ACTUATE THERAPEUTICS

Corporate Overview
November 2025

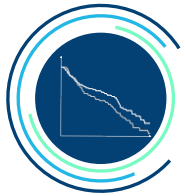
Forward-Looking Statements

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 2025, 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 2025, 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: 0.63

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/registration trial in planning for refractory Ewing Sarcoma patients

Oral Dose Tablet Successfully Developed

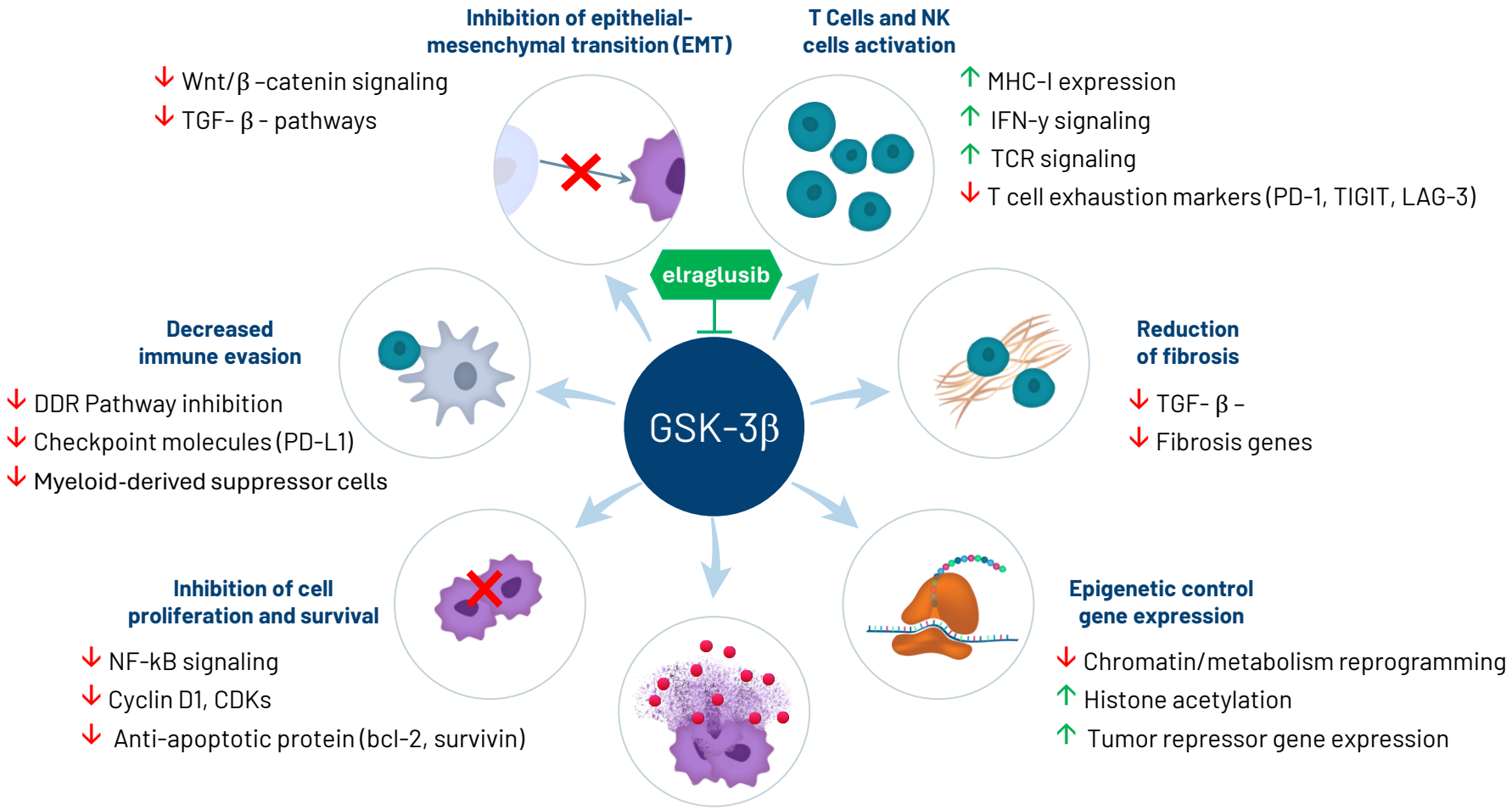
- Oral liquid successfully evaluated in Healthy Volunteer Phase 1 study
- Solid dose achieved >95% bioavailability in preclinical studies
  - Phase 1/2 study planned in advanced cancer patients including refractory metastatic melanoma

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

Elraglusib Injection (IV)	Program	Preclinical	Phase 1	Phase 2	Phase 3	Milestones
Pancreatic Cancer (with GnP) 1st line metastatic	Adult Actuate-1801 Part 3B				*In Planning***	- Updated Phase 2 data to be 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*
Pancreatic Cancer (with FOLFIRINOX) 1st line metastatic	Investigator Initiated Trial	MASSACHUSETTS GENERAL HOSPITAL				- Study closed to enrollment - Data Readout: Mid 2026
Advanced Pancreatic Cancer (with mFOLFIRINOX + retifanlimab)	Investigator Initiated Trial	Incyte UPMC HILLMAN CANCER CENTER				- Enrollment open
Advanced Refractory Cancers – Ewing Sarcoma (EWS) Cohort Only	Pediatric Actuate-1902			*In Planning***		- Phase 1 topline data: Q4 2025 - Initiate Phase 2/Registration trial: 2H 2026
Elraglusib (oral tablet)						
Phase 1 dose escalation in advanced, refractory solid cancers	Adult Actuate-2401		*In Planning***			- Study initiation: 1H 2026
Phase 2 treatment of CPI refractory metastatic melanoma and other advanced refractory cancers	Adult /Pediatric			*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 paths towards product registrations in the U.S. and EU
**Contingent upon future funding

GnP: gemcitabine/nab-paclitaxel; CPI: Checkpoint Inhibitor

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Elraglusib Advancing Under a Master Protocol 1801

Accelerated Study Design from Phase 1 to Phase 2 for Elraglusib Injection (IV)

Establishes process for transition from elraglusib monotherapy (Part 1) to evaluation of multiple chemotherapy combinations (Part 2) to Phase 2 efficacy studies (Part 3) under one protocol[1]

1801 - Part 1

First In Human Monotherapy Dose Escalation

Avg 3+ lines of prior therapy (n=67)

BOR: CR, PR, SDs
DCR (16 wks): 42%

48% of patients went on to subsequent therapies

1801 - Part 2

Dose Escalation in Combination with Standard Dosing Chemotherapy

All patients required to have previously failed the combination chemo prior to enrollment (n=171)

