



Corporate Overview

December 2024



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 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 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; 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discontinue clinical trials or result in other negative consequences; that this presentation includes preliminary and unpublished data which may be subject to change following the availability of more data or following a more comprehensive review of the data; that we do not have, and may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 based on our estimates regarding expenses, capital requirements and needs for additional financing. 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 Quarterly Report on Form 10-Q filed with the SEC on November 13, 2024 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.

Company Highlights



Advancing a potentially class-leading GSK-3 β inhibitor, elraglusib with a novel, multimodal MOA, in multiple advanced cancer Phase 2 trials



Clinical responses (CRs/PRs) and Disease Control observed across cancer histologies

Extended survival and increased responses are observed in mPDAC and relapsed/ refractory Ewing sarcoma. Preliminary evidence of clinical benefit has also been observed in patients with metastatic melanoma and relapsed/refractory colorectal and lung cancer



Oral version of elraglusib successfully evaluated in Healthy Volunteer Phase 1

- Phase 1 dose escalation study planned in advanced cancer patients



Broad composition of matter IP protection and development incentives

- Orphan Drug Designations for pancreatic and other cancer types; Fast Track Designation for pancreatic cancer

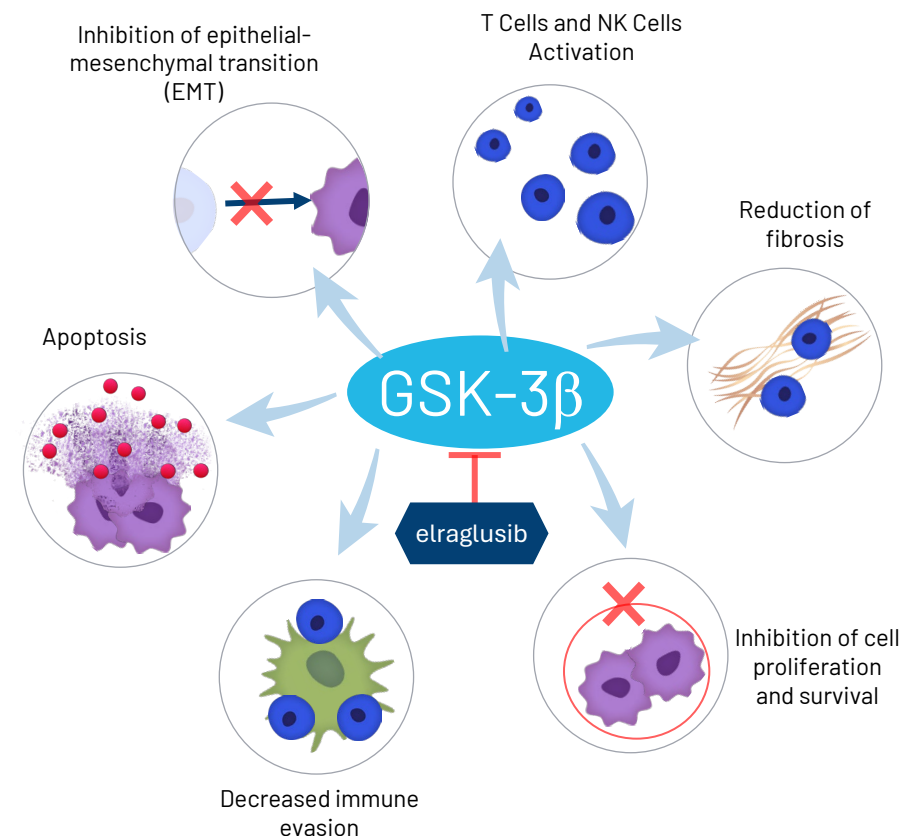
IPO: August 2024

NASDAQ: ACTU

HEADQUARTERS: Fort Worth, TX

Elraglusib: Multimodal MOA Supported by Clinical Data

- Elraglusib is an ATP-competitive inhibitor of GSK-3 β
 - GSK-3 β has been shown to potentially contribute to tumor progression in many treatment naive and refractory/resistant tumors
 - Pleiotropic effects as signaling adaptor
- Elraglusib downregulates well-credentialed molecular pathways that can lead to chemotherapy and drug resistance
 - NF- κ B pathway-anti-apoptotic protein expression
 - Alterations in TGF- β and pro-inflammatory cytokines suggest role in fibrosis in addition to immunomodulation
 - DDR pathways (ATR/ATM) including mismatch repair (PMS2)
 - Increase responsiveness of resistant/refractory tumors to chemo and immune therapy—"cold" tumors turned to "hot"
 - Inhibition of oncogenic epithelial-mesenchymal transitions



Strategic Pipeline Growth for GSK-3β Associated Diseases

Elraglusib Injection (IV)	Program	Preclinical	Phase 1	Phase 2	Phase 3	Milestones
Pancreatic Cancer (with GnP) 1st line metastatic ★	Adult Actuate-1801 Part 3B					Topline Data: Q1 2025*
Pancreatic Cancer (with GnP) 1st line metastatic ★	Adult - Phase 3 RCT				<i>In Planning</i>	TBD**
Advanced Refractory Cancers - Ewing Sarcoma Cohort Only	Pediatric Actuate-1902					Topline Data: 2H 2025
Elraglusib (oral tablet)						
Phase 1 in Advanced, refractory solid cancers	Adult Actuate-2401		<i>In Planning</i>			TBD**
Advanced, refractory cancers (solid and hematological)	Adult /Pediatric			<i>In Planning</i>		TBD**

★ *Fast track designation*

 Ongoing Trial

* Based on our meetings with the FDA to discuss our development plan in pancreatic cancer, the current Phase 2 study design cannot be used to support Accelerated Approval. However, if the future mOS data is positive in favor of the elraglusib/GnP combination, we would initiate further conversations with the FDA to discuss possible registration.

