ACTUATE THERAPEUTICS

Corporate Overview

January 2026

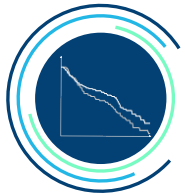
Forward-Looking Statements

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 second 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 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 the second 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. 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 13, 2025, our Quarterly Reports on Form 10-Q, and other filings with the SEC. This presentation also contain 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.

Company Highlights

Class-Leading GSK-3β Inhibitor

- Highly specific small molecule kinase-inhibitor with excellent drug-like properties
- >500 patients treated to date



Compelling Survival Data in mPDAC

- Statistically significant improvements in overall survival (OS) in global Phase 2 trial in 1L mPDAC
  - 40% improvement in mOS
  - 100% improvement in 1-year survival
  - Hazard Ratio: 0.62

Broad Therapeutic Potential

- Clinical activity (CRs/PRs and extended disease control) in multiple other oncology indications, including Ewing Sarcoma, Melanoma, mCRC, and NSCLC
  - Phase 2 pivotal trial in planning for refractory Ewing Sarcoma patients

Oral Dose Tablet Successfully Developed

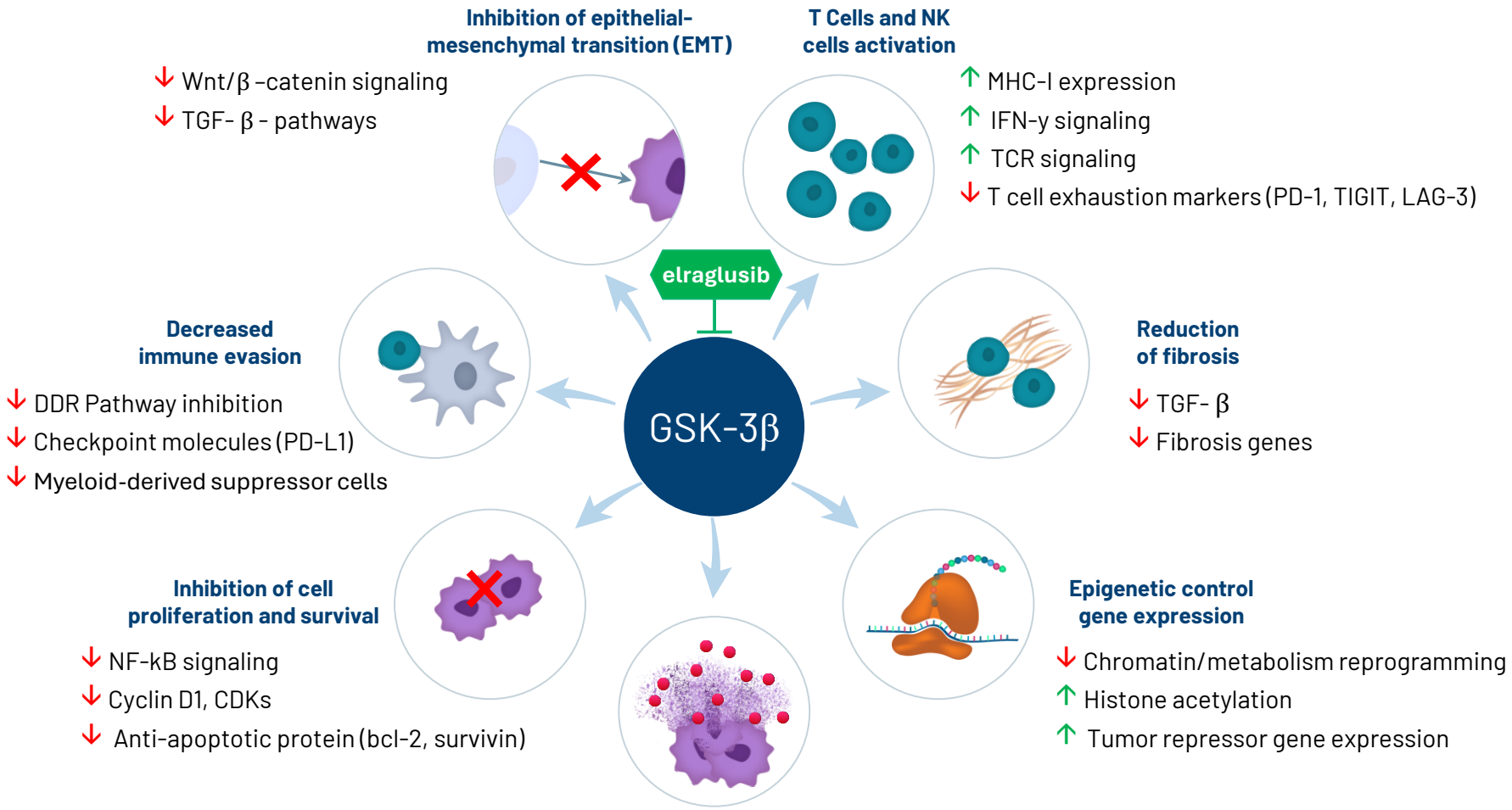
- Oral liquid successfully evaluated in Healthy Volunteer Phase 1 study
- Solid dose achieved >95% bioavailability in preclinical studies
  - Phase 1/2 study planned in advanced cancer patients including refractory metastatic melanoma

Extended IP Protection

- Broad composition of matter IP protection until 2038 before PTE
- Orphan Drug Designations for pancreatic and other cancer types
- Fast Track Designation for pancreatic cancer
- Rare Pediatric Disease Designations for Ewing Sarcoma and neuroblastoma

GSK-3β: Glycogen Synthase Kinase 3 beta; mPDAC: Metastatic Pancreatic Ductal Adenocarcinoma Cancer; mOS: Median Overall Survival; CR: Complete Response; PR: Partial Response; mCRC: Metastatic Colorectal Cancer; NSCLC: Non-Small Cell Lung Cancer; PTE: Patent Term Extension

Elraglusib: Multimodal MOA Supported by Clinical Data



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Strategic Pipeline Growth for IV and Oral Elraglusib

Pancreatic (PDAC)	Program	Formulation	Phase 1	Phase 2	Phase 3	Milestones
1L metastatic with GnP	Actuate-1801 Part 3B	IV			*In Planning***	- Updated Phase 2 data presented at ASCO GI in January 2026 - FDA meeting request: clarity for registration requirements: 1H 2026* - EMA meeting request: clarity for potential Conditional Approval/ Phase 3 design requirements for full registration: 1H 2026*
1L metastatic with FOLFIRINOX	Investigator Initiated Trial	IV			MASSACHUSETTS GENERAL HOSPITAL	- Study closed to enrollment - Data Readout: Mid 2026
Advanced pancreatic with mFOLFIRINOX + retifanlimab	Investigator Initiated Trial	IV		Incyte	UPMC HILLMAN CANCER CENTER	- Enrollment open
Pediatric Cancers						
Advanced Refractory Cancers - Ewing Sarcoma (EWS) Cohort Only	Actuate-1902	IV		*In Planning***		- Phase 1 final data: Q1 2026 - Initiate Phase 2 trial: 2H 2026
Neuroblastoma	TBD	IV		*In Planning***		- Study initiation: 2H 2026
R/R Melanoma and Other Cancers						
Dose escalation in advanced, refractory solid cancers	Actuate-2601	Oral tablet	*In Planning***			- Study initiation: 1H 2026
Monotherapy - 2L/3L relapsed, CPI refractory metastatic melanoma and other cancers	TBD	Oral tablet		*In Planning***		- Study initiation: 1H 2027

* The Company plans to request meetings with the FDA and EMA in the first half of 2026 to align on requirements for product registrations in the U.S. and EU
**Contingent upon future funding

GnP: gemcitabine/nab-paclitaxel; R/R: Relapsed/Refractory; CPI: checkpoint inhibitor

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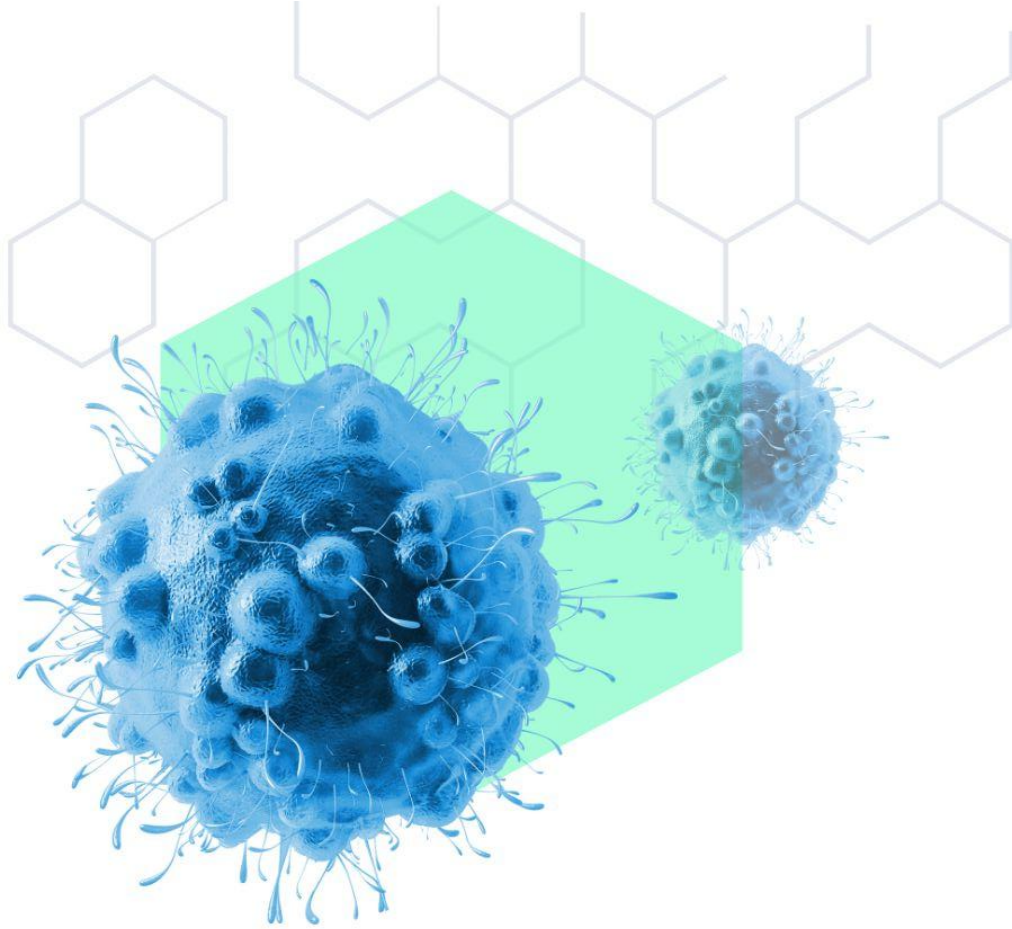