- Elraglusib + Gemcitabine
- Elraglusib + GnP
- Elraglusib + Carboplatin
- Elraglusib + Lomustine
- Elraglusib + Irinotecan
- Elraglusib + Paclitaxel Carboplatin
- Elraglusib + Doxorubicin
- Elraglusib + Pemetrexed Carboplatin

1801 - Part 3

Company Sponsored Phase 2 Studies

1801 - Part 3A

First Line mPDAC
GnP + elraglusib

Simon Two-Stage Trial (International)

1801 - Part 3B

First Line mPDAC
GnP + elraglusib

Randomized Controlled Trial (International)

Completed
Ongoing

1. Database for 1801 Parts 1-3A locked; final CSR in development

BOR: Best Overall Response; SD: Stable Disease; DCR: Disease Control Rate

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mPDAC Represents a High Unmet Need With Significant Commercial Potential

Pancreatic Cancer

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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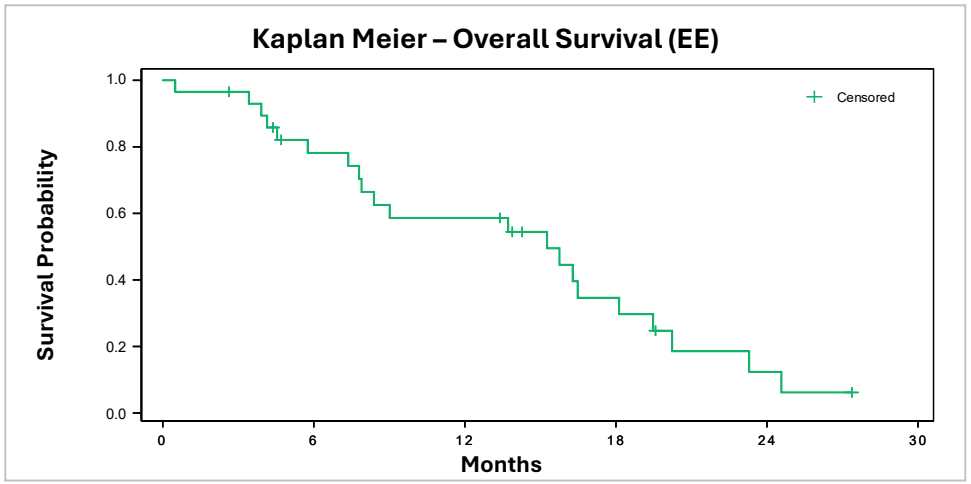
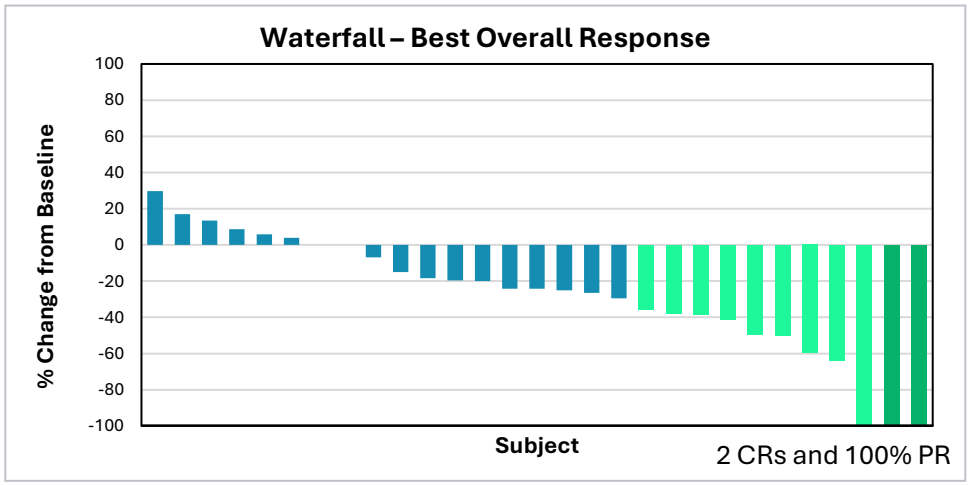
Phase 2 – Clinical Activity with Extended Median Overall Survival

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; 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

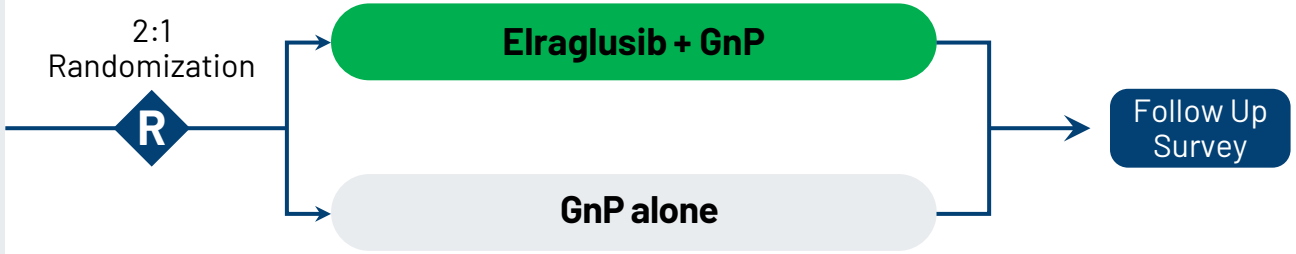
≥ 18 yrs old with metastatic pancreatic adenocarcinoma

Participants must have measurable disease as defined by RECIST1.1

No prior therapy

Total enrollment: 286

Treatment



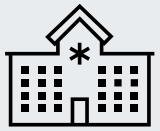
Endpoints

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

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

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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

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%)	154 (99.4%)
Mean (S.D.)	1.83 (2.23)	1.82 (0.22)
Median	1.82	1.81
Min, Max	1.31, 2.77	1.30, 2.41