**Contingent Upon Future Funding

GnP: gemcitabine/nab-paclitaxel

Clinical Study Actuate-1801

Phase 1/2 Study Design for Elraglusib Injection (IV)

Establishes process for transition from elraglusib (9-ING-41) Monotherapy (Part 1) to evaluation of multiple chemotherapy combinations (Part 2) to Phase 2 efficacy studies (Part 3) under one protocol¹



1801 - Part 1

Elraglusib
Monotherapy Dose
Escalation



Completed



Ongoing



1801 - Part 2

Elraglusib Dose Escalation in
Combination with Standard Dosing Chemotherapy
*All patients required to have previously failed the
combination chemo prior to enrollment*

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)

Elraglusib Potential in Metastatic Pancreatic Cancer (mPDAC)



Pancreatic Cancer

Metastatic pancreatic cancer is highly aggressive and accounts for approximately 80-85% of all pancreatic cancer diagnoses. Projected market growth to >\$7 billion by 2030



Survival Rate and Economic Burden

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



Current Treatment

FOLFIRINOX and gemcitabine with nab-paclitaxel are standard but offer limited survival benefits

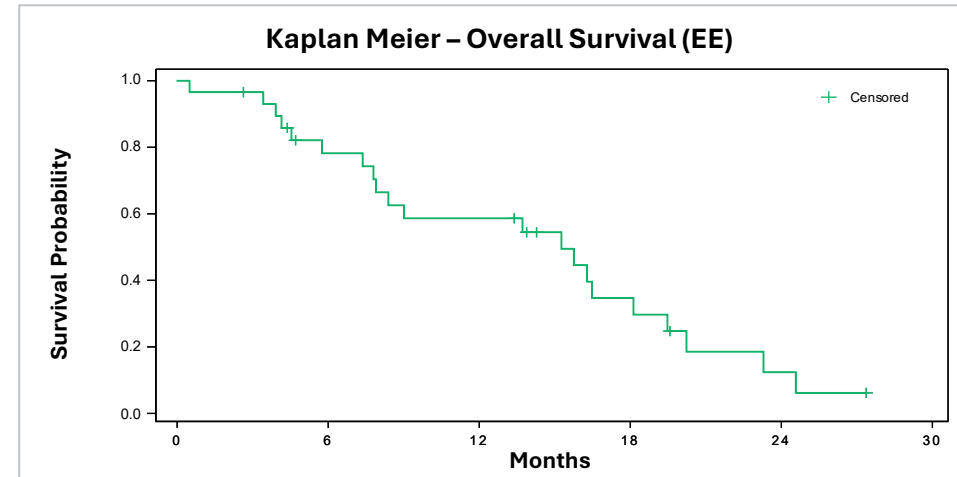


Elraglusib Opportunity

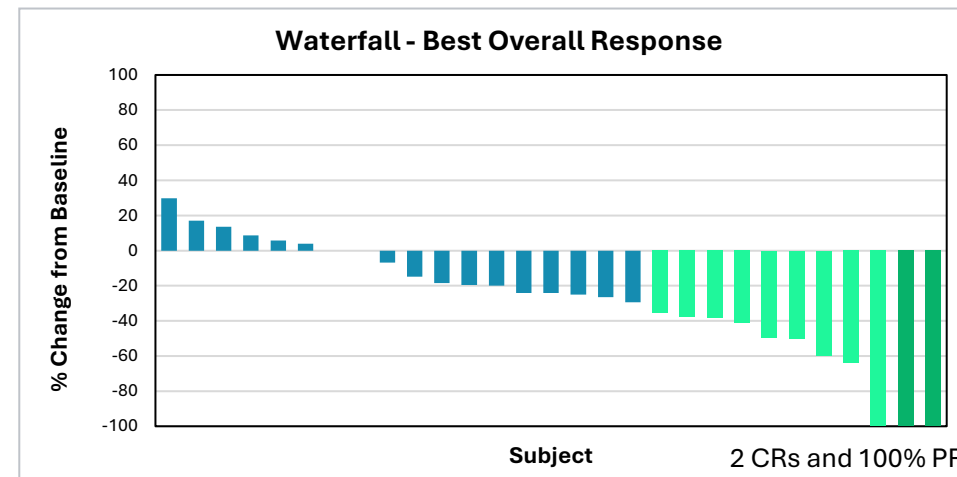
Novel GSK-3 β inhibitor that targets multiple molecular pathways in cancer cells but also impacts the TME and immune response

