ACTUATE THERAPEUTICS

Corporate Overview

September 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 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. In addition, any forward-looking statements are qualified in their entirety by reference to the factors discussed under the heading "Risk Factors" in our final prospectus filed with the SEC on August 13, 2024 pursuant to Rule 424(b)(4) under the Securities Act with respect to our Registration Statement on Form S-1 (File No. 333-279734) and other filings with the SEC.

Company Highlights

Advancing a class-leading GSK-3β 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 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 and Fast Track Designations for pancreatic and other cancer types

IPO: August 2024

NASDAQ: ACTU

HEADQUARTERS: Fort Worth, TX

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Elraglusib: Multimodal MOA Supported by Clinical Data

- Elraglusib is an ATP-competitive inhibitor of GSK-3β

- GSK-3β 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

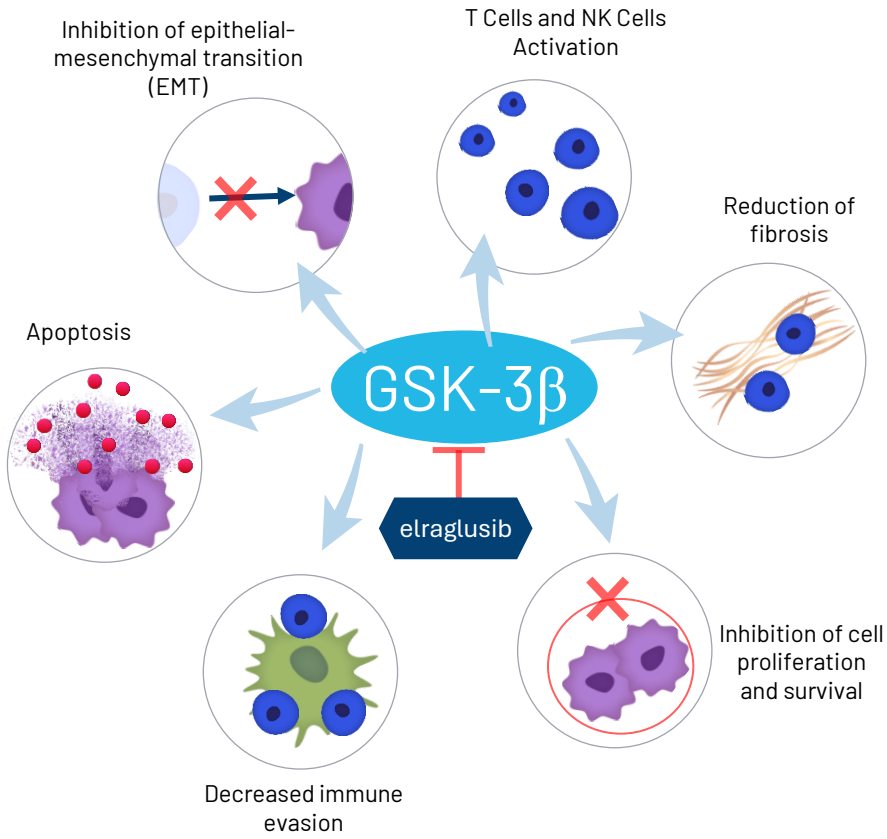
- NF-kB pathway-anti-apoptotic protein expression

- Alterations in TGF-b 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



DDR: DNA Damage Response Source, Walz et al., Clinical Cancer Research 2017; DOI: 10.1158/1078-0432.

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Strategic Pipeline Growth for GSK-3β Associated Diseases

Elraglusib (injection)	Program	Preclinical	Phase 1	Phase 2	Phase 3	Milestones
Pancreatic Cancer (with GnP) 1st line metastatic	Adult Actuate-1801				★	Administrative analysis of interim data: Q4 2024 Topline Data: Q1 2025
Ewing Sarcoma Patients Only	Pediatric Actuate-1902					Topline Data: 2H 2025
Elraglusib (oral)						
Advanced, refractory solid cancers	Adult Actuate-2401	*In planning*				TBD
Advanced, refractory cancer (solid and hematological)	Pediatric	*In planning*				TBD

