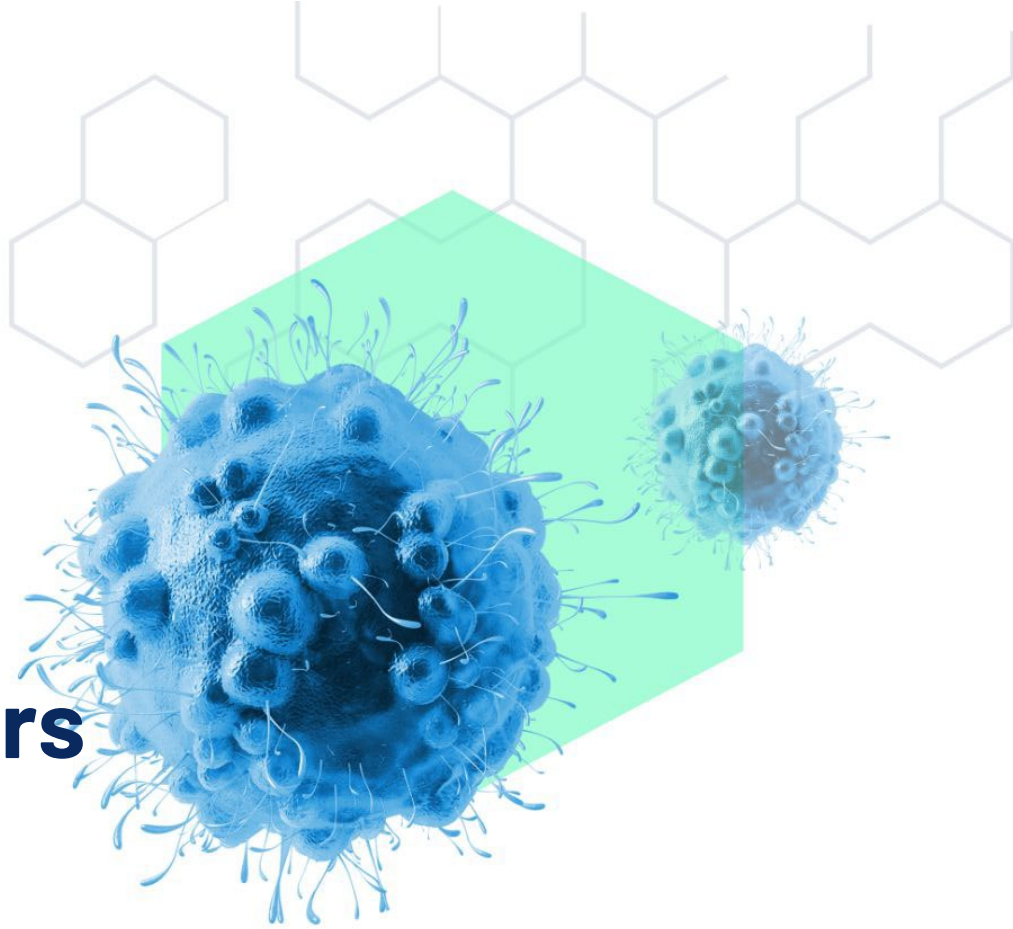
Metastatic Pancreatic Cancer	CPI Refractory, Metastatic Melanoma	Metastatic Colorectal Cancer	Refractory Metastatic NSCLC
TAM: ~$4 billion	TAM: ~$10 billion	TAM: ~$12 billion	TAM: ~$27 billion

Potential to be ready for pivotal studies in 2H 2027

PDAC: https://www.fortunebusinessinsights.com/pancreatic-cancer-treatment-market-101989
Melanoma: https://www.thebusinessresearchcompany.com/report/metastatic-melanoma-therapeutics-global-market-report

CRC: https://www.gminsights.com/industry-analysis/colorectal-cancer-therapeutics-market
NSCLC: https://www.databridgemarketresearch.com/reports/global-non-small-cell-lung-cancer-market

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Elraglusib in Rare Pediatric Cancers

EWS and NBL: Rare Diseases with High Unmet Need

High Unmet Need

Ewing Sarcoma (EWS):

5-year survival:

- 10-15% for relapsed/refractory or after recurrence [1]
- 7% for patients with disease-free interval <2 years[2]

Neuroblastoma (NBL):

- Leading cause of cancer mortality in peds < 5 yr
- Survival rates ~ 50%[3]

No uniformly effective SOC for relapsed/refractory Ewing Sarcoma or advanced NBL

Strategic and Commercial Potential

- Accelerated pathways to registration
- Combined NBL + EWS treatment market size: $700M - $1B[4,5]
  - Significant market upside with EWS maintenance therapy development
- Priority Review Voucher eligible for either NBL or EWS

1. Stahl M, Ranft A, Paulussen M, et al.: Risk of recurrence and survival after relapse in patients with Ewing sarcoma. Pediatr Blood Cancer 57(4): 549-53, 2011
2. Van Mater and Wagner. Onco Targets Ther. 2019;12:2279-2288.
3. Bagatell R, DuBois SG, Naranjo A, et al. Children's Oncology Group's 2023 blueprint for research: Neuroblastoma. Pediatr Blood Cancer 2023;70 Suppl 6(Suppl 6):e30572. DOI: 10.1002/pbc.30572.
4 Ewing Sarcoma Treatment Market (2025-2035 outlook); IMARC Group. https://www.researchnester.com/reports/ewing-sarcoma-treatment-market/6962?utm
5. Neuroblastoma Market Size, Epidemiology, In-Market Drugs Sales, Pipeline Therapies, and Regional Outlook 2025-2035. IMARC Group. https://www.imarcgroup.com/neuroblastoma-market