Phase 2 – Clinical Activity with Extended Median Overall Survival

- 1801 Part 3A in mPDAC
- Simon's Two-Stage trial design - Stage 1
- Evaluate the combination of elraglusib and gemcitabine/nab-paclitaxel (GnP)
 - mOS of 15.3 (EE population)
 - 2 CRs confirmed
 - 9 PRs confirmed
 - DCR: 52%, ORR: 38%
 - Met Simon's stage 1 threshold of DCR>50%
- 42 total patients enrolled (ITT)



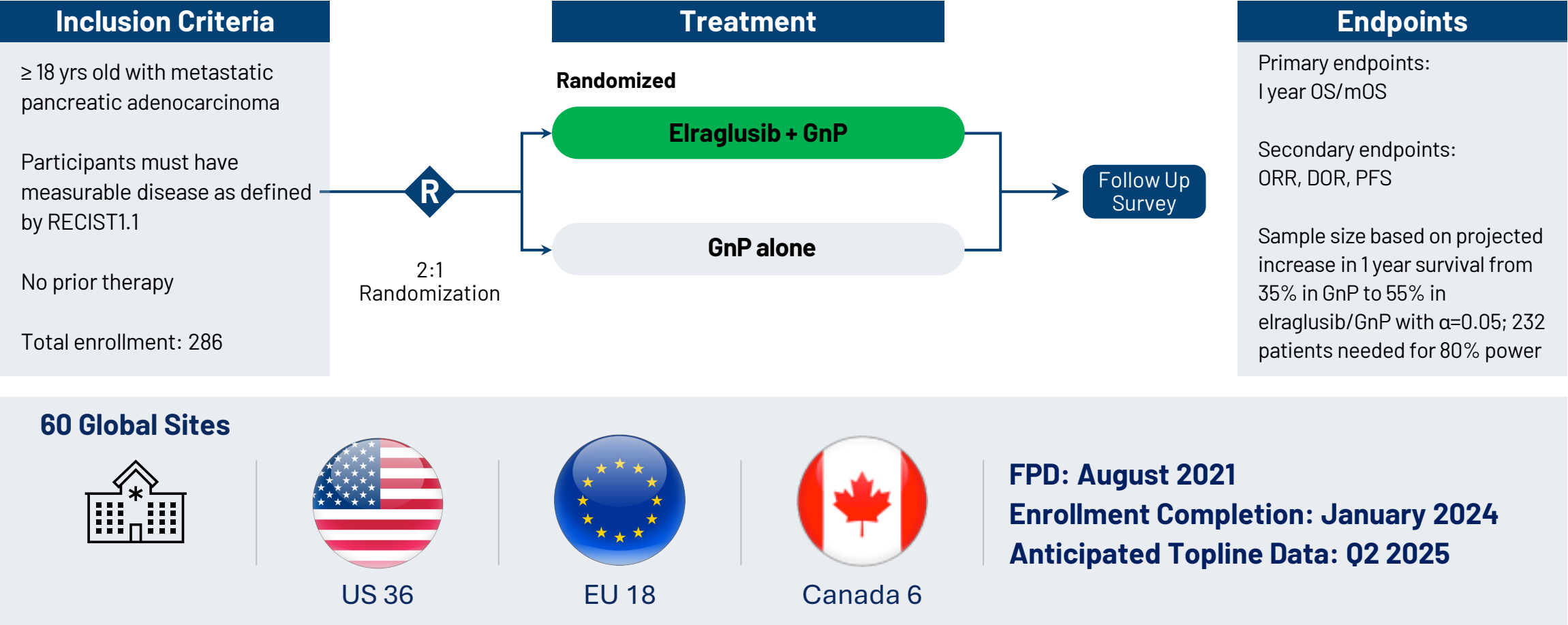
Subjects	29
Event	21 (72%)
Censored	8 (28%)
Median Survival	15.26
95% CL	(7.895, 18.13)



*13 subjects had no response data entered

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

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



Phase 2 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%)	155 (100%)
Site of Metastases		
Pancreas	73 (93.6%)	127 (81.9%)
Liver	61 (78.2%)	117 (75.5%)
Lymph Node	29 (37.2%)	71 (45.8%)
Lung	27 (34.6%)	57 (36.8%)