★ *Fast track designation*

Ongoing Trial

GnP: gemcitabine/nab-paclitaxel
FPFD: First patient first dose
RP2D: Recommended Phase 2 Dose

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Clinical Study Actuate-1801

Phase 1/2 Study Design for Elraglusib Injection

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 protocol

1801 - Part 1

Elraglusib Monotherapy Dose Escalation

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

1801 - Part 3

Company Sponsored Phase 2 Studies

1801 - Part 3A

First Line mPDAC GnP + elraglusib Simon Two-Stage (International)

1801 - Part 3B

First line mPDAC GnP + elraglusib Randomized Controlled Trial (International)

Completed

Ongoing

GnP: gemcitabine/nab-paclitaxel

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Safety Profile of Elraglusib

As Monotherapy and in combination with chemotherapy

Treatment-Emergent Adverse Events of Any Grade Reported in ≥20% of Patients Treated with elraglusib in Actuate 1801 Part 1 and 2

Patients, n (%)				
Adverse event	Elraglusib monotherapy Part 1 (N=67)		Elraglusib with chemotherapy Part 2 (N=171)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TEAE	67 (100)	37 (55.2)	171 (100)	124 (72.5)
Serious TEAE	29 (43.3)	26 (38.8)	72 (42.1)	67 (39.2)
Leading to treatment discontinuation	6 (9)	4 (6)	36 (21.1)	30 (17.5)
Leading to death	5 (7.5)	5 (7.5)	18 (10.5)	18 (10.5)
TEAEs of any Grade in ≥20% of Patients				
Visual impairment	34 (50.7)	0	104 (60.8)	1 (0.6)
Fatigue	32 (47.8)	2 (3)	86 (50.3)	8 (4.7)
Nausea	25 (37.3)	1 (1.5)	77 (45)	3 (1.8)
Diarrhea	21 (31.3)	3 (4.5)	52 (30.4)	6 (3.5)
Anemia	17 (25.4)	4 (6)	80 (46.8)	43 (25.2)
Vomiting	17 (25.4)	1 (1.5)	47 (27.5)	5 (2.9)
Headache	16 (23.9)	0	36 (21.1)	1 (0.6)
Abdominal pain	12 (17.9)	3 (4.5)	38 (22.2)	6 (3.5)
Neutrophil count decrease	2 (3)	2 (3)	45 (26.3)	36 (21.1)
Platelet count decrease	1 (1.5)	0	50 (29.2)	27 (15.8)
White blood cell count decrease	Not reported	Not reported	42 (24.6)	28 (16.3)

Treatment-Emergent Adverse Events of Any Grade Reported in ≥20% of Patients Treated with elraglusib (December 31, 2023) in Actuate 1801 Part 3B (ongoing)

Patients, n (%)				
Adverse event	Elraglusib with Nab-Paclitaxel + Gemcitabine (N=139)		Nab-Paclitaxel + Gemcitabine (N=62)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TEAE	128 (92.1)	105 (75.5)	54 (87.1)	33 (53.2)
Serious TEAE	63 (45.3)	60 (43.2)	25 (40.3)	23 (37.1)
Leading to Stoppage of Any Study Drug	19 (13.7)	16 (11.5)	8 (12.9)	8 (12.9)
Leading to death	13 (9.4)	13 (9.4)	8 (12.9)	8 (12.9)
TEAEs of any Grade in ≥20% of Patients				
Visual impairment	80 (57.6)	0	3 (4.8)	0
Neutropenia[1]	67 (48.2)	63 (45.3)	17 (27.4)	11 (17.7)
Fatigue	64 (46)	15 (10.8)	18 (29)	1 (1.6)
Nausea	61 (43.9)	10 (7.2)	19 (30.6)	1 (1.6)
Diarrhea	57 (41)	11 (7.9)	19 (30.6)	2 (3.2)
Anemia[2]	45 (32.4)	25 (18)	14 (22.6)	8 (12.9)
Alopecia	43 (30.9)	1 (0.7)	18 (29)	0
Decreased appetite	41 (29.5)	5 (3.6)	9 (14.5)	2 (3.2)
Thrombocytopenia[3]	38 (27.3)	11 (7.9)	12 (19.4)	2 (3.2)
Vomiting	36 (25.9)	2 (1.4)	15 (24.2)	1 (1.6)
Constipation	36 (25.9)	2 (1.4)	14 (22.6)	1 (1.6)