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Durable Responses in Heavily Pre-treated Ewing Sarcoma Patients

Phase 1 Solid Tumor Study (n=40)

9 elra monotherapy, 12 elra + irinotecan, 19 elra + cyclophosphamide/topotecan

Elraglusib + cyclo/topo patients

- 10/19 patients responded/achieved disease control
- 12 EWS, 6 R/R patients responded/achieved disease control
- 3 objective responses (2 CRs, 1 PR)

CMR

- 18-year-old EWS patient
- Refractory to 6 prior lines of tx
- CMR with partial response; 60% reduction in lung target lesion
- No evidence of recurrence after >2 years

CR at First Scan

- 20-year-old EWS patient
- Refractory to 4 prior lines of tx
- CR by CT, CMR by PET
- No evidence of disease >3 years after termination of treatment

EWS: Ewing Sarcoma; CMR: Complete Metabolic Response; CR: Complete Response; PR: Partial Response.

Clinical Data in NBL Support Participation in BEACON2 Trial

Background

~38% patients with advanced relapsed/refractory disease responded with stable disease or better in Phase 1 clinical study of elraglusib + chemotherapy

Complete Response

- Last line NBL patient with unfavorable molecular profile
- Achieved CR within 9 cycles of treatment
- Completed 12 cycles of treatment

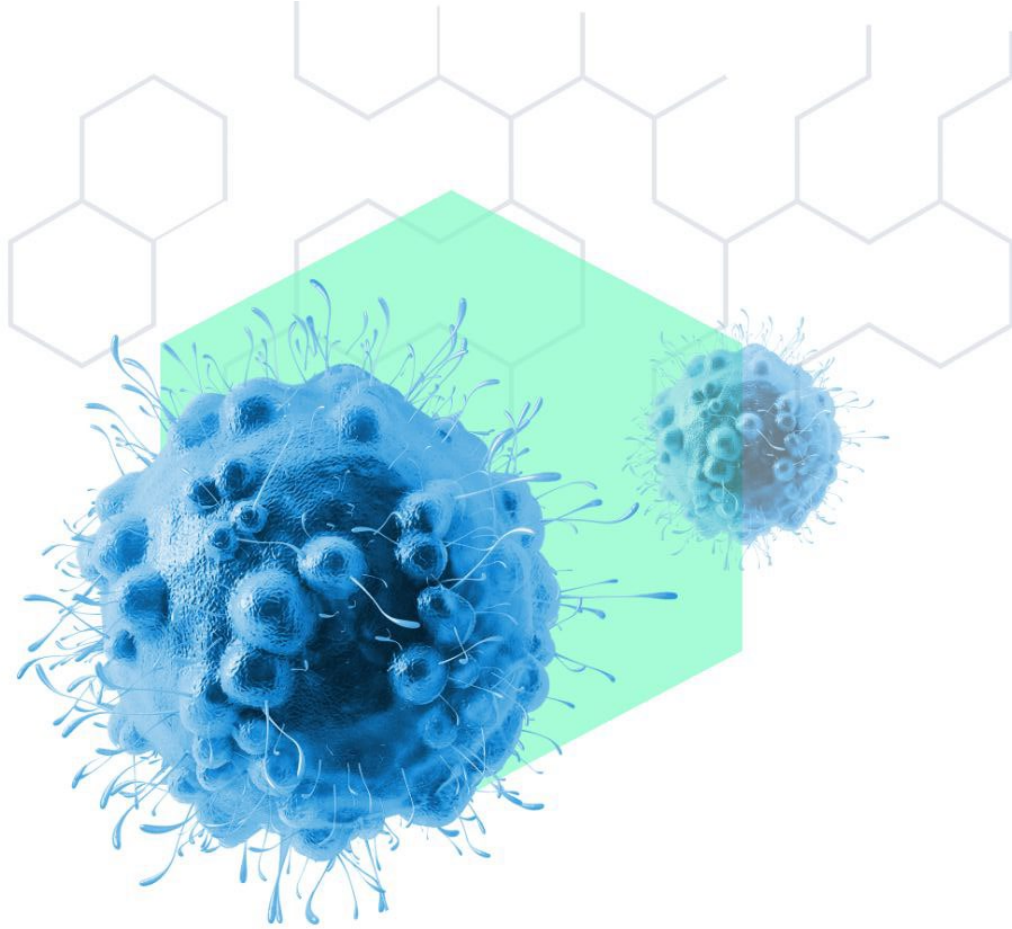
Advancing pediatric indications towards registration study in R/R neuroblastoma

- Agreement to participate in BEACON2 clinical trial with Cancer Research UK Clinical Trials Unit / University of Birmingham signed in June 2026

- Planned 2-stage clinical trial design:
  Stage 1: Up to 20 patient run-in; elra + SOC (dinutuximab beta + chemotherapy)
  Stage 2: RCT of approximately 75 patients: elra + SOC vs SOC alone
  FPFD: Target 1H2027

dinutuximab beta: 14G2A, an anti-GD2 antibody

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Nasdaq Global Market: ACTU