Predefined Safety Population
Draft unaudited data as of November 15th, 2024

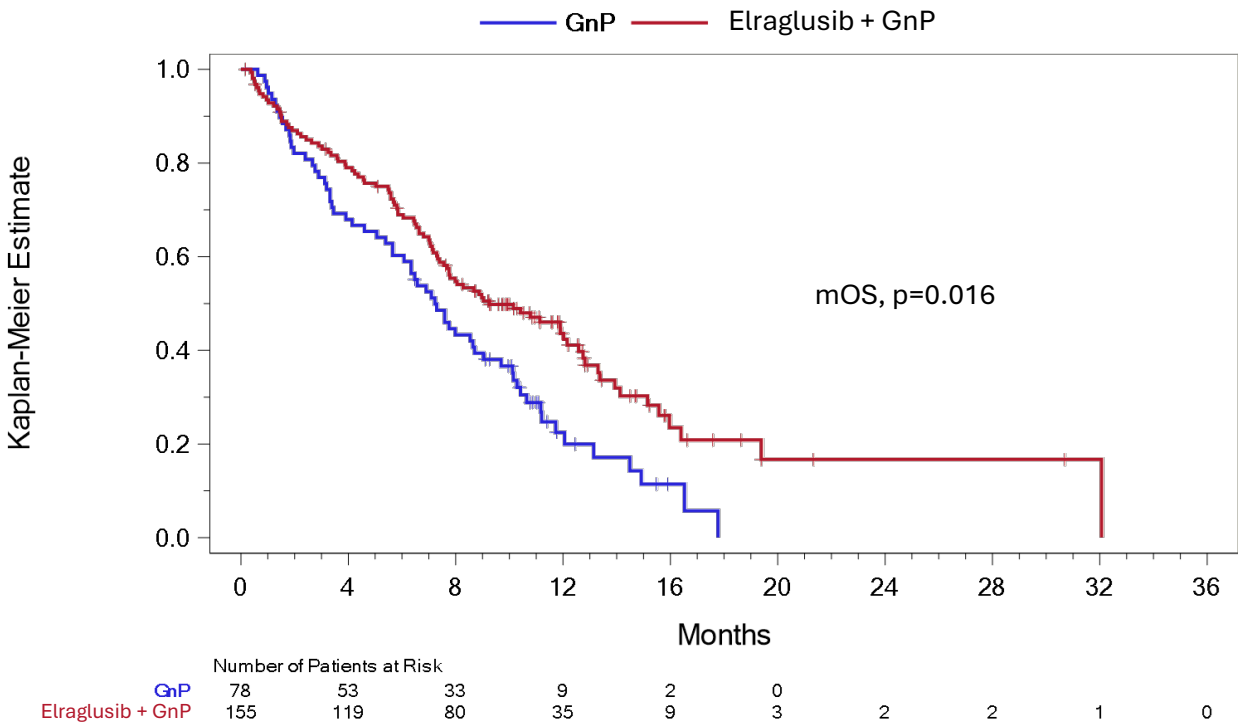
The final data and results may change as the study continues through completion

Doubling of 1 year OS and 37% Reduction in Risk of Death vs GnP

Administrative Analysis of Interim Data from Nov 15th, 2024, Demonstrates a Hazard Ratio of 0.63

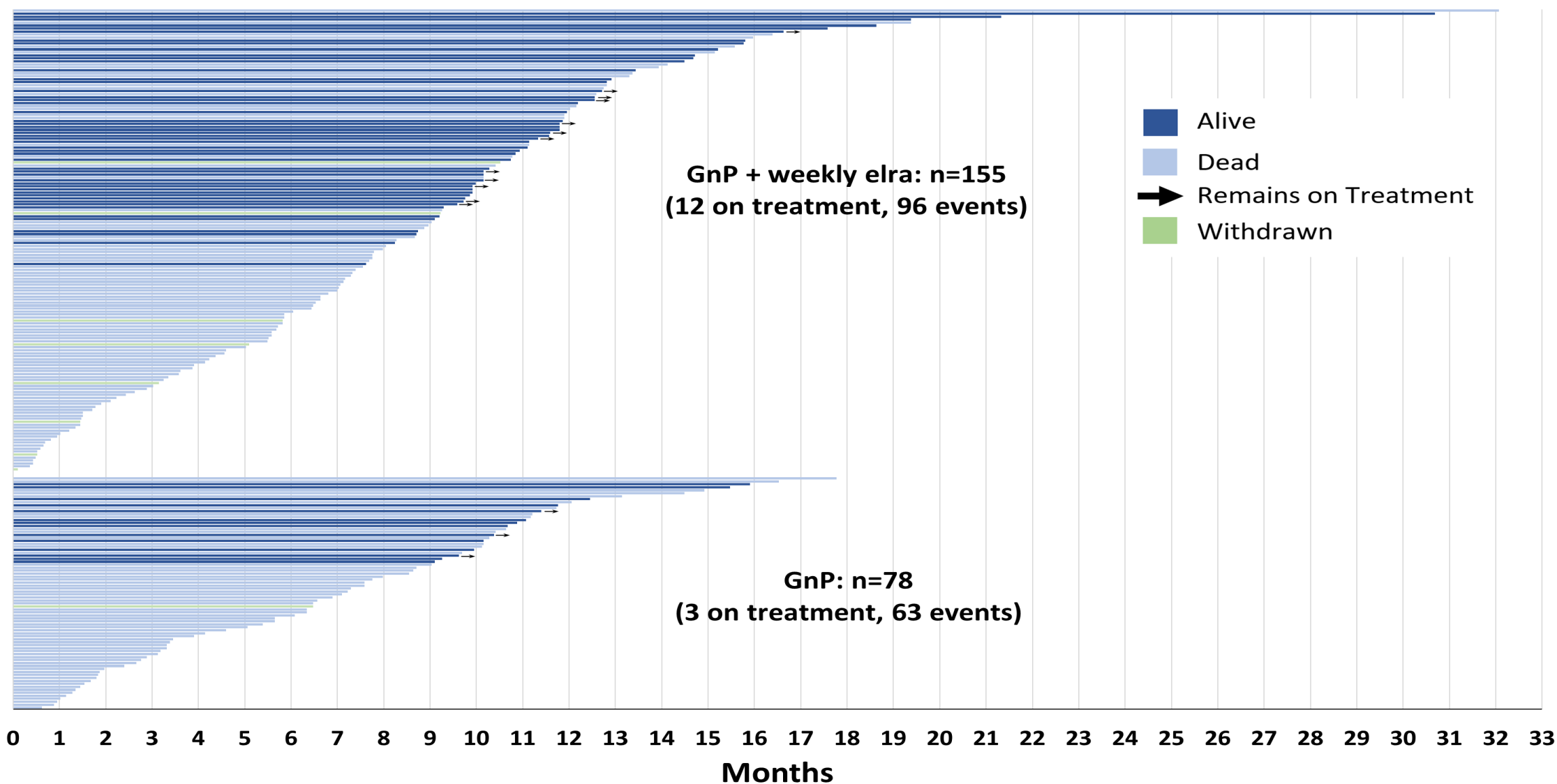
	GnP (78)	Elraglusib/GnP (155)
Primary Endpoint: 1 Year OS (%) p=0.002	22.5	43.6
Primary Endpoint: mOS (months) HR=0.63; log-rank p=0.016	7.2	9.3
Events(% events)	63 (80.8%)	96 (61.9%)
18-month OS (%)	0	20.9
24-month OS (%)	0	16.7
mPFS (months) HR=0.91; P=NS	4.9	5.6
Events(% events)	70 (89.7%)	128 (82.6%)
DCR	33.3%	42.6%
ORR n(%)	16 (20.5%)	43 (27.7%)