Elraglusib in PDAC

mPDAC Represents a High Unmet Need With Significant Commercial Potential

Market Size

Metastatic pancreatic cancer is highly aggressive and accounts for approximately 80-85% of all pancreatic cancer diagnoses. Projected market growth to >$5 billion by 2030[1]

Survival Rate and Economic Burden

The prognosis remains poor with a 5-year survival rate of less than 10%[2] and a high economic burden with annual treatment costs exceeding $100,000 per patient[3]

Current Treatment

FOLFIRINOX and GnP are standard but offer limited survival benefits. Elraglusib is currently in clinical trials with FOLFIRINOX and GnP

Elraglusib Opportunity

Novel GSK-3β inhibitor that targets multiple molecular pathways in cancer cells but also impacts the TME and immune response

1. Pancreatic Cancer Treatment Market Size Report, 2030, https://www.grandviewresearch.com/industry-analysis/pancreatic-cancer-treatment-market
2. Hu JX, Zhao CF, Chen WB, Liu QC, Li QW, Lin YY, Gao. World J Gastroenterol. 2021 Jul 21;27(27):4298-4321. doi: 10.3748/wjg.v27.i27.4298. PMID: 34366606; PMCID: PMC8316912
3. Soefje SA. Managing the economic impact of advanced pancreatic cancer. Am J Manag Care. 2019 Jan;25(1 Suppl):S11-S16. PMID: 30681820

TME: Tumor microevironment

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PDAC: A Disease with Urgent Unmet Needs

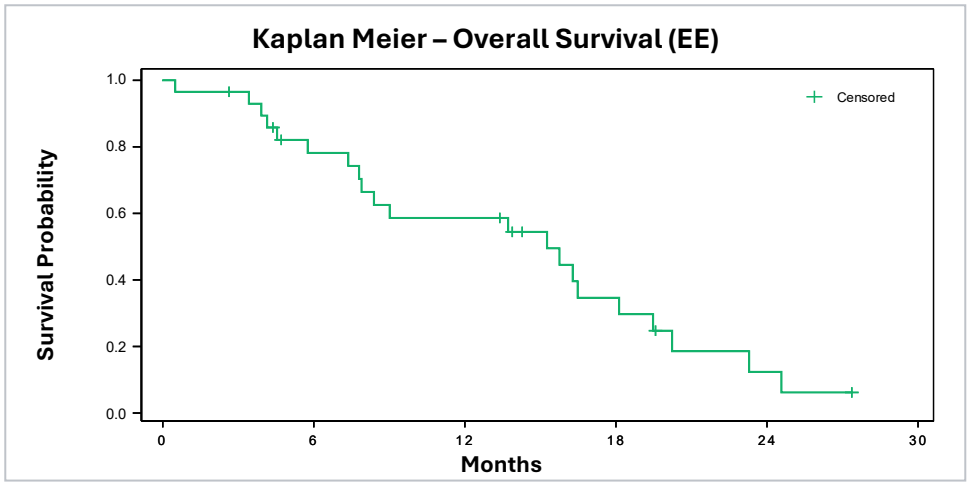
- Most patients with PDAC present with advanced or metastatic disease with poor survival
- Median survival remains <1 year, with real world data for mOS ranging from 6-9 months
- Apart from PARP inhibitors as maintenance therapy in a subset of patients with gBRAC1/2 metastatic PDAC patients, there is an urgent need for more novel therapeutic targets for PDAC patients

Study	Comparison	mOS (months)	1 year OS (%)
MPACT (Von Hoff et al. 2013)	GnP vs Gem	**8.5** vs 6.7 **HR 0.72**; p<0.001	35.0 vs 22.0
NAPOLI-3 (Wainberg et al., 2024)	GnP vs NALIRIFOX	**9.2** vs 11.1 **HR 0.83**; p<0.036	39.5 vs 45.6
Cockrum et al. (2025)	GnP and FFX Real-world review	**GnP 6.9** (3.6-9.8) FFX 9.2 (4.7-11.4)	N/A

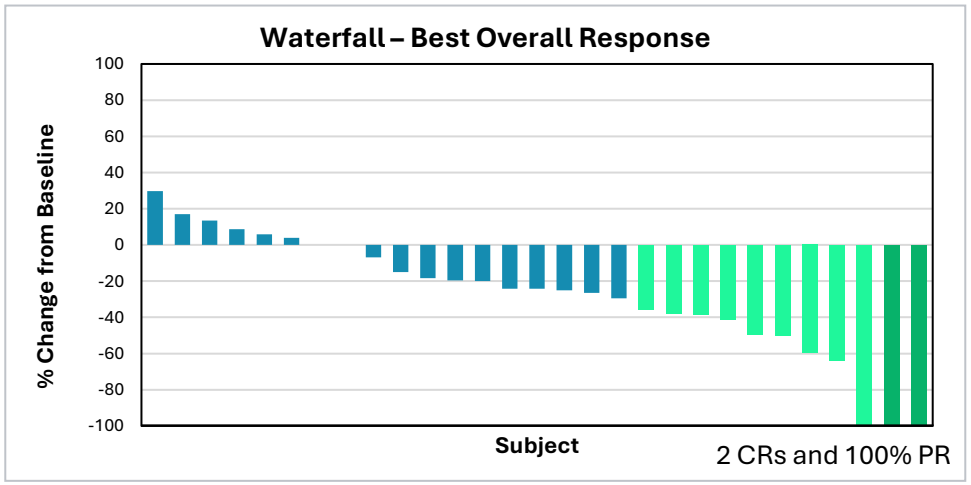
Phase 2 – Clinical Activity with Extended Median Overall Survival

1801 Part 3A in mPDAC

- Simon Two-Stage trial design - Stage 1
- Evaluate the combination of elraglusib and GnP
  - mOS of 15.3 (EE population)
  - 2 CRs confirmed
  - 9 PRs confirmed
  - DCR: 52%, ORR: 38%
  - Met Simon stage 1 threshold of DCR>50%
- 42 total patients enrolled (ITT)*



Subjects	29
Event	21 (72%)
Censored	8 (28%)
Median Survival	15.26
95% CL	(7.895, 18.13)



The encouraging preliminary efficacy prompted a pivot to a randomized Phase 2 trial

Historical Control: Wainberg, Zev A et al., The Lancet, Volume 402, Issue 10409, 1272 – 1281; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4631139/
*13 subjects had no response data entered
EE: efficacy evaluable; DCR: disease control rate; ORR: overall response rate; ITT: intent to treat

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1801-Part 3B: Phase 2 RCT in First-Line Metastatic PDAC

Inclusion Criteria

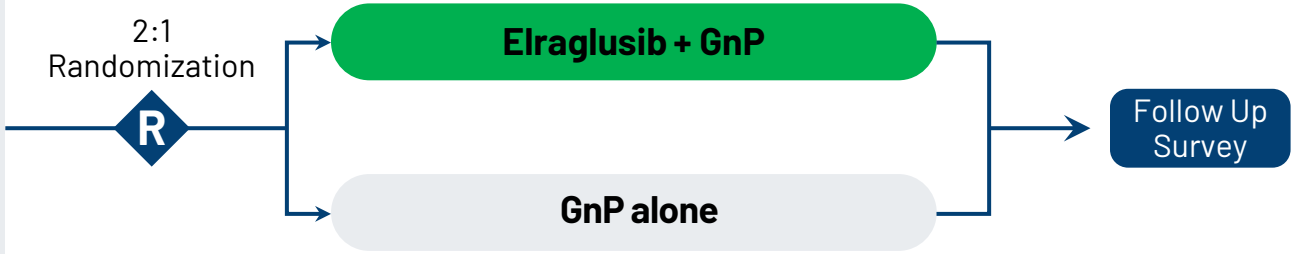
≥ 18 yrs old with metastatic pancreatic adenocarcinoma

Participants must have measurable disease as defined by RECIST1.1

No prior therapy

Total enrollment: 286

Treatment



Endpoints

Primary endpoints:
1 year OS/mOS

Secondary endpoints:
ORR, DOR, PFS

Sample size based on projected increase in 1 year survival from 35% in GnP to 55% in elraglusib/GnP with α=0.05; 80% power

60 Global Sites

US 36

EU 18

Canada 6

FPD: August 2021
Enrollment Completion: January 2024
Topline Data: Reported at ASCO 2025
Updated Data: Reported at ASCO GI 2026

RCT: randomized, controlled trial; DOR: duration of response; PFS: progression-free survival, FPD: First Patient Dosed

Study 1801 Part 3B RCT Patient Demographics

Demographics	GnP (n=78)	Elraglusib + GnP (n=155)
Sex		
Female	35 (44.9%)	75 (48.4%)
Male	43 (55.1%)	80 (51.6%)
Age (years)		
n (%)	78 (100%)	155 (100%)
Mean (S.D.)	66.2 (9.9)	65.1 (9.1)
Median	68.0	65.0
Min, Max	42.0, 85.0	42.0, 86.0
Race		
Asian	2 (2.6%)	5 (3.2%)
Black or African American	6 (7.7%)	7 (4.5%)
White	65 (83.3%)	128 (82.6%)
Multiracial	0	1 (0.6%)
Unknown/Not Reported	5 (6.4%)	14 (9.0%)
Ethnicity		
Hispanic or Latino	0	8 (5.2%)
Not Hispanic or Latino	77 (98.7%)	141 (91.0%)
Unknown/Not Reported	1 (1.3%)	6 (3.9%)
Body Surface Area (BSA) (m2)		
n (%)	78 (100%)	155 (100%)
Mean (S.D.)	1.83 (0.26)	1.83 (0.23)
Median	1.82	1.81
Min, Max	1.31, 2.77	1.30, 2.62