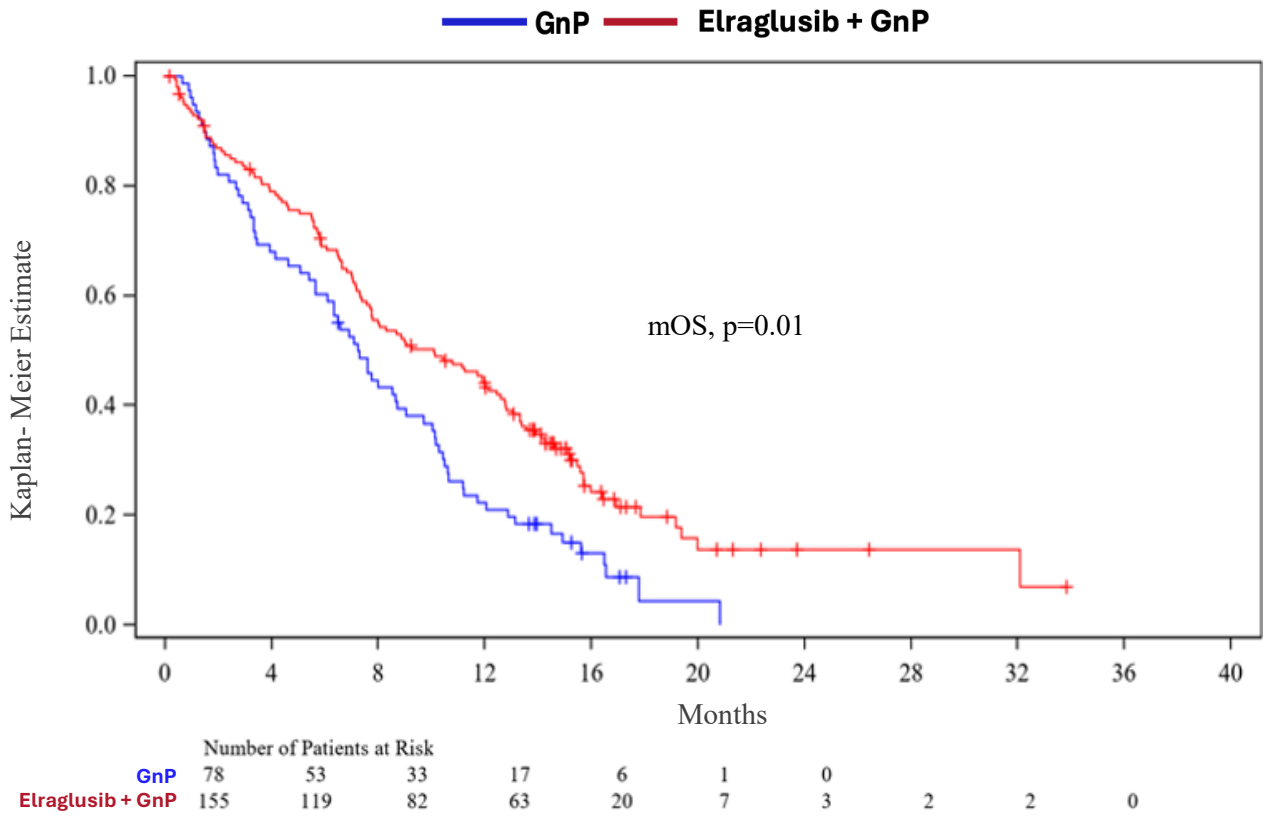
Demographics	GnP (n=78)	Elraglusib + GnP (n=155)
Eastern Cooperative Oncology Group Performance Status		
0	31 (39.7%)	64 (41.3%)
1	45 (57.7%)	89 (57.4%)
2	2 (2.6%)	2 (1.3%)
Disease Status		
Metastatic at Initial Diagnosis	59 (75.6%)	109 (70.3%)
Metastatic at Study Entry	77 (98.7%)	154 (99.4%)
Site of 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%)	58 (37.4%)

Predefined Safety Population
Draft unaudited data as of March 27, 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 37% Reduction in Risk of Death vs GnP

	GnP (n=78)	Elraglusib/GnP (n=155)
Primary Endpoint: mOS (months) HR=0.63; log-rank p=0.01	**7.2**	**10.1**
12-month OS (%) p=0.0005	**22.3**	**44.1**
Events (% events)	**70 (89.7%)**	**114 (73.5%)**
18-month OS (%)	**4.4**	**19.7**
24-month OS (%)	**0**	**13.8**
mPFS (months) HR=0.90; P=NS	**5.1**	**5.6**
Events (% events)	**75 (96.2%)**	**136 (87.7%)**
DCR	**56.4%**	**61.3%**
ORR n (%)	**17 (21.8%)**	**45 (29.0%)**



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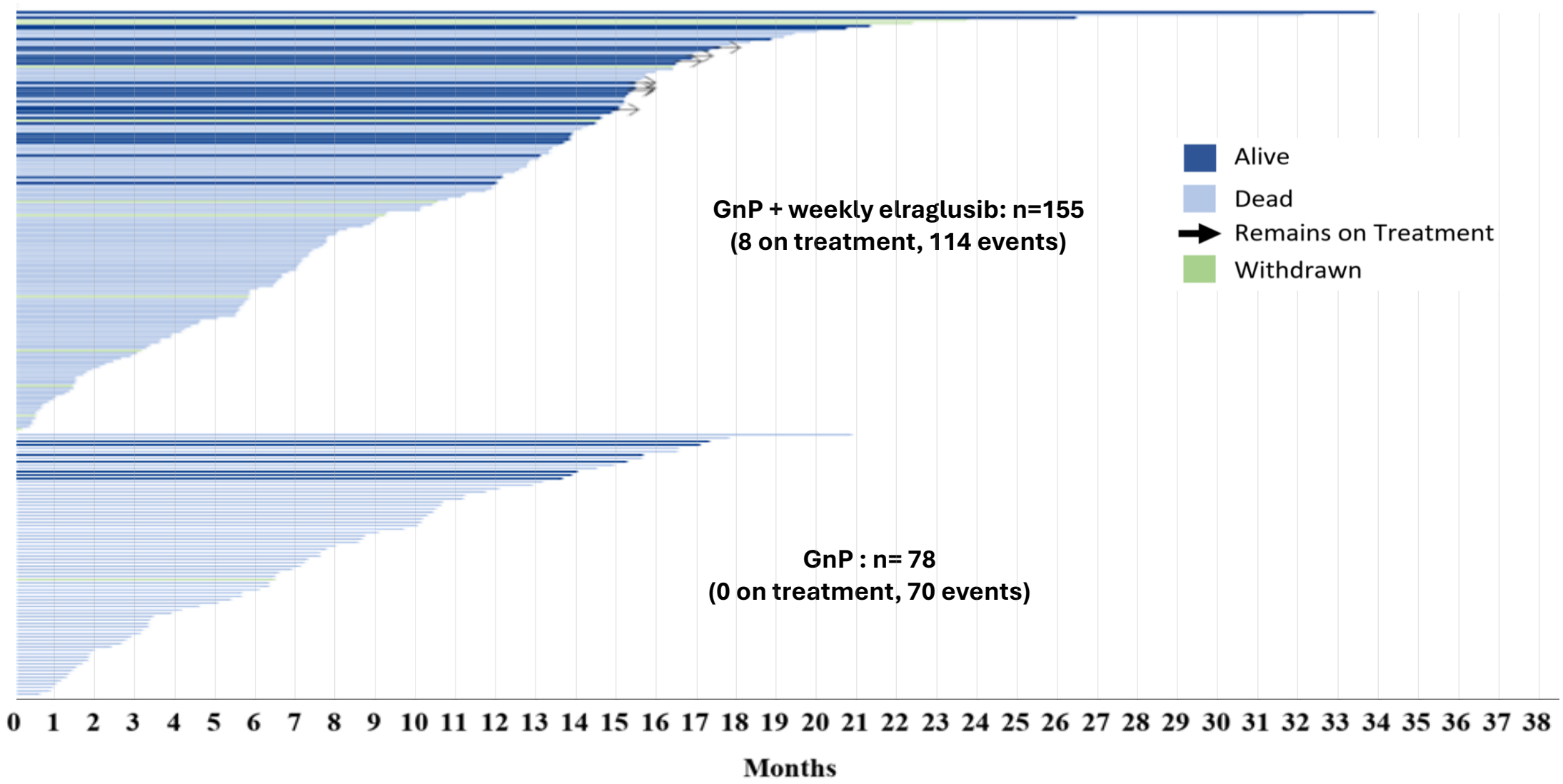
Durable and Sustained Responses Observed Relative to GnP