The administrative analysis of interim data indicates that >80% of the patients in the GnP control group progressed and were no longer receiving GnP



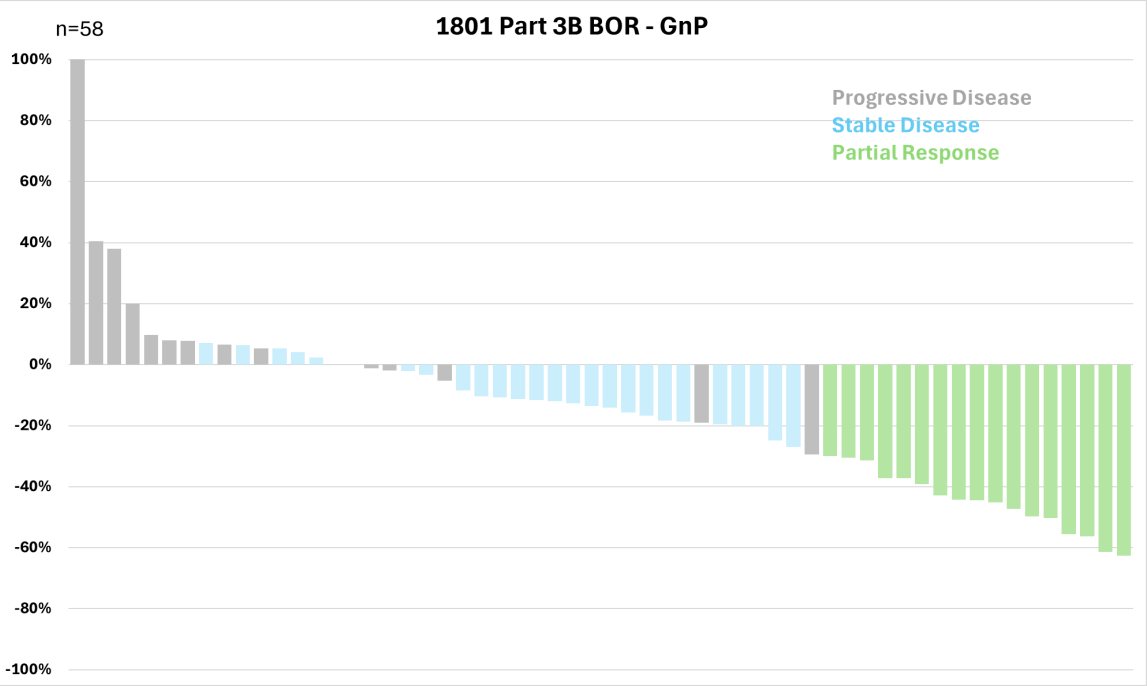
The final data and results may change as the study continues through completion