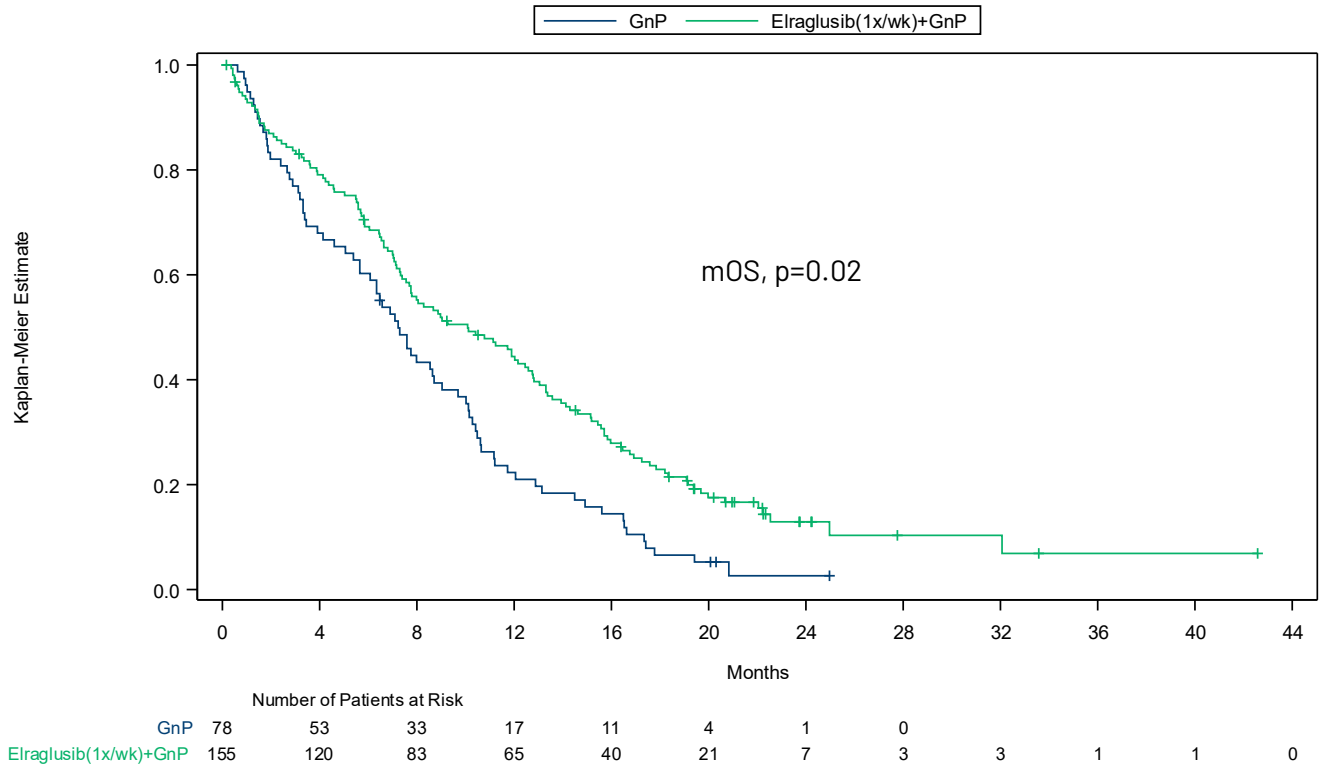
Demographics	GnP (n=78)	Elraglusib + GnP (n=155)
Eastern Cooperative Oncology Group Performance Status		
0	31 (39.7%)	64 (41.3%)
1	45 (57.7%)	89 (57.4%)
2	2 (2.6%)	2 (1.3%)
Disease Status		
Metastatic at Initial Diagnosis	60 (76.9%)	108 (69.7%)
Metastatic at Study Entry	77 (98.7%)	154 (99.4%)
Site of Metastases		
Pancreas	68 (87.2%)	123 (79.4%)
Liver	61 (78.2%)	112 (72.3%)
Lymph Node	27 (34.6%)	69 (44.5%)
Lung	26 (33.3%)	59 (38.1%)

Predefined Safety Population
Draft unaudited data as of Nov 22, 2025
The final data and results may change as the study continues through completion

Study 1801 Part 3B Meets Primary Endpoint of Improved Survival

Doubling of 1 year OS and 38% Reduction in Risk of Death vs GnP

	GnP (n=78)	Elraglusib/GnP (n=155)
Primary Endpoint: mOS (months) HR=0.62; log-rank p=0.02	**7.2**	**10.1**
12-month OS (%) p=0.0004	**22.3**	**44.4**
Events (% events)	**74 (94.9%)**	**128 (82.6%)**
18-month OS (%)	**6.6**	**22.9**
24-month OS (%)	**2.6**	**12.9**
mPFS (months) HR=0.83; P=NS	**5.1**	**5.6**
Events (% events)	**77 (98.7%)**	**143 (92.3%)**
DCR	**29.5**	**39.4**
ORR n (%)	**17 (21.8%)**	**44 (28.4%)**



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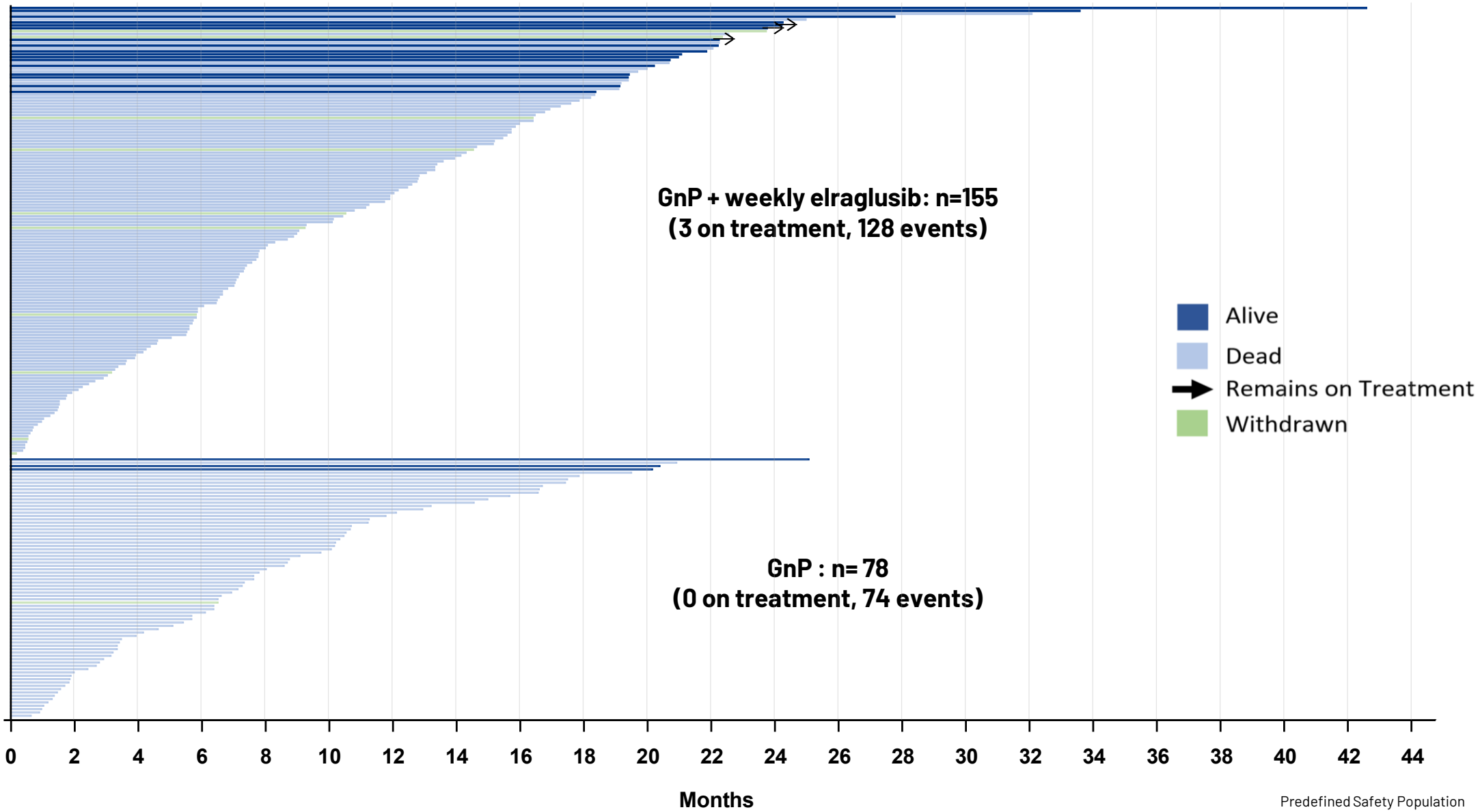
Durable and Sustained Responses Observed Relative to GnP