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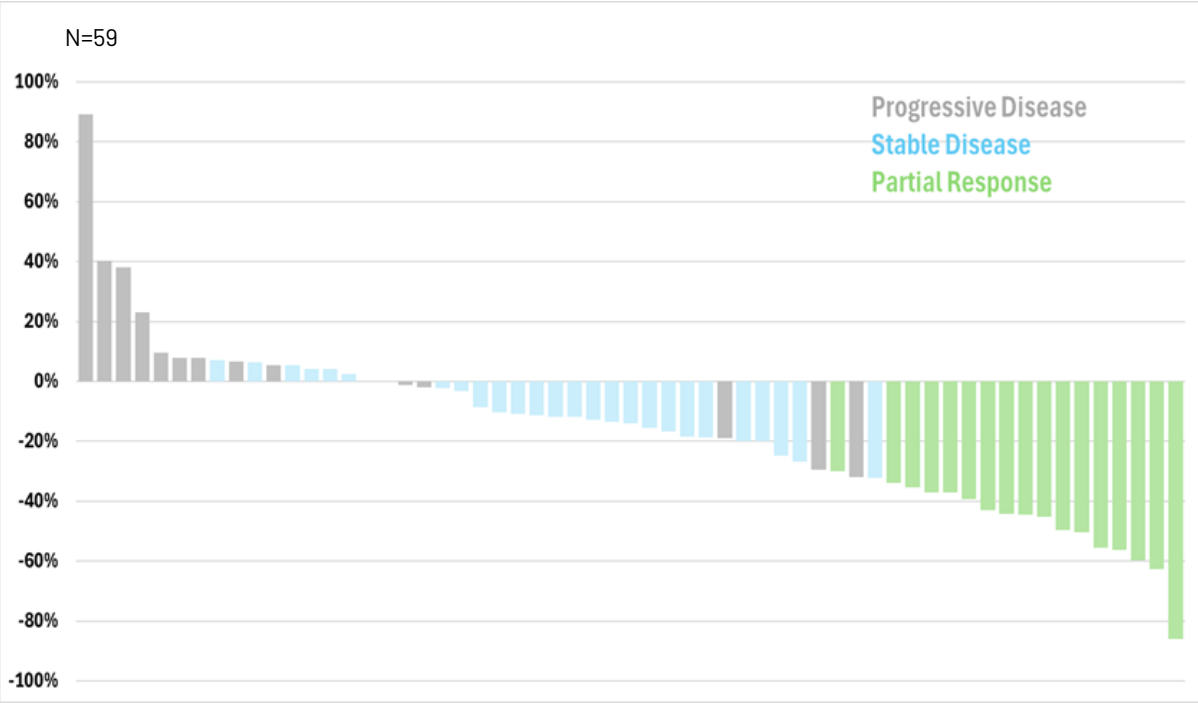
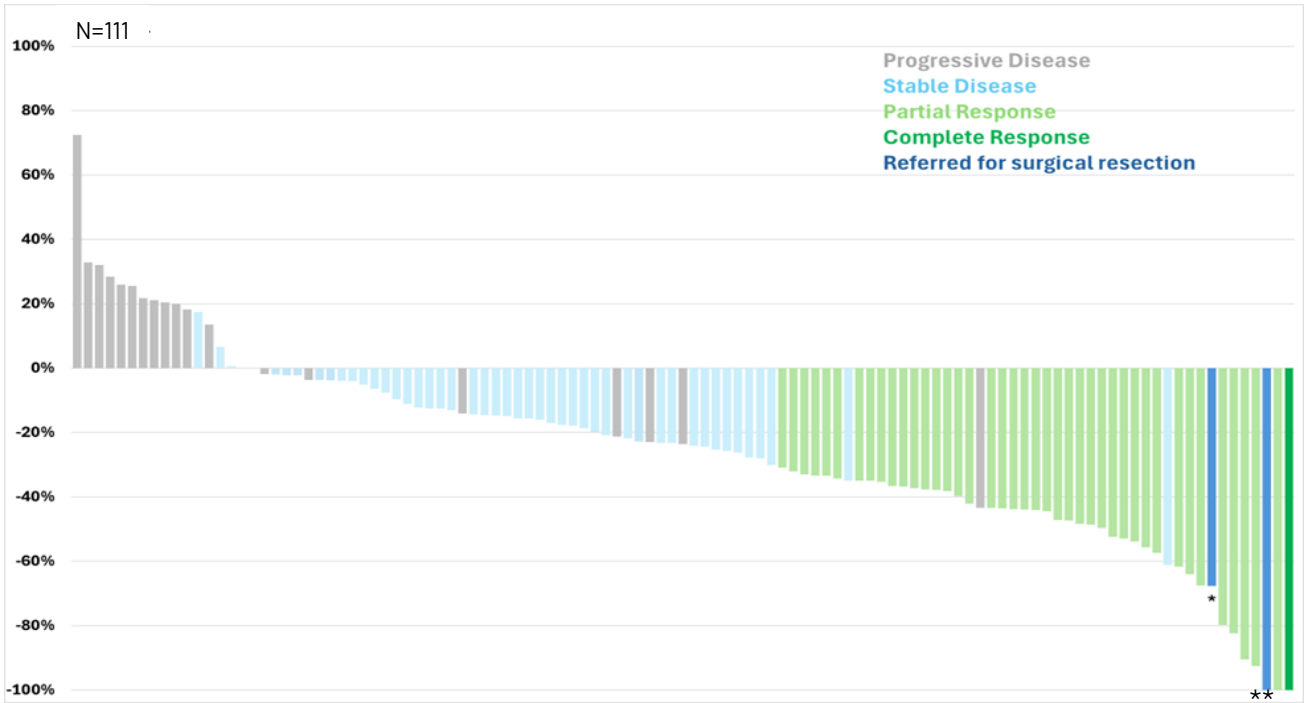
Elraglusib Arm Demonstrated Strong Improvement in ORR and Depth of Response vs. GnP