1. Includes PT terms neutropenia and neutrophil count decreased
2. Includes PT terms anemia and hemoglobin decreased
3. Includes PT terms thrombocytopenia and platelet count decreased

Key Takeaways

Most adverse events when used as monotherapy were reported as mild to moderate

- Transient visual impairment described as transient alterations in color and skin tones under fluorescent light
- No permanent changes to eye structure or vision
- Visual impairment and fatigue are the two most frequent adverse events attributed to elraglusib
- Visual impairment decreases after a few cycles of treatment

Part 2: 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 marked growth to $4.9 billion by 2026

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

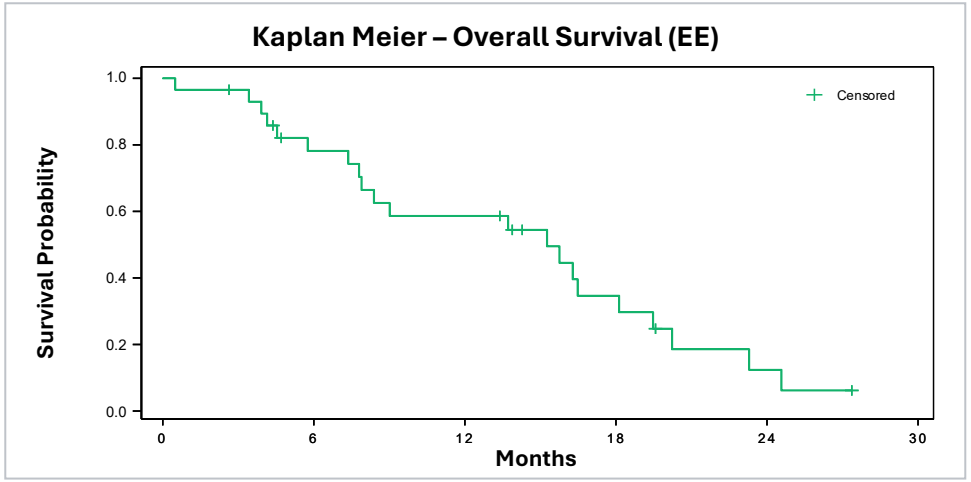
Elraglusib Opportunity

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

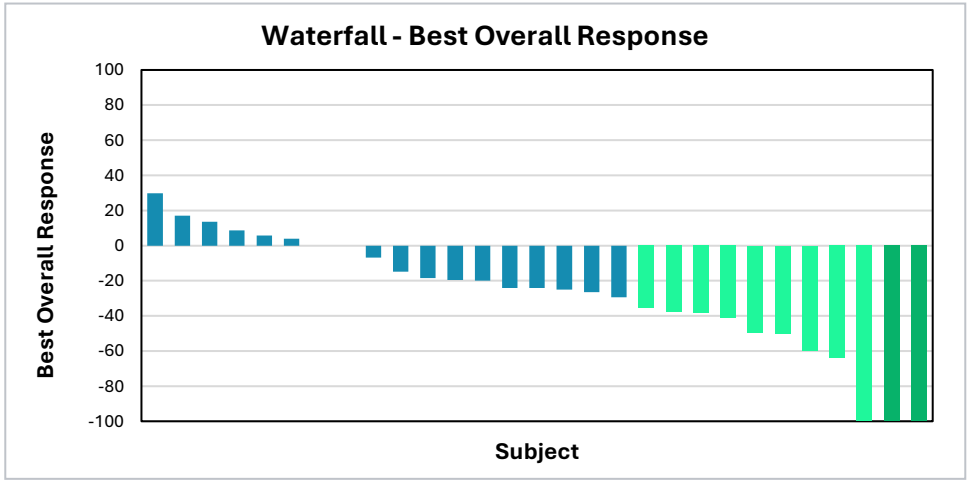
Hu JX, Zhao CF, Chen WB, Liu QC, Li QW, Lin YY, Gao . World J Gastroenterol. 2021 Jul 21;27(27):4298-4321. doi: 10.3748/wjg.v27.i27.4298. PMID: 34366606; PMCID: PMC8316912.
Soefje SA. Managing the economic impact of advanced pancreatic cancer. Am J Manag Care. 2019 Jan;25(1 Suppl):S11-S16. PMID: 30681820.