Administrative Analysis of 1801 Part 3B OS Swim Plot

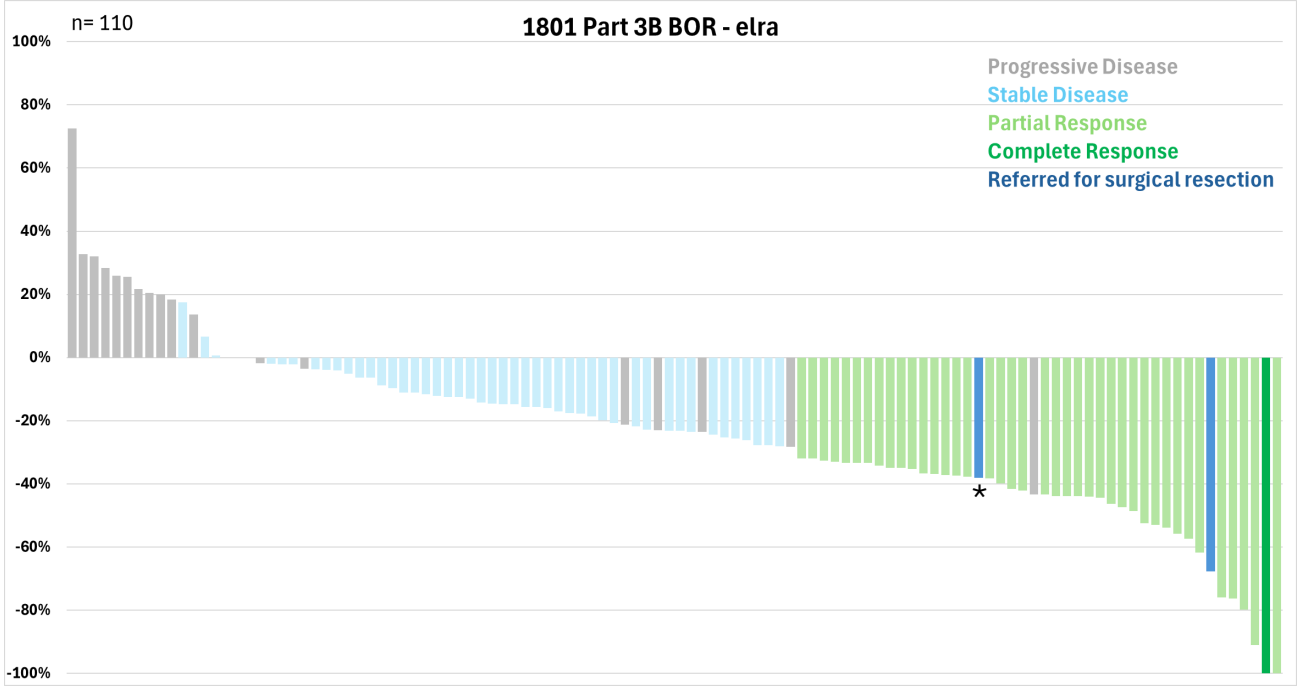


Phase 2 RCT in First-Line Metastatic PDAC - Best Overall Response

1801 Part 3B: GnP Best Overall Response



1801 Part 3B: GnP + Weekly Elra Best Overall Response



* Patient reported as 100% tumor reduction as of November 22, 2024

Predefined Safety Population
Draft unaudited data as of November 15th, 2024

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

Adverse event	Patients, n (%)			
	Elraglusib + GnP		GnP	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	(N=155)		(N=78)	
Any TEAE	155 (100)	139 (89.7)	77 (98.7)	63 (80.8)
Serious TEAE	84 (54.2)	79 (50.9)	45 (57.7)	44 (56.1)
Leading to Stoppage of Any Study Drug	26 (16.8)	17 (10.9)	16 (20.5)	14 (17.9)
Leading to death	19 (12.3)	19 (12.3)	13 (16.7)	13 (16.7)
TEAEs of any Grade in ≥20% of Patients				
Visual Impairment	103 (66.5)	1 (0.6)	7 (9.0)	0
Fatigue	96 (61.9)	25 (16.1)	40 (51.3)	4 (5.1)
Neutropenia*	94 (60.6)	80 (51.6)	32 (41.0)	23 (29.5)
Diarrhea	92 (59.4)	15 (9.7)	37 (47.4)	6 (7.7)
Nausea	88 (56.8)	11 (7.1)	38 (48.7)	4 (5.1)
Alopecia	71 (45.8)	0	26 (33.3)	0
Anemia**	67 (43.2)	38 (24.5)	35 (44.9)	23 (29.5)
Decreased appetite	62 (40.0)	9 (5.8)	20 (25.6)	5 (6.4)
Thrombocytopenia***	57 (36.8)	15 (9.7)	22 (28.2)	6 (7.7)
Vomiting	57 (36.8)	5 (3.2)	29 (37.2)	1 (1.3)
Edema peripheral	52 (33.5)	3 (1.9)	21 (26.9)	0
Constipation	48 (31.0)	3 (1.9)	23 (29.5)	1 (1.3)
Pyrexia	43 (27.7)	2 (1.3)	19 (24.4)	1 (1.3)
Abdominal pain	42 (27.1)	14 (9.0)	15 (19.2)	2 (2.6)
Weight decreased	42 (27.1)	5 (3.2)	15 (19.2)	4 (5.1)
Peripheral sensory neuropathy	38 (24.5)	4 (2.6)	18 (23.1)	0
Hypokalemia	34 (21.9)	7 (4.5)	20 (25.6)	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

Key Takeaways

- Visual impairment and fatigue were major TEAE attributed to elraglusib as a single agent in 1801 Part 1 and were mild to moderate¹
 - Transient visual impairment described as transient alterations in color and skin tones under fluorescent light
 - No permanent changes to eye structure or vision
- Overall rate of a TEAE and/or a 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