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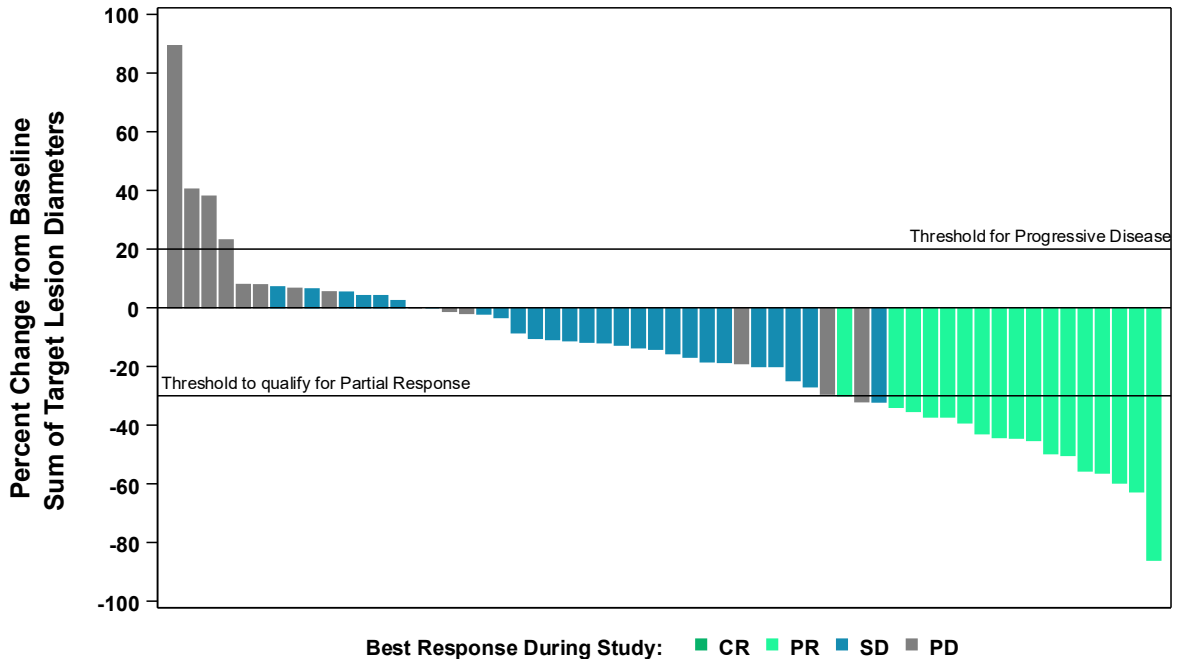
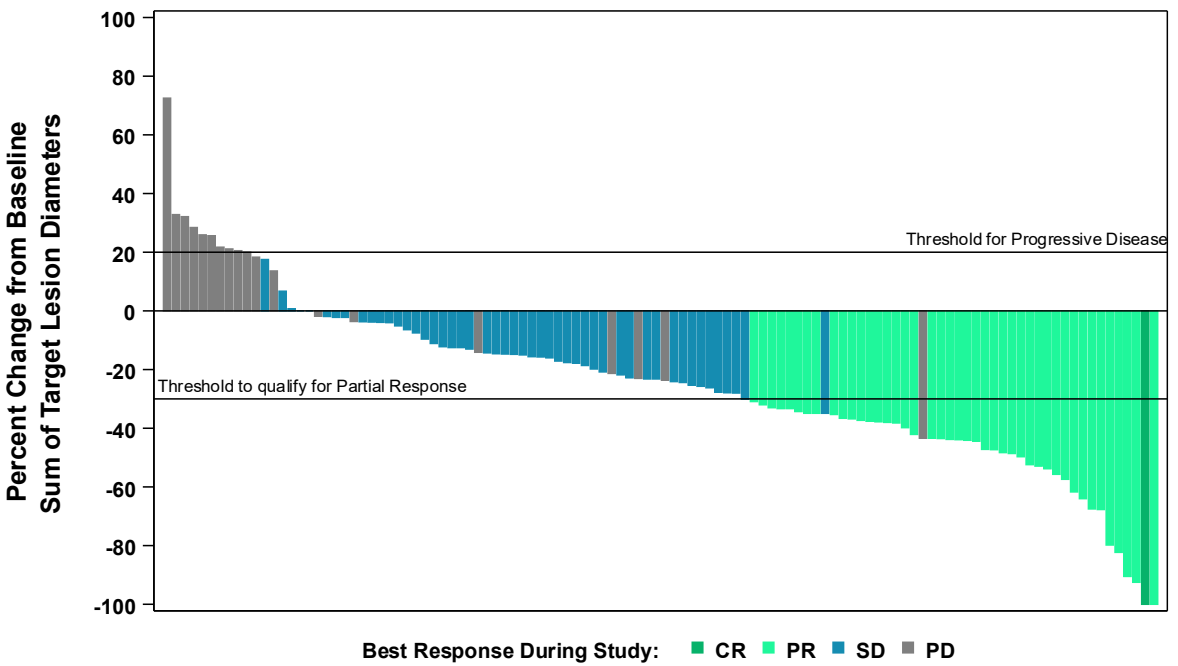
Elraglusib Arm Demonstrated Strong Improvement in ORR and Depth of Response vs. GnP

GnP Best Overall Response



Elraglusib + GnP Best Overall Response



- One patient had a partial response on treatment, then was referred for a Whipple procedure and subsequently came off treatment
- One patient had a partial response on treatment, then was referred for a Whipple procedure and then reported a CR with 100% of the primary tumor removed

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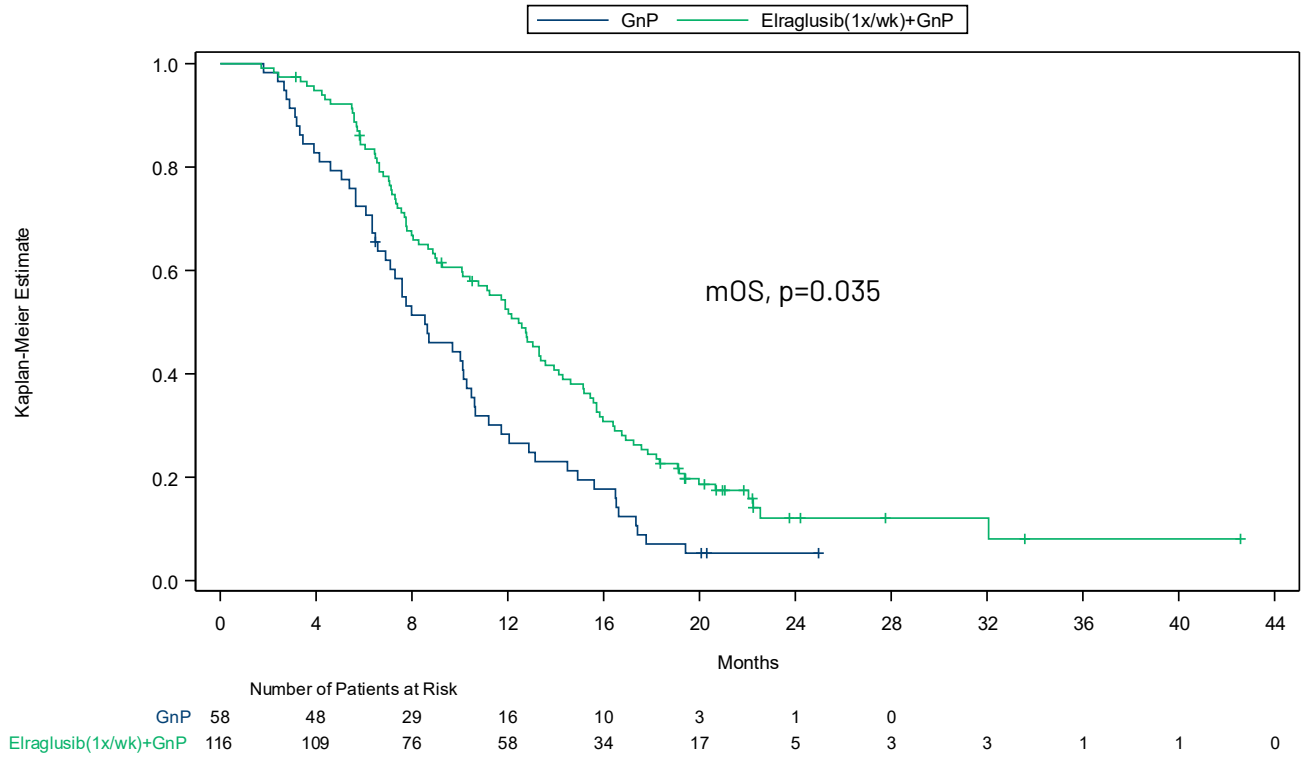
Subgroup of Patients Treated for One Cycle (4 weeks) - Significant Benefit in OS

Near Doubling of 1 year OS and 42% Reduction in Risk of Death vs GnP

	GnP (n=58)	Elraglusib/GnP (n=116)
Primary Endpoint: mOS (months) HR=0.58; log-rank p=0.035	**8.5**	**12.5**
12-month OS (%)	**28.3**	**52.5**
Events (% events)	**54 (93.1%)**	**96 (82.8%)**
18-month OS (%)	**7.1**	**24.4**
24-month OS (%)	**5.3**	**12.1**
mPFS (months) HR=0.75; P=NS	**5.6**	**6.9**
Events (% events)	**57 (98.3%)**	**110 (94.8%)**
DCR	**44.8%**	**54.3%**
ORR n (%)	**17 (29.3%)**	**44 (37.9%)**



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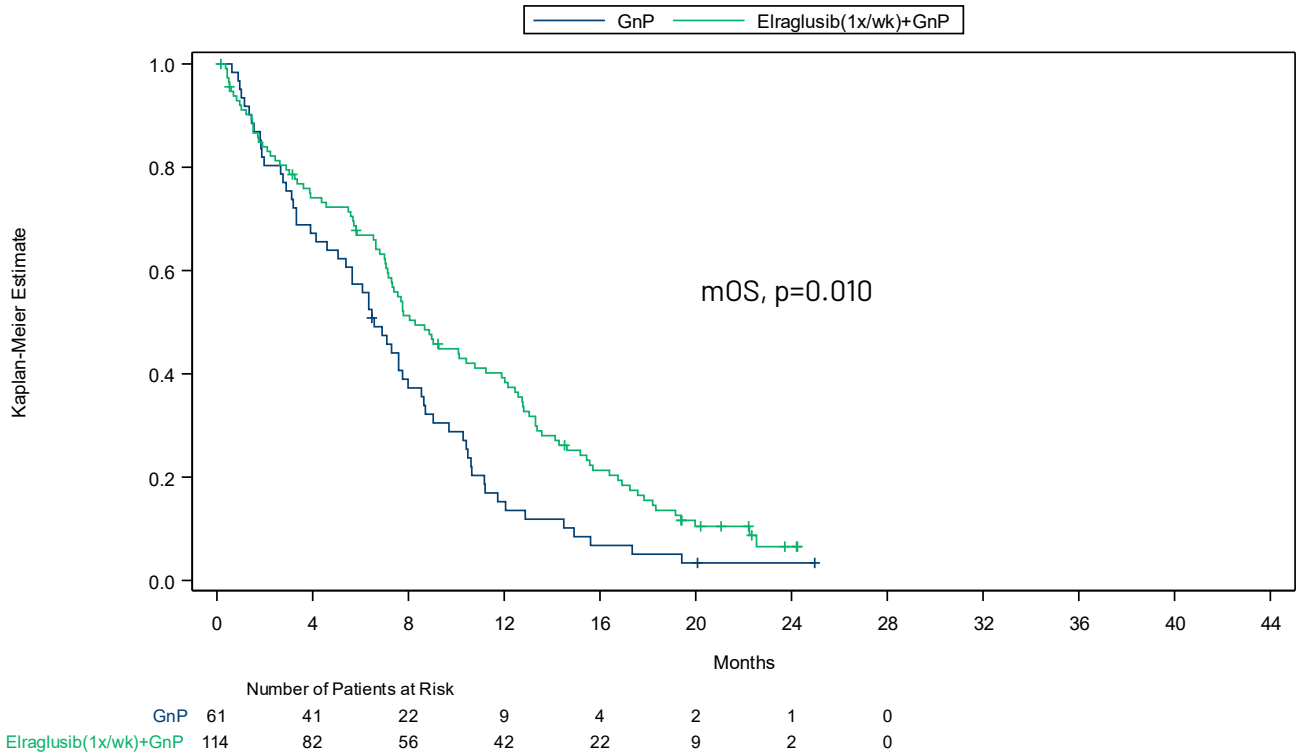
Patients with Liver Metastases – Significant Benefit in mOS and mPFS