Phase 2 – Clinical Activity with Extended Median Overall Survival

- Simon's two-stage 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

Wainberg, Zev A et al., The Lancet, Volume 402, Issue 10409, 1272 – 1281; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4631139/
RCT: randomized, controlled trial; PDAC: pancreatic ductal adenocarcinoma; ITT: intent to treat; mITT: modified intent-to-treat; EE: efficacy evaluable;
CR: complete response; PR: partial response; DCR: disease control rate; ORR: overall response rate;

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Phase 2 RCT in First-Line Metastatic PDAC

Inclusion Criteria

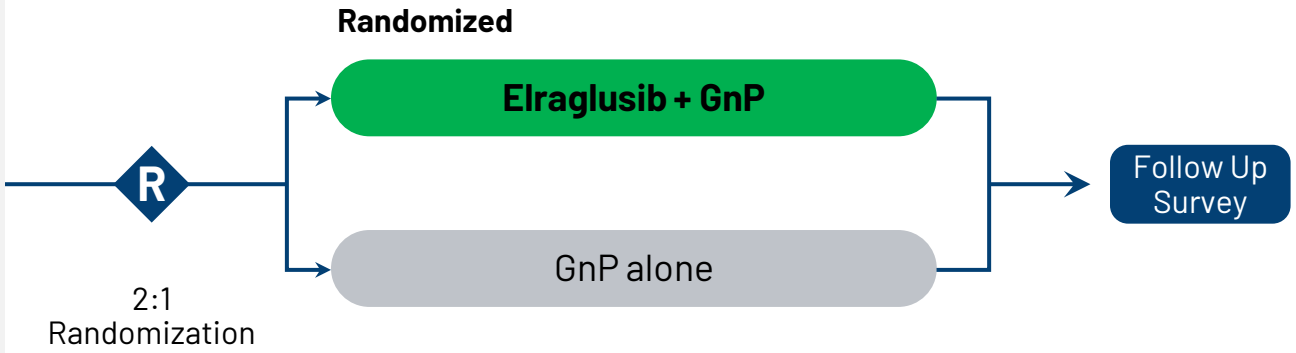
≥ 18 yrs with metastatic pancreatic adenocarcinoma

Participants must have measurable disease as defined RECIST1.1

No prior therapy

Total enrollment: 286

Treatment



Endpoints

Primary endpoint: mOS

Secondary endpoints: ORR, DOR, PFS

Sample size based on increase in 1 year survival from 35% in GnP to 55% in elraglusib/GnP with α=0.05; 232 patients needed for 80% power

60 Global Sites

US 36

EU 18

Canada 6

FPD: August 2021
Enrollment Completion: January 2024
Anticipated Topline Data: Q1 2025

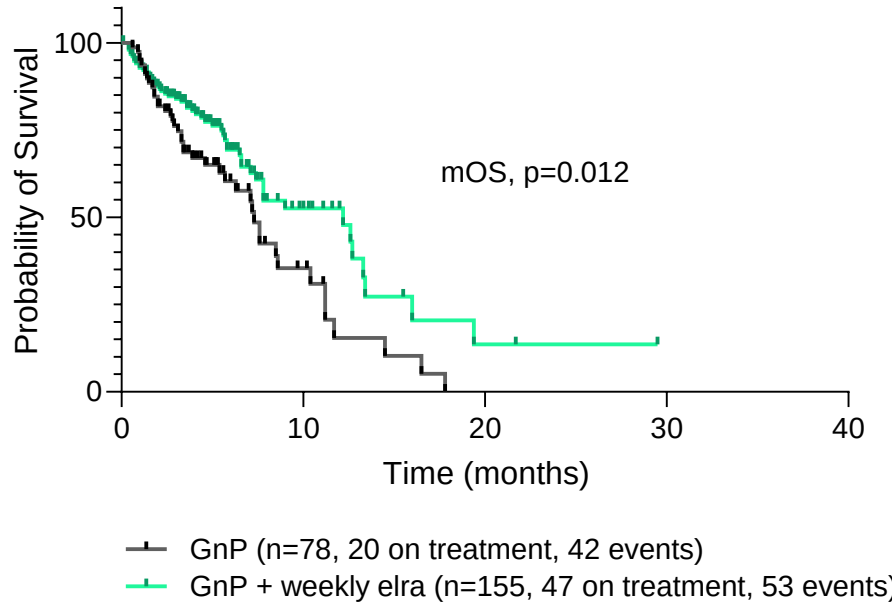
RCT: randomized, controlled trial; PDAC: pancreatic ductal adenocarcinoma; OS: overall survival;
ORR: overall response rate; DOR: duration of response; PFS: progression-free survival, FPD: First Patient Dosed