GnP Best Overall Response



Elraglusib + GnP Best Overall Response



*Patient had a partial response on treatment, then was referred for a Whipple procedure and subsequently came off treatment

**Patient had a partial response on treatment, then was referred for a Whipple procedure and then reported a complete response with 100% of the primary tumor removed

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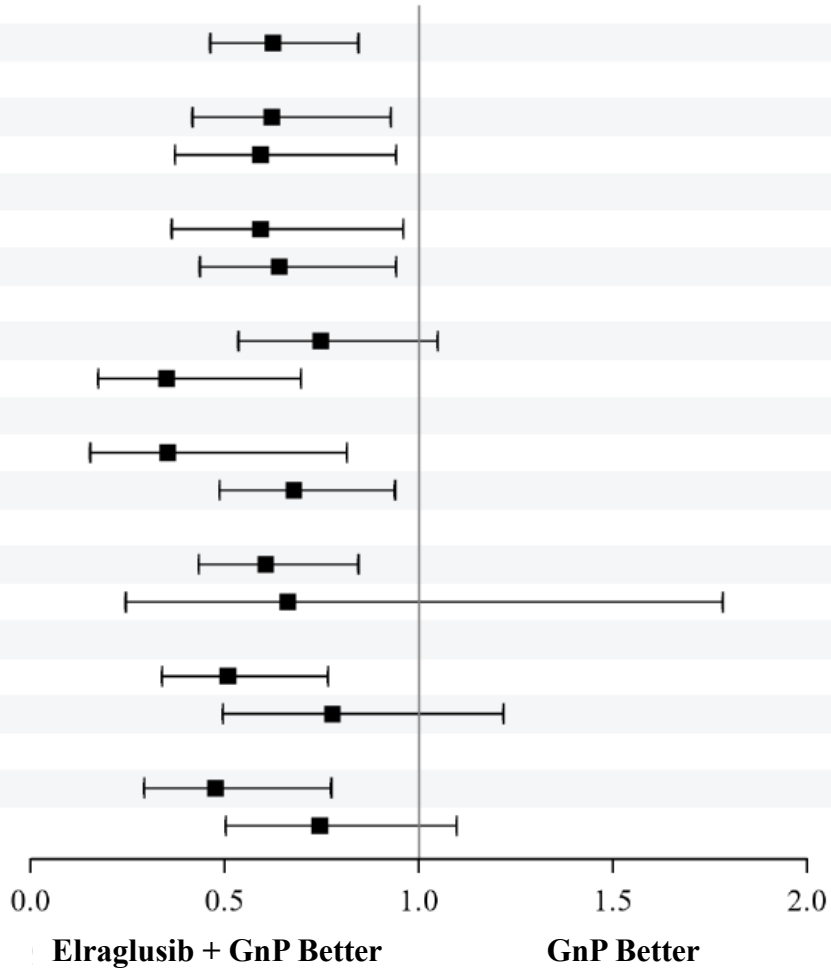
Clinical Benefit Observed For Elraglusib + GnP Across All Subgroups Evaluated

Subgroup	GnP, event/patients	Elraglusib + GnP, event/patients	HR (95% CI)
Overall	70/78	115/155	0.62 (0.46, 0.84)
Liver Mets at Baseline			
Yes	39/44	70/87	0.62 (0.42, 0.93)
No	31/34	45/68	0.59 (0.37, 0.94)
ECOG at Baseline			
0	27/31	48/64	0.59 (0.36, 0.96)
>= 1	43/47	67/91	0.64 (0.44, 0.94)
Region			
North America	54/60	95/117	0.75 (0.54, 1.05)
Rest of World	16/18	20/38	0.35 (0.18, 0.70)
CA 19-9 at Baseline			
< 37 U/mL	11/12	16/23	0.35 (0.15, 0.82)
>= 37 U/mL	59/66	96/129	0.68 (0.49, 0.94)
Race			
White	57/65	92/128	0.60 (0.43, 0.84)
Non-White	8/8	11/13	0.66 (0.25, 1.78)
Sex			
Male	40/43	60/80	0.51 (0.34, 0.77)
Female	30/35	55/75	0.78 (0.50, 1.22)
Age			
< 65 years	27/29	50/70	0.48 (0.29, 0.77)
>= 65 years	43/49	65/85	0.74 (0.50, 1.10)



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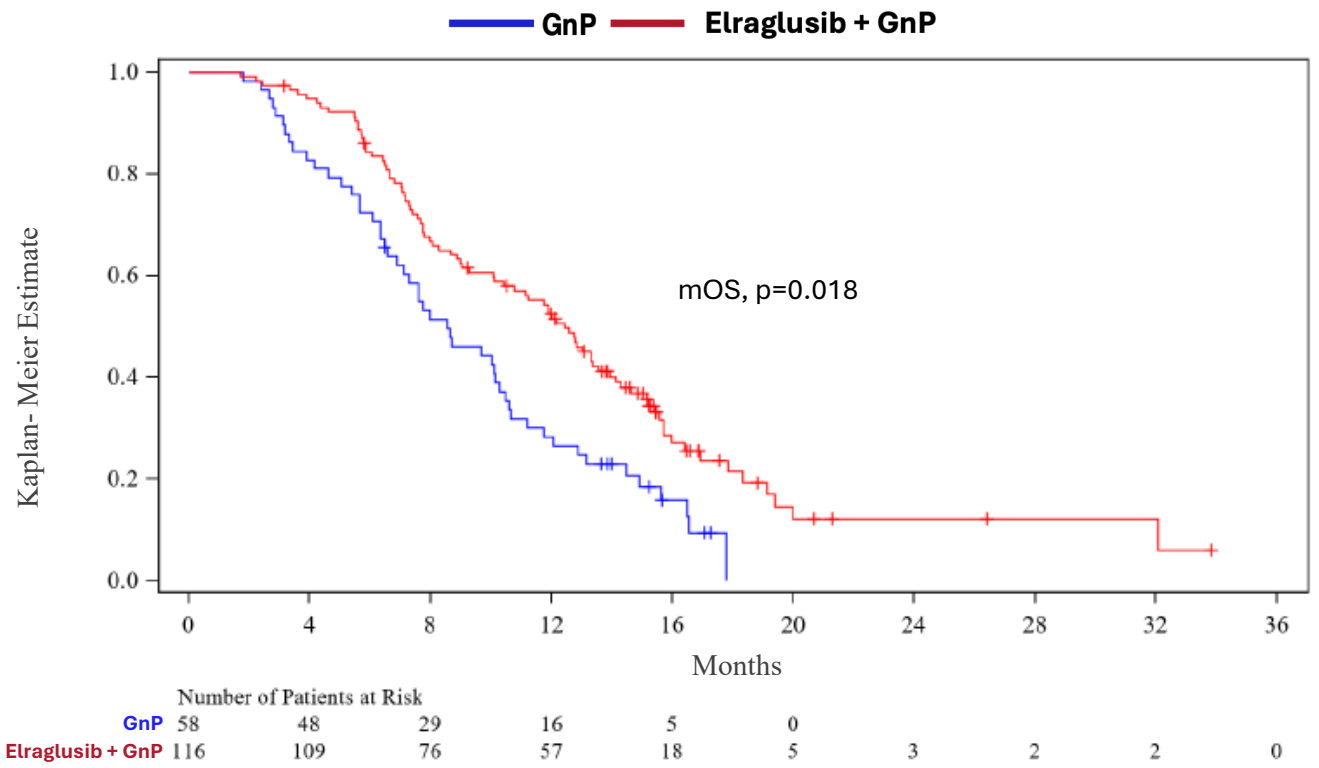
Subgroup of Patients Treated for One Cycle (4 weeks) - Significant Benefit in OS