2.5X Increase in 1 year OS and a 35% Reduction in Risk of Death vs GNP

	GnP (n=61)	Elraglusib/GnP (n=114)
Primary Endpoint: mOS (months) HR=0.65; log-rank p=0.010	**6.6**	**8.3**
12-month OS (%) p=0.0003*	**15.2**	**39.2**
Events (% events)	**58 (95.1%)**	**99 (86.8%)**
18-month OS (%)	**5.1**	**15.5**
24-month OS (%)	**3.4**	**6.5**
mPFS (months) HR=0.73; P=0.031	**3.9**	**4.8**
Events (% events)	**60 (98.4%)**	**107 (93.9%)**
DCR	**23.0%**	**36.0%**
ORR n (%)	**12 (19.7%)**	**33 (28.9%)**



*z-test

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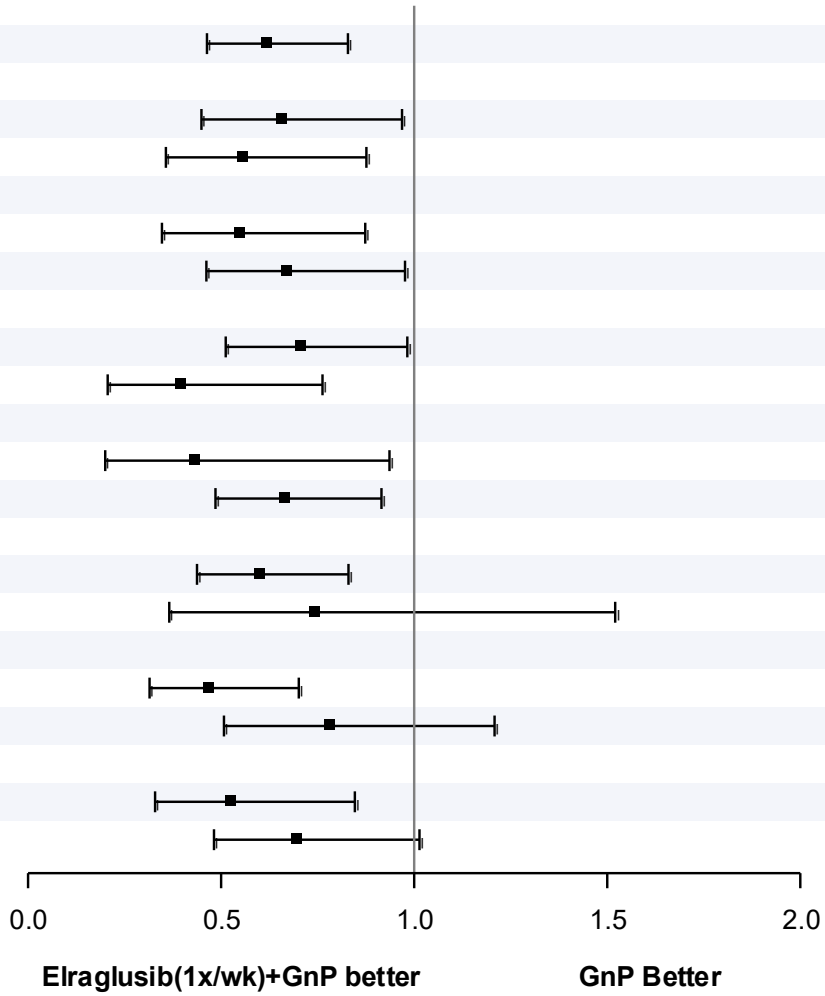
Clinical Benefit Observed For Elraglusib + GnP Across All Subgroups Evaluated

Subgroup	GnP, event/patients	Elraglusib(1x/wk)+GnP, event/patients	HR (95% CI)
Overall	74/78	128/155	0.62 (0.46, 0.83)
Liver Mets at Baseline			
Yes	41/44	76/87	0.66 (0.45, 0.97)
No	33/34	52/68	0.56 (0.36, 0.88)
ECOG at Baseline			
0	30/31	52/64	0.55 (0.35, 0.87)
>= 1	44/47	76/91	0.67 (0.46, 0.98)
Region			
North America	58/60	104/117	0.71 (0.51, 0.98)
Rest of World	16/18	24/38	0.40 (0.21, 0.76)
CA 19-9 at Baseline			
< 37 U/mL	11/12	18/23	0.43 (0.20, 0.94)
>= 37 U/mL	62/65	107/129	0.67 (0.49, 0.92)
Race			
White	61/65	105/128	0.60 (0.44, 0.83)
Non-White	13/13	23/27	0.75 (0.37, 1.52)
Sex			
Male	42/43	70/80	0.47 (0.31, 0.70)
Female	32/35	58/75	0.78 (0.51, 1.21)
Age			
< 65 years	27/29	54/70	0.53 (0.33, 0.85)
>= 65 years	47/49	74/85	0.70 (0.48, 1.01)



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Subsequent Anti-Cancer Therapy Is Balanced Between Both Arms

	GnP (N = 78)	Elraglusib/GnP (N = 155)
Subsequent anti-cancer therapy, n (%)	30 (38%)	79 (51%)
Systemic anti-cancer therapy, n (%)	29 (37%)	79 (51%)
FOLFIRINOX	10 (13%)	18 (12%)
FOLFOX	4 (5%)	3 (2%)
FOLFOXIRI	2 (3%)	6 (4%)
FOLFIRI	3 (4%)	7 (5%)
GnP	0 (0%)	10 (6%)
5-FU/liposomal irinotecan/LV	2 (3%)	6 (4%)
Other*	8 (10%)	29 (19%)
Radiotherapy, n (%)	1 (1%)**	0 (0%)

*Other primarily represents various other chemotherapy regimens
**Patient also received anti-neoplastic therapy with radiation

LV: leucovorin

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Safety Profile of Elraglusib in Combination with GnP

Actuate 1801 Part 3B (ongoing)

TEAEs of Any Grade Reported in ≥20% of Patients Treated with elraglusib

Patients, n (%)				
Adverse event	Elraglusib + GnP (N=155)		GnP (N=78)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TEAE	155 (100)	140 (90.3)	77 (98.7)	62 (79.5)
Serious TEAE	87 (56.1)	82 (52.9)	44 (56.4)	43 (55.1)
Leading to Stoppage of Any Study Drug	43 (27.7)	26 (16.8)	22 (28.2)	17 (21.8)
Resulting in death	19 (12.3)	19 (12.3)	13 (16.7)	13 (16.7)
TEAEs of any Grade in ≥20% of Patients				
Visual Impairment	106 (68.4)	1 (0.6)	7 (9.0)	0
Fatigue	97 (62.6)	26 (16.8)	40 (51.3)	4 (5.1)
Neutropenia*	97 (62.6)	83 (53.6)	32 (41.0)	25 (32.1)
Diarrhea	92 (59.4)	15 (9.7)	38 (48.7)	6 (7.7)
Nausea	90 (58.1)	11 (7.1)	38 (48.7)	4 (5.1)
Alopecia	71 (45.8)	0	27 (34.6)	0
Anemia**	70 (45.2)	39 (25.2)	37 (47.4)	26 (33.3)
Decreased appetite	66 (42.6)	9 (5.8)	19 (24.4)	6 (6.7)
Thrombocytopenia***	58 (37.4)	17 (11.0)	25 (32.1)	6 (7.7)
Vomiting	59 (38.1)	5 (3.2)	30 (38.5)	1 (1.3)
Edema peripheral	57 (38.1)	3 (1.9)	26 (33.3)	0
Constipation	49 (31.6)	3 (1.9)	24 (30.8)	1 (1.3)
Pyrexia	44 (28.4)	2 (1.3)	20 (25.6)	1 (1.3)
Abdominal pain	46 (29.7)	14 (9.0)	16 (20.5)	2 (2.6)
Weight decreased	46 (29.7)	5 (3.2)	17 (21.8)	3 (3.8)
Peripheral sensory neuropathy	40 (25.8)	4 (2.6)	18 (23.1)	0
Hypokalemia	35 (22.6)	8 (5.2)	24 (30.8)	4 (5.1)
Asthenia	33 (21.3)	9 (5.8)	19 (24.4)	5 (6.4)
Dysgeusia	32 (20.6)	0	16 (20.5)	0
Leukopenia	31 (20.0)	22 (14.2)	12 (15.4)	9 (11.5)
Neuropathy peripheral	21 (13.5)	1 (0.6)	18 (23.1)	0

TEAE: Treatment-Emergent Adverse Event; SAE: Serious Adverse Event

Key Takeaways

- Overall rate of a TEAE and/or an SAE observed were similar in the elraglusib + GnP-treated patients as compared to GnP-treated patients
- Treatment discontinuation due to TEAEs were similar across the treatment groups
- Visual impairment and fatigue were major TEAEs attributed to elraglusib as a single agent in 1801 Part 1 and were mild to moderate in the 1801 3B [1]
  - Transient visual impairment described as transient alterations in color and skin tones under fluorescent light
  - No permanent changes to eye structure or vision

[1] Carneiro et al. Clin Cancer Res 2024 Feb 1;30(3):522-531

*Includes Preferred Terms (PT) neutropenia and neutrophil count decreased

** Includes PT anemia and hemoglobin decreased

***Includes PT thrombocytopenia and platelet count decreased

Predefined Safety Population

Draft unaudited data as of Nov 22, 2025

The final data and results may change as the study continues through completion

mPDAC Future Development and Registration Plans

- Regulatory discussions planned with FDA and EMA on registration pathway
- Registration trial design to be harmonized to support approval in both the US and EU