¹Carneiro 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

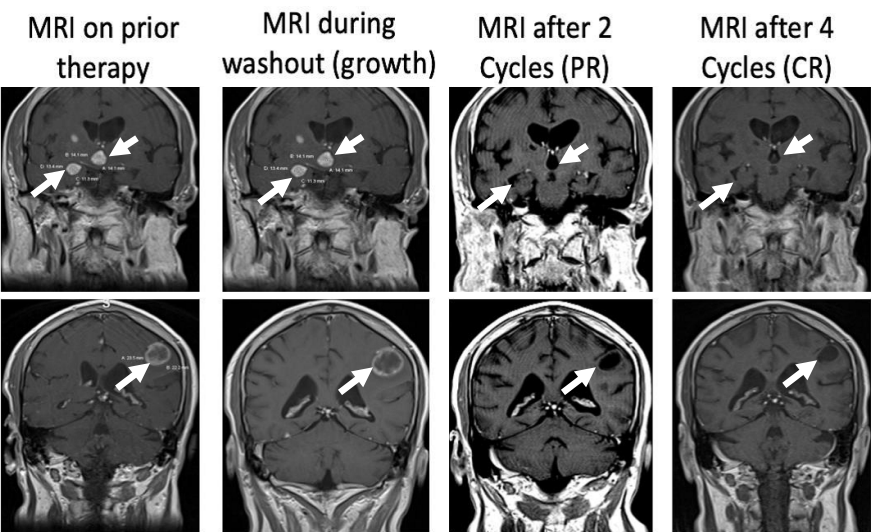
Clinical Activity in Areas of High Unmet Need in 1801 Part 1 and 2

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 >5.5 years as of November 15, 2024)**

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
- **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



Elraglusib Potential in High Unmet Need-Pediatric Oncology



Developing Elraglusib for the Treatment of Refractory Ewing Sarcoma

Ewing sarcoma is the second most common malignant bone tumor in children, adolescents, and young adults, with >200 cases diagnosed in the US each year



Patients that have metastasis and disease recurrence after chemotherapy have short survival of 3-8 months¹



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



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

Objective Responses and Prolonged Survival in Ewing Sarcoma



8 patients with EWS and EWS-related sarcomas with disease progression prior to joining the study received the combination of elraglusib+cyclophosphamide/topotecan in 1902