Significant Improvements in mOS vs GnP

Administrative Analysis of Interim Data from April 30th, 2024, Demonstrates a mOS of 12.2 months

	GnP (78)	Elraglusib/GnP (155)
mOS (months) HR=0.60; log-rank p=0.012	**7.3**	**12.2**
Events (% events)	**42 (53.8%)**	**53 (34.2%)**
12-month OS (%)	**15.5**	**52.5**
18-month OS (%)	**0**	**20.5**
24-month OS (%)	**0**	**13.6**
mPFS (months) HR=0.90; P=NS	**4.6**	**4.8**
Events (% events)	**50 (64.1%)**	**79 (51%)**
ORR n (%) Evaluable for response	**12 (24%)**	**32 (30.8%)**

The administrative analysis of interim data indicates that >50% 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

RCT: randomized, controlled trial; PDAC: pancreatic ductal adenocarcinoma; OS: overall survival; ORR: overall response rate; DOR: duration of response; PFS: progression-free survival

Predefined Safety Population
Draft unaudited data as of April 30, 2024

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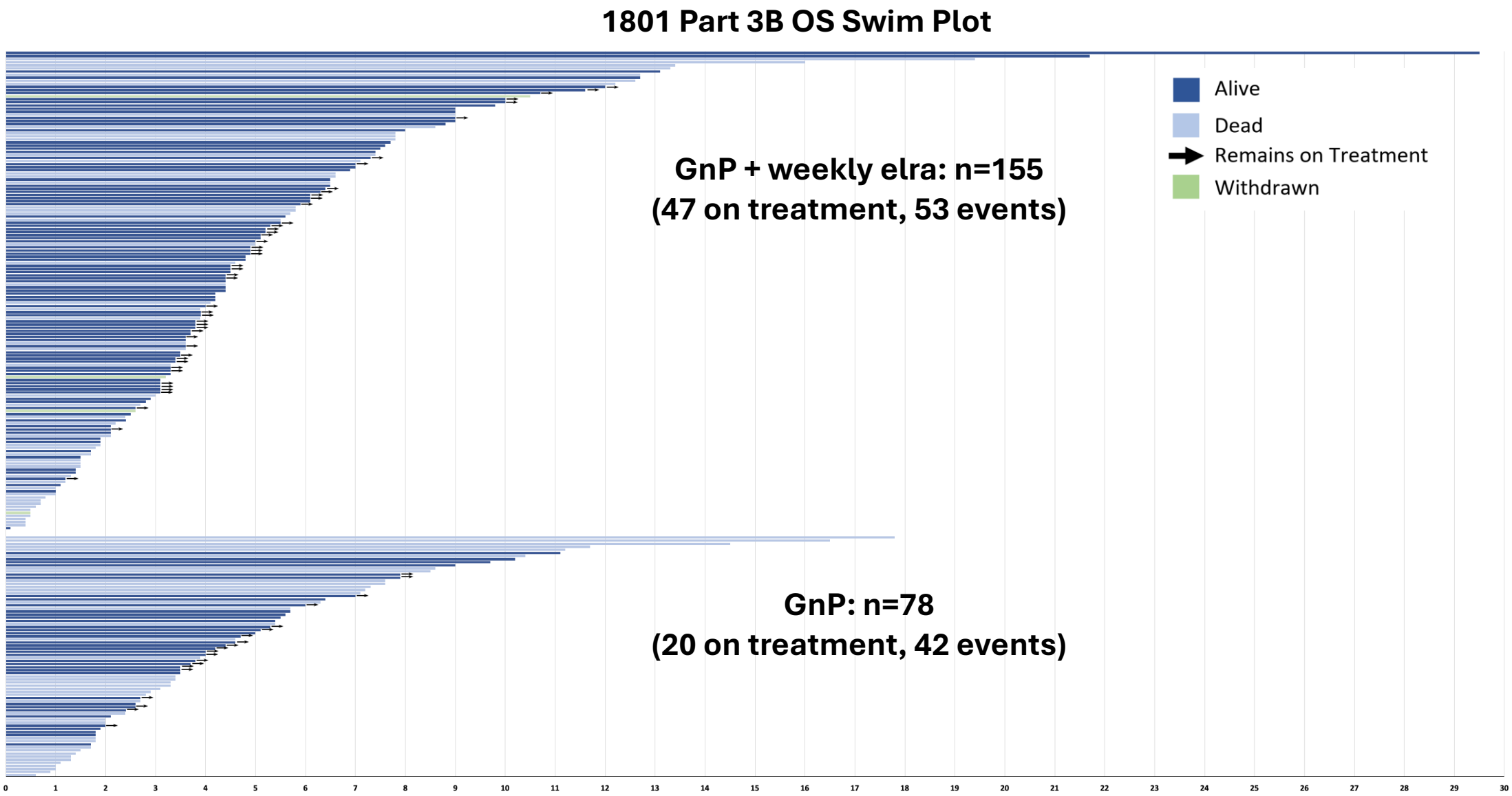
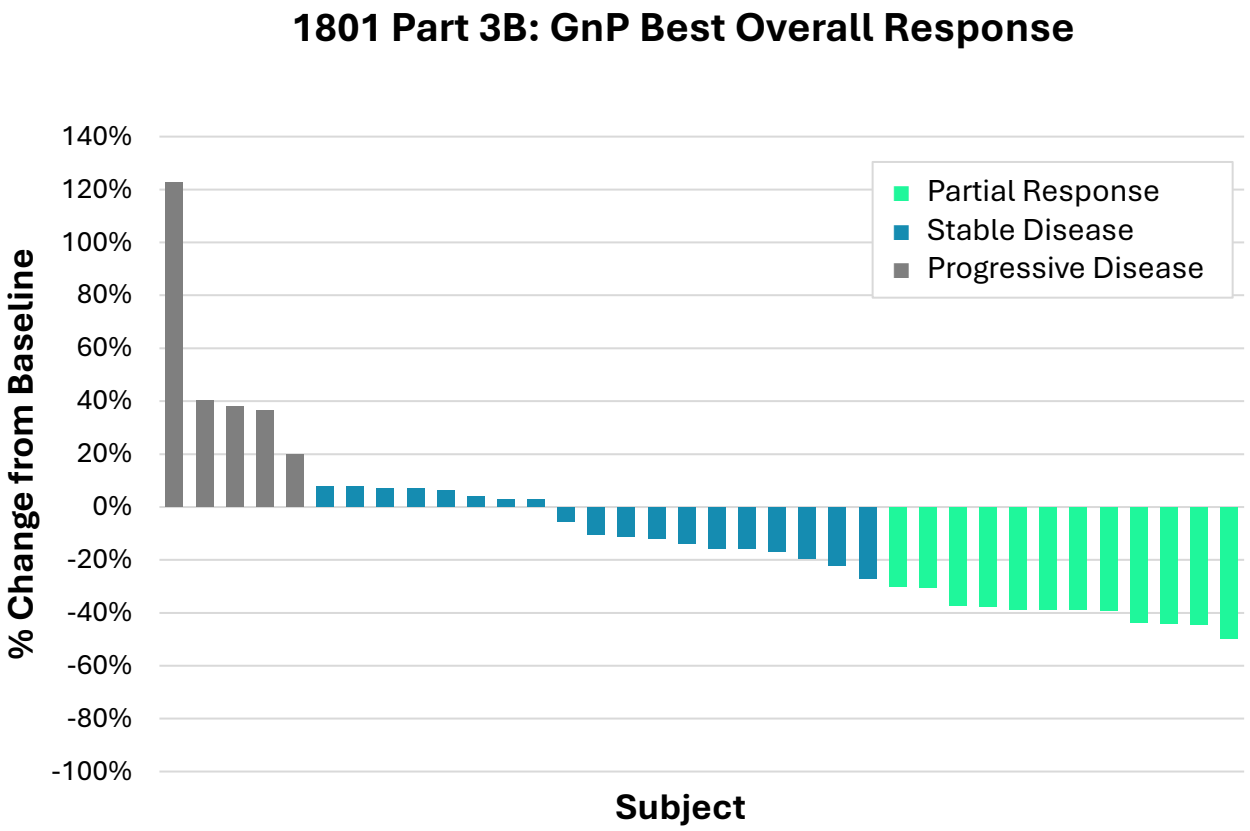
Administrative Analysis Swim Plot