Inclusion Criteria

≥ 18 yrs old with mPDAC

Participants must have measurable disease as defined by RECIST1.1

No prior therapy

Total planned enrollment: 600

Treatment

Endpoints

Primary endpoints: mOS

Secondary endpoints:
ORR, DOR, PFS

Estimated sample size based on α=0.05 and 90% power

~120 Global Sites

Study Initiation: 2H 2026*

US | EU | UK | Canada | Asia-Pac

*Contingent upon future funding

ACTUATE THERAPEUTICS

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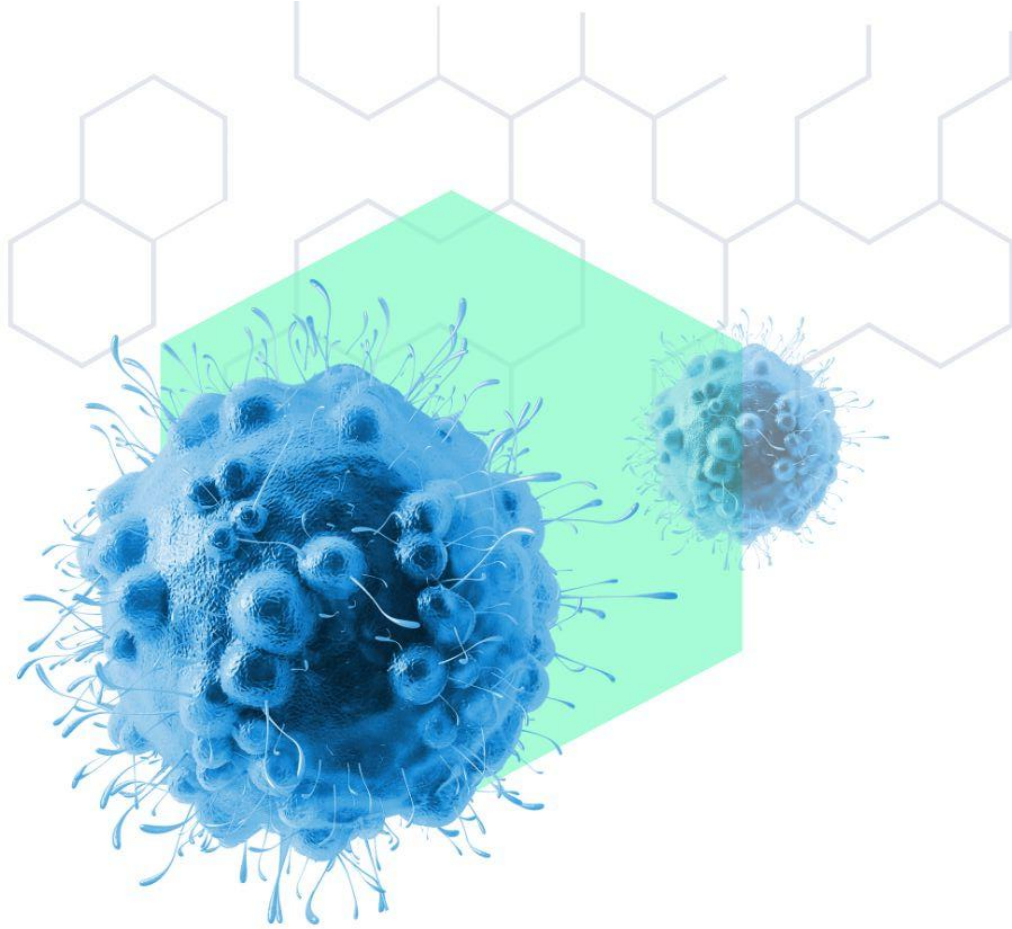


Elraglusib in Pediatric Cancers

Elraglusib Shows Promise in Difficult to Treat Pediatric Cancers

GSK-3β represents a credentialed target in pediatric cancers

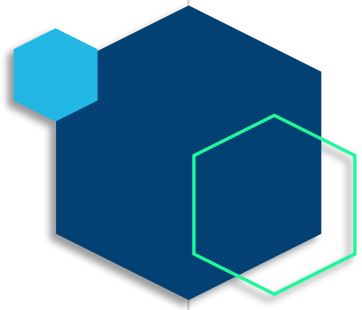
- Ewing's (EWS) and related small round cell sarcomas with EWSR1 translocations/fusions
- Neuroblastoma
- Primary bone cancer: osteosarcoma
- Ependymoma
- CNS tumors: Medulloblastoma

GSK-3β mediates resistance in pediatric tumors

- GSK-3 inhibitors have been shown to increase expression of NK cell activation antigens in Ewing sarcoma, an immunologically "cold" tumor
- Elraglusib may activate immune cell-mediated killing of Ewing sarcoma
- Based on MOA, elraglusib may also synergize with PI3K and mTOR inhibitors

Key Elraglusib Pediatric Regulatory Designations:

- US Orphan Drug Designations
  - Pediatric neuroblastoma
  - Soft tissue sarcomas (STS)
- US FDA Rare Pediatric Disease Designations
  - Pediatric neuroblastoma
  - Ewing sarcoma (EWS)
- EU Orphan Medicinal Product Designation (OMPD)
  - Soft Tissue Sarcoma



PI3K: Phosphoinositide 3-kinase (e.g. idelalisib); mTOR: mammalian target of rapamycin (e.g. sirolimus)

Phase 1 Elraglusib Trial Demonstrated Clinical Responses in Pediatric Cancers

1902 Trial Update

Clinical responses and disease control observed in 15 of 40 patients with difficult-to-treat refractory pediatric cancers

- 10 of 19 patients treated with elraglusib plus cyclophosphamide/topotecan showed clinical responses and disease control

1902 – Phase 1 (Enrollment Closed)

3-Arm Dose Escalation Study

- Elraglusib monotherapy (n=9)
- Elraglusib + irinotecan (n=12)
- Elraglusib + cyclo/topo (n=19)

Indications Treated:

- EWS
- Neuroblastoma
- CNS cancers
- Osteosarcoma
- Pediatric Lymphoma
- Pediatric Meningioma

EWS

- Two CMRs observed in patients with relapsed/refractory metastatic EWS and
  - One patient had CR at their 1st scan as BOR
    - Stopped all treatments after four months and continued to be in complete remission with no evidence of disease >3 years after termination of treatment
  - One patient had BOR of CMR (no detectable lesions by FDG-PET)
    - Continues on monotherapy with no recurrence after >2 years

Neuroblastoma

- One CR observed in a patient with r/r metastatic neuroblastoma
- One patient achieved a 35% reduction in tumor burden between baseline and week 9 (Cycle 3)

Six elraglusib plus cyclophosphamide/topotecan patients (osteosarcoma, anaplastic ependymoma, glioblastoma multiforme, and four EWS) with prior treatments ranging from 2 to 11, achieved BORs of stable disease. One patient with ependymoma experienced stable disease with a prolonged time to progression of 54 weeks

Objective responses and durable survival highlight development opportunity in Ewing Sarcoma

CMR: complete metabolic response; BOR: best overall response

Elraglusib Pediatric Development Plans

- Actuate has been engaging with KOLs and patient advocacy groups in US, EU, UK, and Japan on Phase 2 study designs
- Pre-IND meeting with FDA planned to discuss registration pathway in EWS
- Discussions initiated and ongoing with US, EU, UK, and Japan KOLs regarding clinical development support and non-dilutive funding
  - National Pediatric Cancer Foundation (NPCF)
  - National Cancer Center Hospital, Tokyo, Japan
  - Pediatric Research Network GmbH
- Plans to initiate global Phase 2 trials in 2H 2026*