1 patient has **CR** which continues for > 2 years

1 patient has a **durable ongoing CMR*** with no detectable lesions by FDG-PET

1 patient with DSRCT had **PR** with 52% reduction in tumor

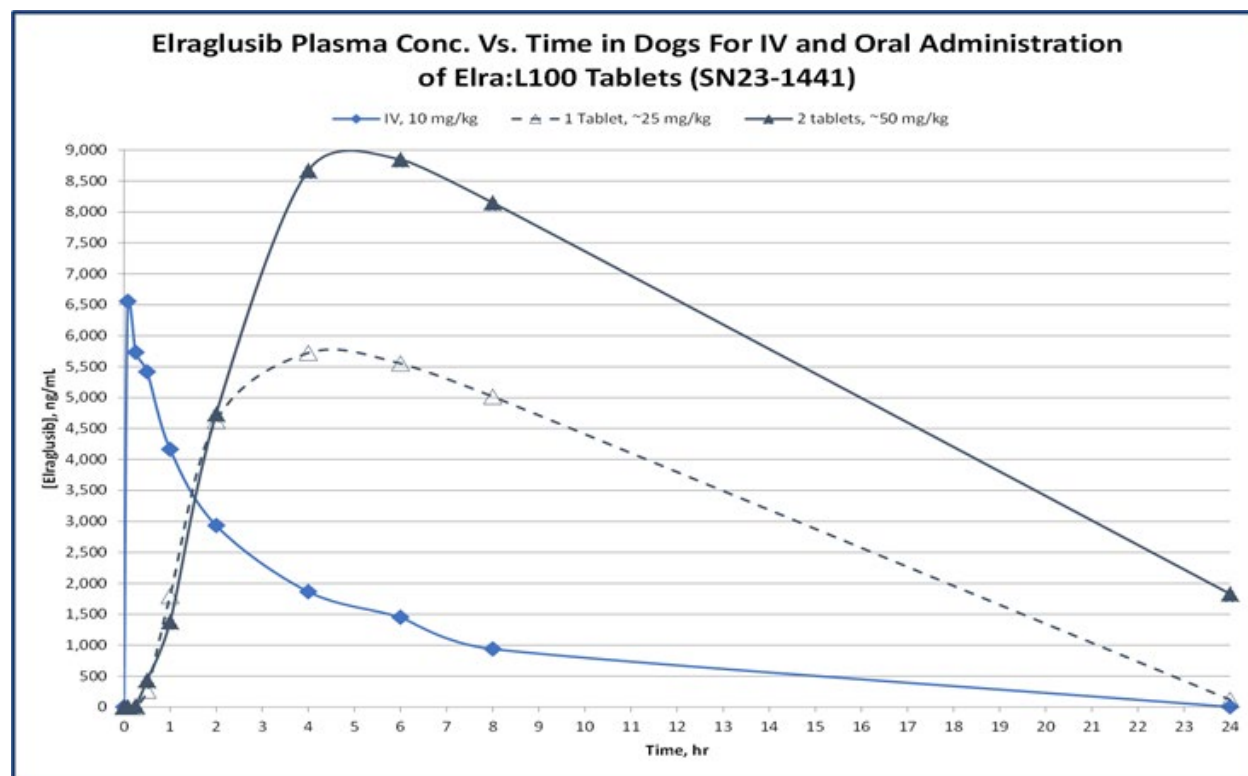
2 patients had BOR of SD

4/8 patients remain alive

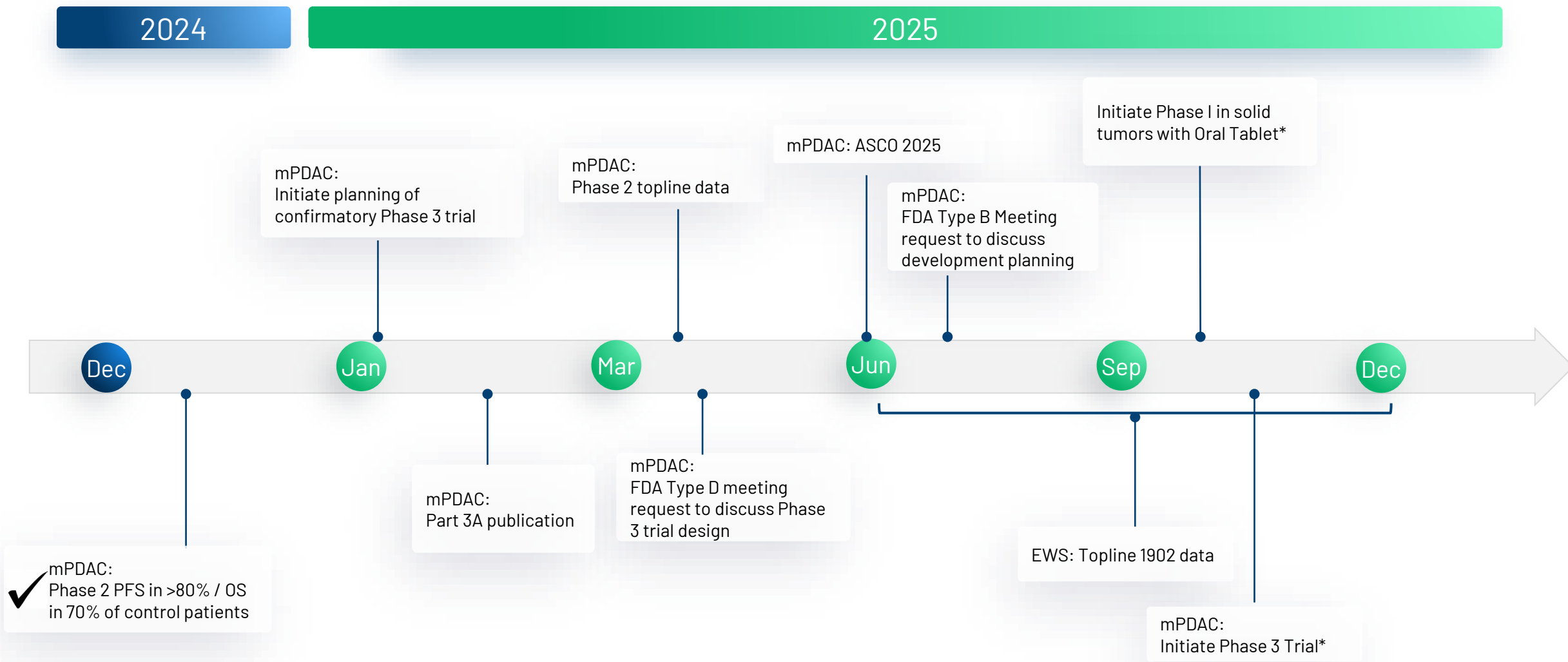
Elraglusib Oral Formulations Provide Similar Drug Exposures to IV

- Decreased cost of manufacturing at commercial scale compared to IV formulations
- Phase 1 Study of Oral Solution in Normal Healthy Volunteers (NHV) showed >50% bioavailability vs IV after a single dose
 - Exposure and pharmacodynamic effects exhibited in fed/fasted patients
- Oral Solid >95% bioavailability vs IV when dosed with food
- Phase 1 dose escalation study using Elraglusib Oral Tablet in advanced cancer patients (not healthy volunteers) in planning stage

Elraglusib Arithmetic Mean Concentration-Time Profiles



Key Near Term Anticipated Development Plans and Milestones



*Timing Contingent Upon Future Funding

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



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



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



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



Investment Highlights



Leading Therapeutic Profile

Extensive data on activity from leading research institutions and promising clinical data in multiple cancer histologies



Significant Unmet Needs

Developing elraglusib to address therapeutic shortcomings in key difficult-to-treat and refractory tumors



Complementary Mechanisms of Action

Focus on mediating cancer cell survival and chemoresistance through regulation of NF- κ B and regulating antitumor immune response



Robust IP Portfolio

Expansive, global patent portfolio with significant exclusivity runway



Clearly Defined Regulatory Path

Multiple key regulatory designations available (Fast Track, Orphan Drug) with registration path clinical trials underway and in development



Seasoned Leadership Team

Distinguished leadership and recognized world leading scientific advisory team



The Passion to Pursue More