Near Doubling of 1 year OS and 43% Reduction in Risk of Death vs GnP

	GnP (n=58)	Elraglusib/GnP (n=116)
Primary Endpoint: mOS (months) HR=0.57; log-rank p=0.018	**8.5**	**12.5**
12-month OS (%)	**28.3**	**52.5**
Events (% events)	**50 (86.2%)**	**85 (73.3%)**
18-month OS (%)	**0**	**21.5**
24-month OS (%)	**0**	**12.1**
mPFS (months) HR=0.78; P=NS	**5.6**	**6.9**
Events (% events)	**55 (94.8%)**	**105 (90.5%)**
DCR	**44.8%**	**53.4%**
ORR n (%)	**17 (29.3%)**	**44 (37.9%)**



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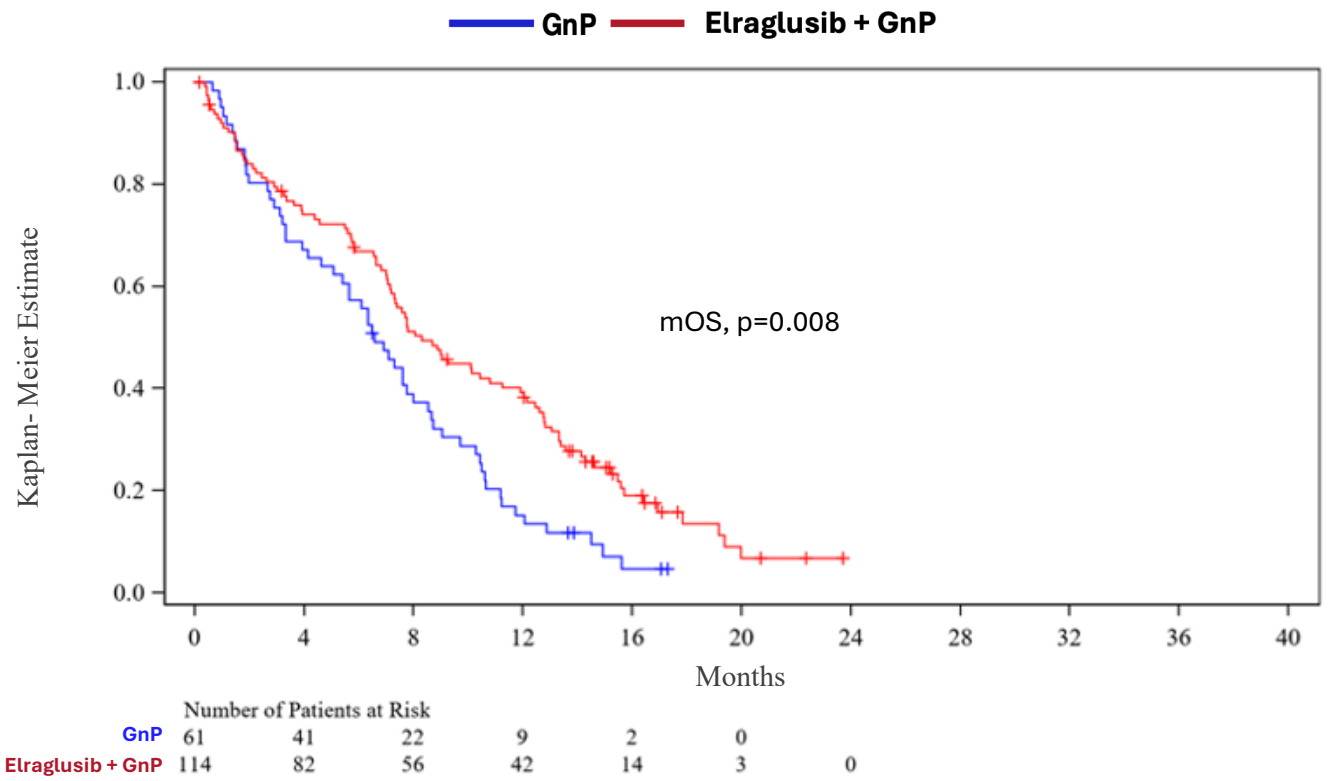
Patients with Liver Metastases – Significant Benefit in mOS and mPFS

2.5X Increase in 1 Year Survival and a 38% Reduction in Risk of Death

	GnP (n=61)	Elraglusib/GnP (n=114)
Primary Endpoint: mOS (months) HR=0.62; log-rank p=0.008	**6.6**	**8.3**
12-month OS (%) p=0.0003*	**15.2**	**39.2**
Events (% events)	**56 (91.8%)**	**92 (80.7%)**
18-month OS (%)	**0**	**13.6**
24-month OS (%)	**0**	**0**
mPFS (months) HR=0.72; P=0.039	**3.9**	**4.9**
Events (% events)	**59 (96.7%)**	**104 (91.2%)**
DCR	**27.9%**	**36.8%**
ORR n (%)	**12 (19.7%)**	**34 (29.8%)**



*z-test

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Subsequent Anti-Cancer Therapy Is Balanced Between Both Arms