NATIONAL PEDIATRIC CANCER FOUNDATION

ZENTRUM für Forschungsförderung in der PÄDIATRIE

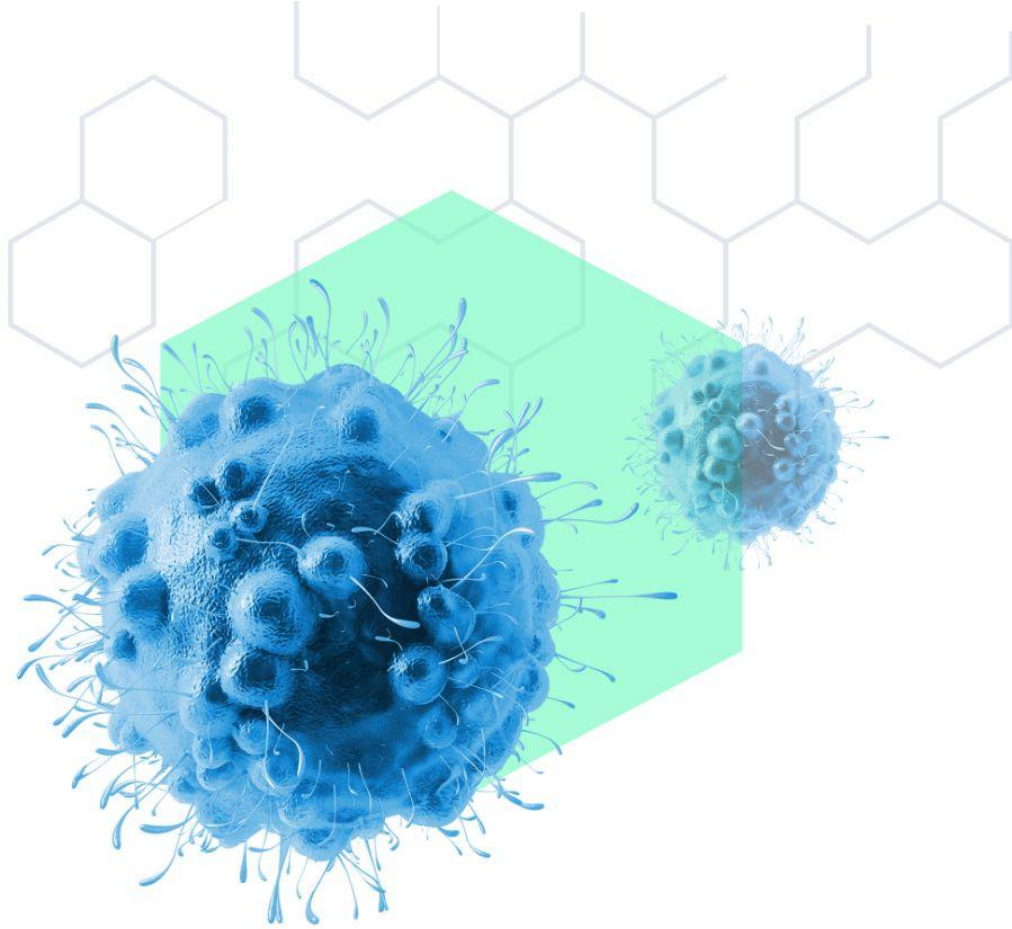
Pädiatrisches Forschungsnetzwerk

National Cancer Center Japan

*dependent on funding

ACTUATE THERAPEUTICS

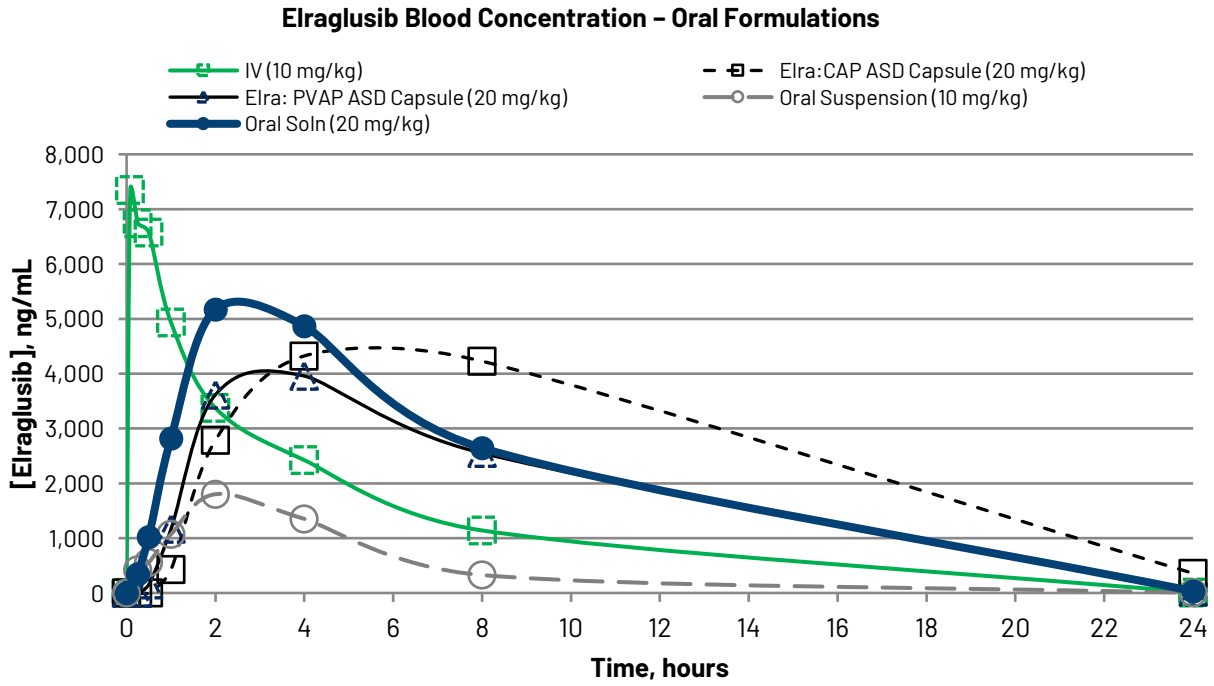
Elraglusib in Metastatic Melanoma and Other Cancer Indications



Elraglusib Tablet to be Utilized in New Indications

Tablet has excellent drug-like properties

- Two tablets could replace one IV bag and allow for daily dosing
- Preclinical studies show Tablet >95% bioavailability
- Pharmacokinetics to date have been largely dose-proportional



Route	Potency	Target Dose (mg/kg)	Half-life (hr)	T_{max} (hr)	C_{max} (ng/mL)	AUC_{last} (hr*ng/mL)	Dose-limiting Toxicity
IV	N/A	10	2.63	0.0830	6,560	**22,300**	No
Oral	250 mg	25	3.01	4.50	6,090	**77,000**	No (MTD)
Oral	500 mg	50	7.63	6.00	9,230	**137,000**	Yes

MTD: Maximum Tolerated Dose

ACTUATE THERAPEUTICS

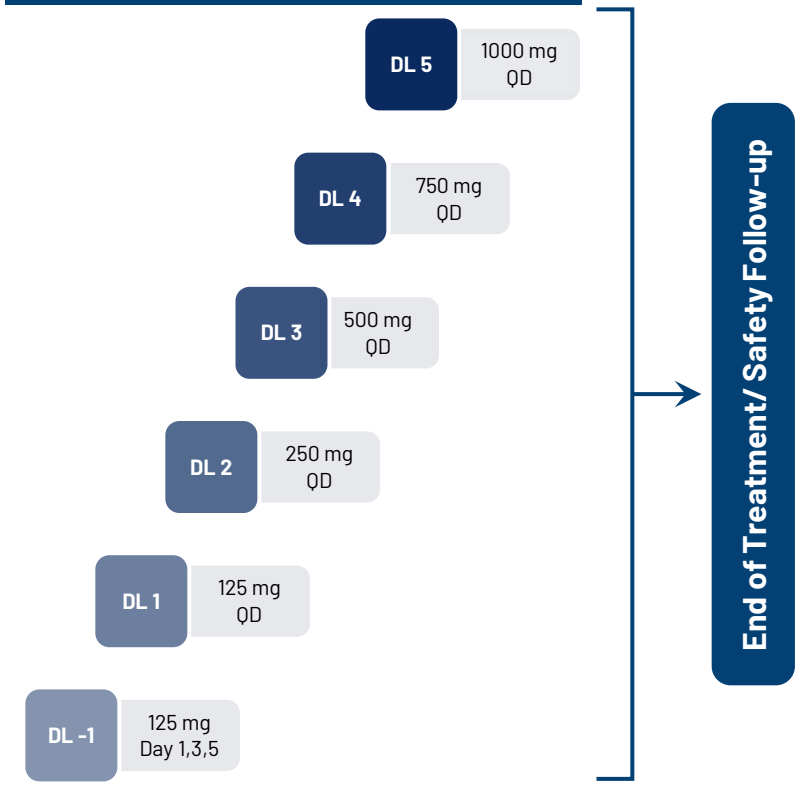
Elraglusib Tablet Clinical Development Plan

Phase 1 Study Design

Inclusion Criteria

- CPI refractory metastatic melanoma and other advanced refractory cancers
- Relapsed or refractory to existing therapies OR patient is intolerant to existing therapies
- Adequate organ function
- At least 1 measurable lesion per RECIST v1.1
- ECOG PS ≤ 2

Treatment BOIN 3+3 Design



Endpoints

Primary endpoints: MTD/RP2D and Safety

Secondary endpoints: ORR, DOR, PFS

Study Initiation: 2H 2026*

Phase 2 Study Design

Daily dose at RP2D

CPI refractory metastatic melanoma and other advanced refractory cancers

Planned study initiation 2H 2027*

*Contingent upon future funding
RP2D: Recommended Phase 2 Dose

ACTUATE THERAPEUTICS

Metastatic Melanoma is a High Unmet Need With Significant Commercial Potential

Market Size

Metastatic melanoma is the deadliest form of skin cancer and accounts for the majority of melanoma deaths (~57,000 deaths per year worldwide).[1] U.S. new cases are ~105k per year,[2] and global new cases are ~330k per year.[3] Projected market growth to >$10 billion by 2030[4]

Survival Rate and Economic Burden

The prognosis remains poor with a 5-year survival rate in distant stage patients of only ~35%[5] and a high economic burden with total per-patient costs for advanced disease commonly exceeding US$100,000[6]

Current Treatment

Immune checkpoint inhibitors (anti–PD-1 ± CTLA-4) and, for BRAF-mutant tumors, BRAF/MEK-targeted combinations. Majority of patients experience limited or no response, or develop resistance, to checkpoint inhibitors, and outcomes after progression on immunotherapy remain poor with few effective options. ~50% of patients are CPI refractory[7]

Elraglusib Opportunity

Novel GSK-3β inhibitor with early clinical activity, including an ongoing, durable CR. Elraglusib could be combined with other inhibitors or even potentially used as a single agent in later line settings

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, & Bray F (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians, 71, 209–249.
2. National Cancer Institute. Surveillance, Epidemiology, and End Results (SEER) Program. Cancer Stat Facts: Melanoma of the Skin. SEER website.
3. International Agency for Research on Cancer (IARC). World Health Organization. Global Cancer Observatory (GLOBOCAN 2022). Melanoma of Skin — Fact Sheet.
4. Melanoma Therapeutics Market (2025 - 2030). https://www.grandviewresearch.com/industry-analysis/melanoma-therapeutics-market
5. Sundararajan S, Thida AM, Yadlapati S, et al. Metastatic Melanoma. [Updated 2024 Feb 17]. StatPearls https://www.ncbi.nlm.nih.gov/books/NBK470358/
6. Bateni SB, Nguyen P, Eskander A, et al. Changes in Health Care Costs, Survival, and Time Toxicity in the Era of Immunotherapy and Targeted Systemic Therapy for Melanoma. JAMA Dermatol. 2023;159(11):1195–1204.
7. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Final 10-Year Outcomes with Nivolumab plus Ipilimumab in Advanced Melanoma. New England Journal of Medicine. 2023;389(6):491–505.doi: 10.1056/NEJMoa2300119

ACTUATE THERAPEUTICS

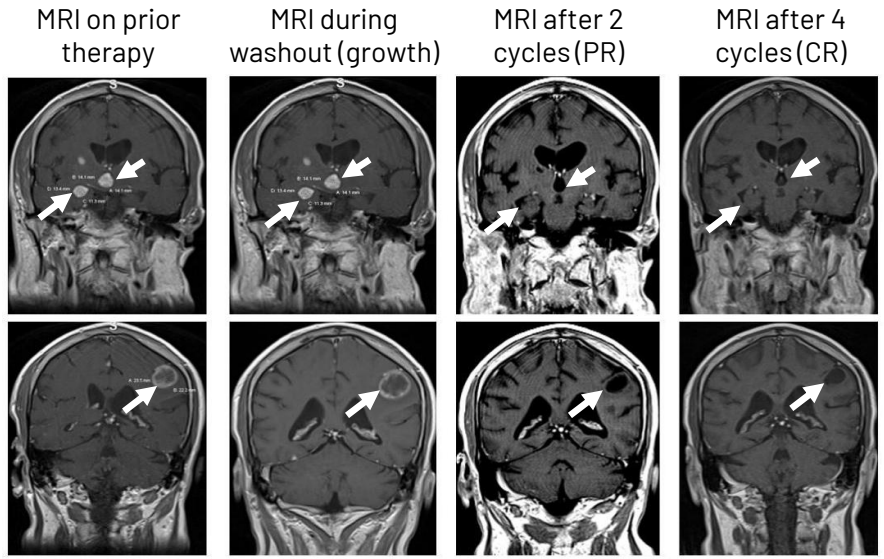
Elraglusib Has Potential in Multiple Indications with High Unmet Need

Actuate 1801 Part 1 evaluated elraglusib as a single agent

- First objective response reported in patient treated with 5 mg/kg elraglusib monotherapy
- Metastatic melanoma diagnosed in 2018; widely metastasized to the brain, lungs, bones, muscles, stomach, lymph nodes, pancreas and adrenal glands
- Refractory to all FDA-approved standard therapies, including several checkpoint inhibitors and BRAF / MEK inhibitor
- **After 12 Weeks on elraglusib:** Brain MRI showed CR by RANO criteria, PET scan showed CMR
- **Durable CMR ongoing (OS >6.5 years as of November 2025)**

Refractory, metastatic melanoma identified as a clinical indication for elraglusib development

- A second patient receiving single-agent elraglusib has ongoing stable disease (SD) (3.1 years as of last documented alive date)
- Also failed all FDA-approved standard therapies including immune checkpoint inhibitors and several experimental treatments
- Patients receiving chemotherapy salvage after anti-PD-1 treatment have a mOS of 6.9 months across all chemotherapy tested[1]
- **Potential for genomic biomarker enrichment to improve the probability of success based on ML models of CPI response**



12 weeks on elraglusib leads to CR by PET-MRI.
Cystic lesions observed in place of prior tumor.