	GnP (n=78)	Elraglusib/GnP (n=155)
Subsequent anti-cancer therapy (%)	37 (47.4%)	78 (50%)
Systemic anti-neoplastic therapy	36 (46%)	78 (50%)
FOLFIRINOX	13 (35%)	23 (28%)
FOLFOX	1 (3%)	0 (0%)
FOLFIRI	3 (8%)	7 (9%)
GnP	3 (8%)	10 (13%)
5-FU/liposomal irinotecan/LV	3 (8%)	7 (9%)
Other*	13 (36%)	31 (40%)
Radiotherapy	1 (3%)**	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 (%)				
	Elraglusib + GnP (N=155)		GnP (N=78)	
Adverse Event	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TEAE	155 (100)	139 (89.7)	77 (98.7)	62 (79.5)
Serious TEAE	86 (55.5)	81 (52.3)	44 (56.4)	43 (55.1)
Leading to Stoppage of Any Study Drug	42 (27.1)	26 (16.8)	20 (25.6)	16 (20.5)
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	105 (67.7)	1 (0.6)	7 (9.0)	0
Fatigue	97 (62.6)	26 (16.8)	39 (50.0)	4 (5.1)
Neutropenia*	95 (61.3)	81 (52.2)	32 (41.0)	24 (30.8)
Diarrhea	91 (58.7)	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**	71 (45.8)	39 (25.2)	35 (44.9)	23 (29.5)
Decreased appetite	64 (40.6)	9 (5.8)	19 (24.4)	6 (7.7)
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	56 (36.1)	3 (1.9)	25 (32.1)	0
Constipation	50 (32.3)	3 (1.9)	24 (30.8)	1 (1.3)
Pyrexia	44 (28.4)	2 (1.3)	20 (25.6)	1 (1.3)
Abdominal pain	45 (29.0)	14 (9.0)	16 (20.5)	2 (2.6)
Weight decreased	42 (27.1)	5 (3.2)	16 (20.5)	4 (5.1)
Peripheral sensory neuropathy	39 (25.2)	4 (2.6)	18 (23.1)	0
Hypokalemia	35 (22.6)	8 (5.2)	24 (30.8)	4 (5.1)
Asthenia	32 (20.6)	9 (5.8)	19 (24.4)	5 (6.4)
Dysgeusia	32 (20.6)	0	16 (20.5)	0
Infusion related reaction	31 (20.0)	4 (2.6)	1 (1.3)	0
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 March 27, 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

2:1 Randomization

R

Elraglusib + GnP

GnP alone

Follow Up Survey

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

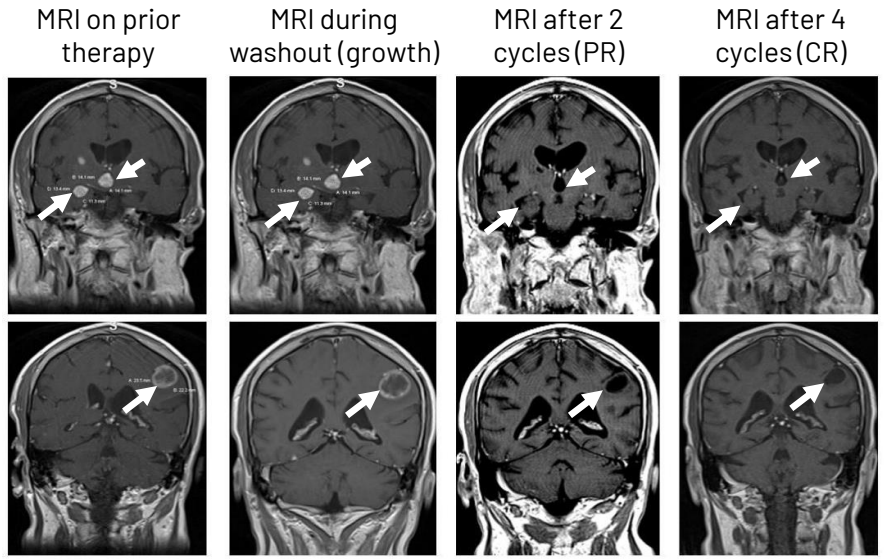
Elraglusib Has Potential in Multiple Indications with High Unmet Need

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 complete response (CR) by RANO criteria, PET scan showed complete metabolic response ("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 Complete Response 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.

Elraglusib Oral Tablet Demonstrates Positive PK Profile

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

- Elraglusib Oral Tablet exceeds plasma exposures of elraglusib IV
- Pharmacokinetics to date have been largely dose-proportional
- Elraglusib Oral Tablet will be given daily, which should achieve steady state plasma levels of drug
- This will allow further exploration of risk-benefit, dose and anti-cancer activity in indications identified as promising in Actuate-1801

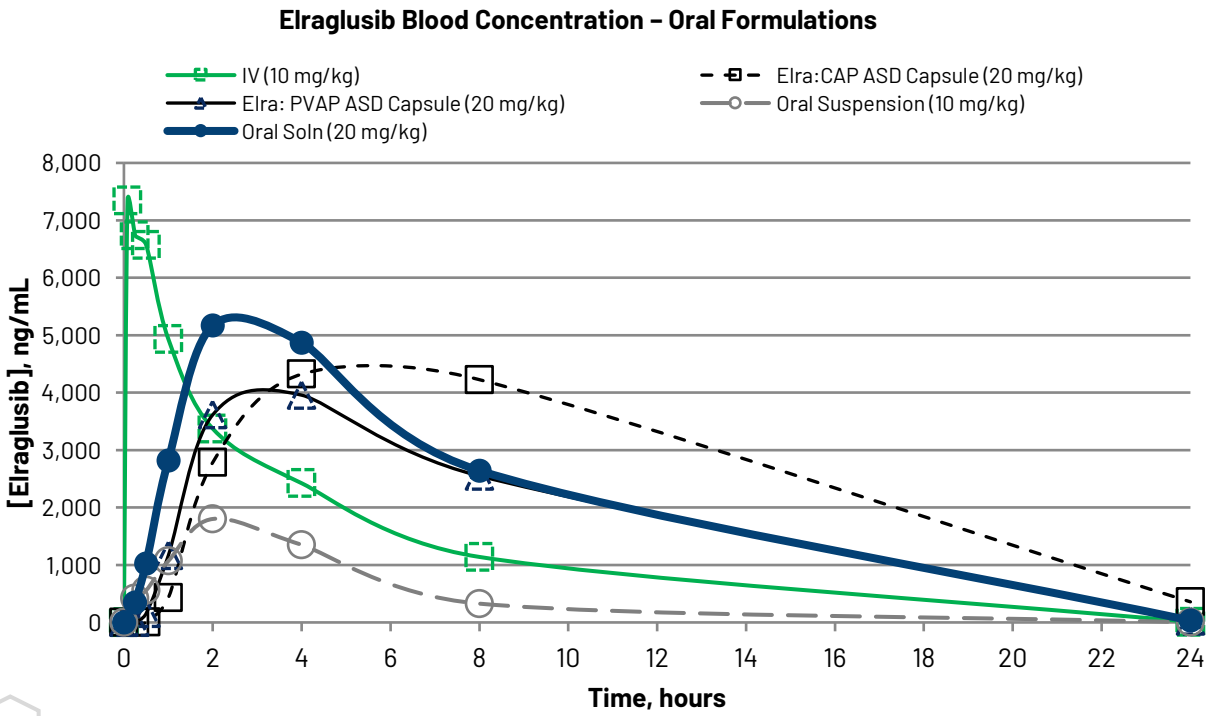
Oral Tablet formulation allows for expansion into new patient populations