Combination	Key Histologies	mOS (1801)
Elraglusib Monotherapy	CPI Refractory, Metastatic Melanoma	9.1 months
Elraglusib/Irinotecan	Refractory, Metastatic Colorectal	6.9 months
Elraglusib/Carboplatin	CPI/Platinum refractory, Metastatic NSCLC	ND

1. Goldinger at el., Eur J Cancer 2022; 162: 22.

GSK-3β is a Therapeutic Target Across Numerous Cancer Histologies

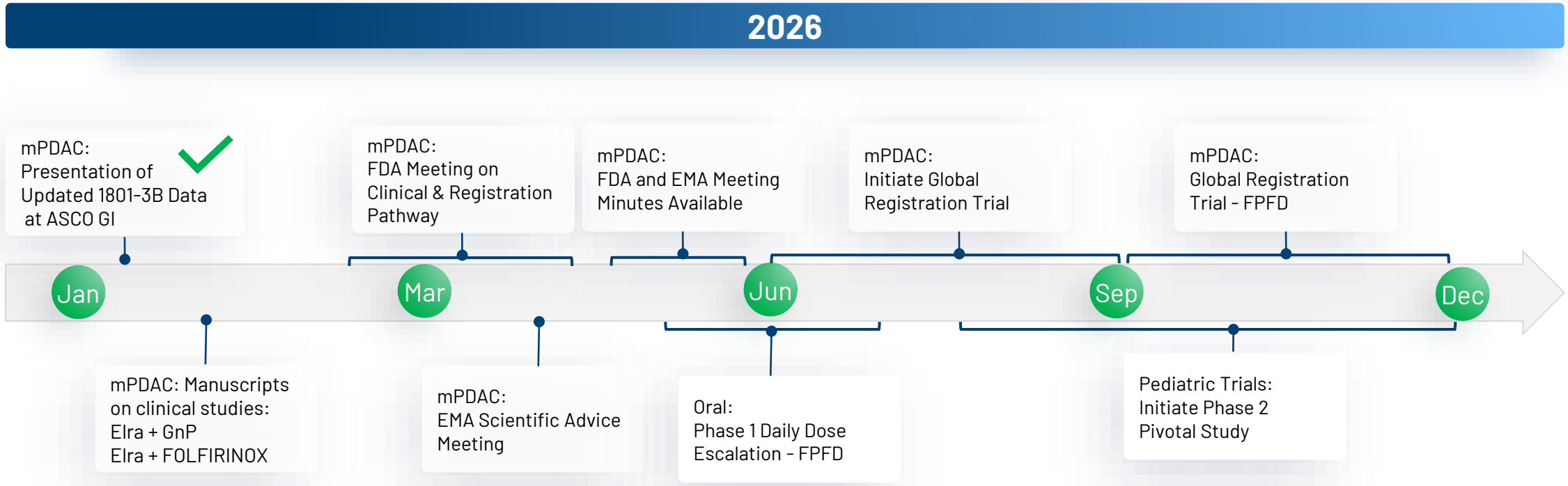
- Extensive preclinical and clinical evidence supports GSK-3β as a therapeutic target in > 20 different cancer types, including solid tumors and hematological malignancies
- Preclinically, elraglusib has shown antitumor activity across 18 cancer types, including solid tumors and hematological malignancies
- Elraglusib demonstrated clinical activity, as monotherapy and/or in combination with standard of care, across 9 different types of cancer

Elraglusib Evaluated Across Multiple Cancers	Elra Preclinical Activity	Elra Clinical Activity
Bladder	✓	
Breast	✓	
Colorectal	✓	✓
CNS	✓	✓
Endometrial/Uterine/Cervical	✓	
Head & Neck	✓	✓
Leukemia	✓	
Lung	✓	✓
Lymphoma	✓	
Melanoma	✓	✓
Multiple Myeloma	✓	
Myelofibrosis	✓	
Neuroblastoma	✓	✓
Ovarian	✓	✓
Pancreatic	✓	✓
Prostate	✓	
Renal	✓	
Sarcomas	✓	✓

Clinical activity represents achievement of an overall survival exceeding 6 months in more than 30% of patients with relapsed or refractory cancer

ACTUATE THERAPEUTICS

Key Near Term Anticipated Development Plans and Milestones



Initiation and timing of future clinical trials contingent upon future funding

FPFD: First Patient First Dose

ACTUATE THERAPEUTICS

Seasoned and Successful Leadership

Experienced leadership team with demonstrated ability to develop and commercialize cancer drugs

Daniel M. Schmitt – Chief Executive Officer and Founder

- 30+ years of biotechnology and pharmaceutical experience across senior executive roles
- Led and contributed to the successful development and launch of multiple pharmaceutical products
- Exosurf, Zovirax, Valtrex, Adenoscan, Ambisome, Duraclon, Campath, Abraxane, enTrust
- Executed ~1B+ in milestone value through licensing, acquisition, and development deals

Fujisawa · SEARLE · IMMTECH · Wellcome · ILEX ONCOLOGY · Northwestern University

Andrew Mazar, PhD – Chief Operating Officer and Scientific Co-Founder

- Co-founder, Chief Scientific Officer and Director, Monopar Therapeutics, Inc. (Nasdaq: MNPR)
- Entrepreneur-in-Residence; Professor of Pharmacology; Founding Director, Center for Developmental Therapeutics, Northwestern University
- Chief Scientific Officer, Attenuon, LLC
- Internationally recognized expert in cancer metastasis and translational oncology
- Eleven drugs from discovery through Phase 2
- >250 peer-reviewed publications and book chapters and inventor on >70 patents
- Serial entrepreneur with seven start-ups founded

Abbott · LungTherapeutics · Monopar Therapeutics · attenuon · NIH National Cancer Institute · Northwestern Chemistry of Life Processes Institute

Paul Lytle – Chief Financial Officer

- 30+ years of finance and accounting experience
- 25+ years of public company experience for Nasdaq listed companies
- Served as co-founder, CFO, and director for multiple biotech companies
- Raised in excess of $500 million in net proceeds from various equity and debt offerings

AVID BIOSERVICES · Mosaic ImmunoEngineering Inc. · Breathe TECHNOLOGIES

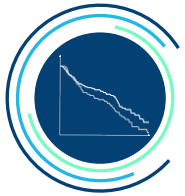
Steven D. Reich, MD – Sr VP, Clinical Development and Acting Chief Medical Officer

- Oncology drug development executive leader for commercial clinical development and strategy
- Directed multi-national medical research groups within pharmaceutical/biotechnology companies and CRO
- Lead investigator for Phase I-III trials and designed and managed Phase I-IV trials for industrial sponsors
- Headed the clinical research programs leading to multiple US, Canadian, and European drug approvals
- Epogen, Targretin, Panretin, Fludara, Inlyta

parexel · Pfizer · Artelo BIOSCIENCES · Ligand · Biogen · Monopar Therapeutics

ACTUATE THERAPEUTICS

Investment Highlights



Compelling Survival Data in mPDAC

Broad Therapeutic Potential in Multiple Oncology Indications

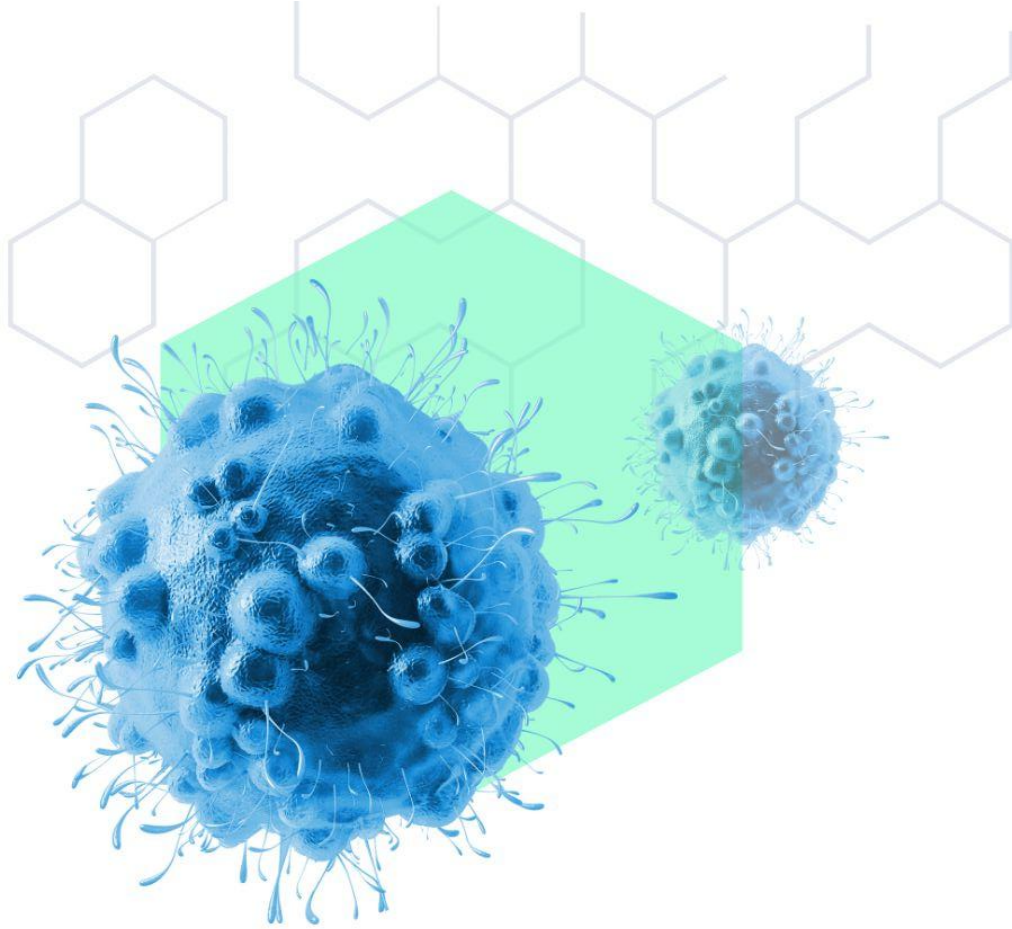
Significant Commercial Potential in Major Markets

Extended IP Protection

Seasoned Leadership Team

ACTUATE THERAPEUTICS

ACTUATE THERAPEUTICS



Nasdaq Global Market: ACTU