MTD: Maximum Tolerated Dose

Elraglusib Oral Tablet Development Plan

Benefits

- Preclinical studies show Oral Solid >95% bioavailability
- Elraglusib oral dosage forms may allow potential expansion into pediatric and adult cancer indications where standard of care is oral
- May improve compliance and patient experience in indications where long DCR is observed



Development Plan – Phase 1/2 Study in Cancer Patients

Phase 1 Daily Dose Escalation Study

- Accelerated dose escalation
  - Design: 3+3 dose escalation to MTD/RP2D
- Adult refractory solid tumor patients
- Planned study initiation 1H 2026*

Phase 2 Treatment Study

- Daily dose at RP2D
- CPI refractory metastatic melanoma and other advanced refractory cancers
- Planned study initiation 1H 2027*

*Contingent upon future funding

RP2D: Recommended Phase 2 Dose

ACTUATE THERAPEUTICS

Ewing Sarcoma: Pediatric Trial Demonstrates Clinical Responses in Multiple Patients

Phase 1/2 study (Actuate-1902) in pediatric cancer patients with recurrent/refractory solid cancers

There are currently no treatment regimens that meaningfully extend life in Ewing sarcoma patients with metastatic, refractory disease

Patients that have metastasis and disease recurrence after chemotherapy have short survival of 3-8 months[1]

Trial Update

- Twelve patients were enrolled in Actuate-1902 and appear to have metastatic, refractory Ewing and Ewing-like sarcoma and had disease progression on their last treatment regimen prior to joining the study
- All twelve patients received the combination of elraglusib+cyclophosphamide/topotecan in 1902
- All twelve patients had received two or more previous chemotherapy regimens
- One patient had CR at their 1st scan as Best Overall Response (BOR)
    - Stopped all treatments after four months and continued to be in complete remission with no evidence of disease almost three years after termination of treatment
- One patient had BOR of CMR (Complete Metabolic Response, no detectable lesions by FDG-PET)
- One patient had BOR of PR (52% reduction in tumor)
- Three patients had BOR of SD
- Study is closed, final data expected by end of Q4 2025

Objective responses and durable survival highlight development opportunity in Ewing Sarcoma

1. Van Mater and Wagner. Onco Targets Ther. 2019;12:2279-2288.

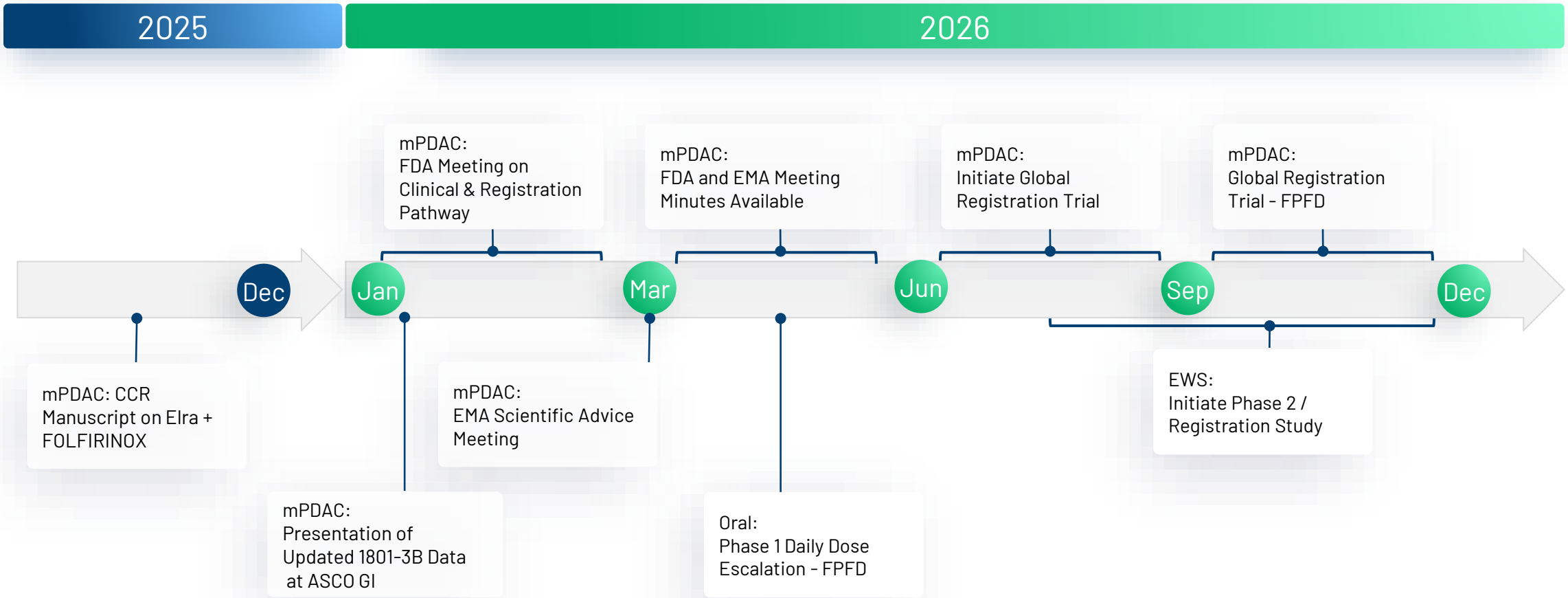
Elraglusib Ewing Sarcoma Development Plan

- Actuate has been engaging with KOLs and patient advocacy groups in US and EU on Phase 2 study
- Pre-IND meeting with FDA planned to discuss registration pathway
- Discussions initiated and ongoing with US, EU, and UK patient advocacy groups regarding clinical development support and non-dilutive funding
  - National Pediatric Cancer Foundation (NPCF)
    - Nonclinical EWS models (University of Colorado)
    - Clinical program partnership with NPCF sites
    - Clinical trial design
- Potential to initiate global Phase 2 registration trial in 2H 2026*

NATIONAL PEDIATRIC CANCER FOUNDATION

*dependent on funding

Key Near Term Anticipated Development Plans and Milestones



FPFD: First Patient First Dose

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

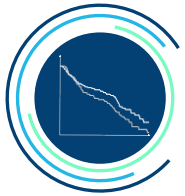
AVID BIOSERVICES · Mosaic ImmunoEngineering Inc. · Breathe TECHNOLOGIES

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

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

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Ticker: ACTU