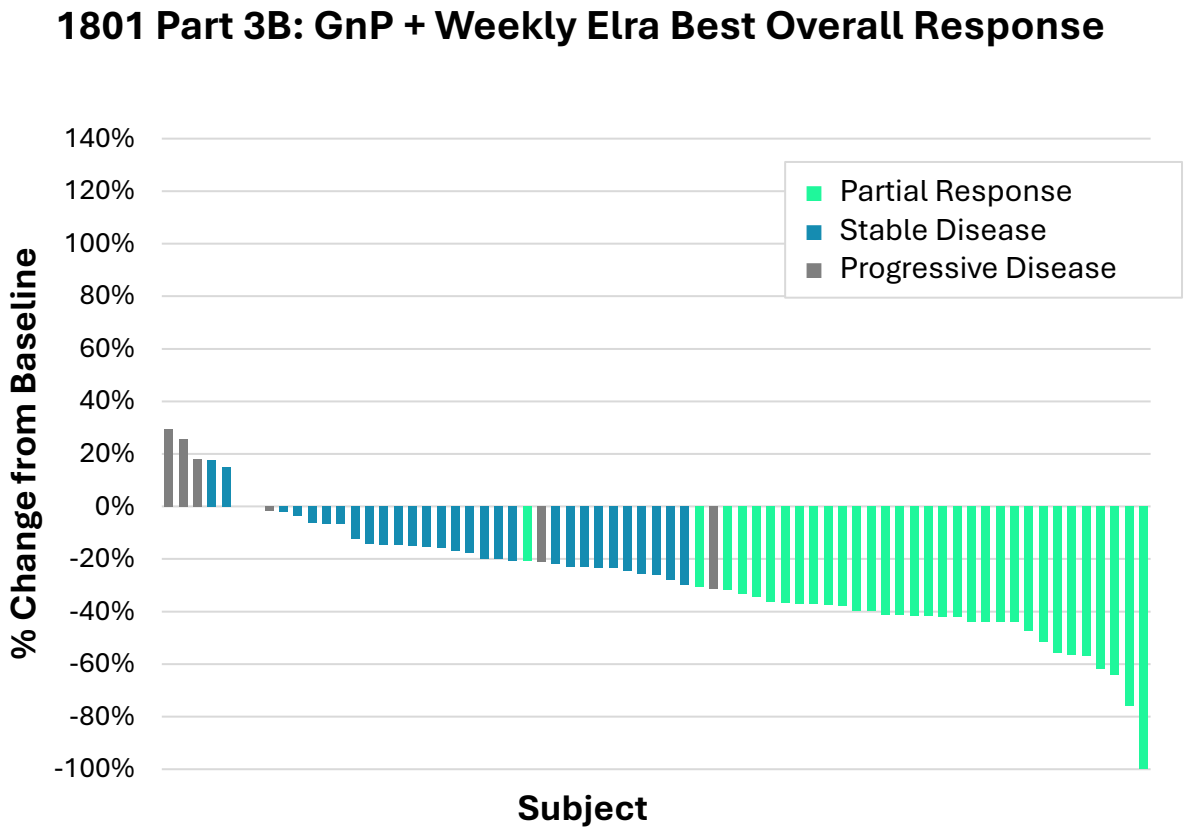


Predefined Safety Population
Draft unaudited data as of April 30, 2024

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

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





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

Predefined Safety Population
Draft unaudited data as of April 30, 2024

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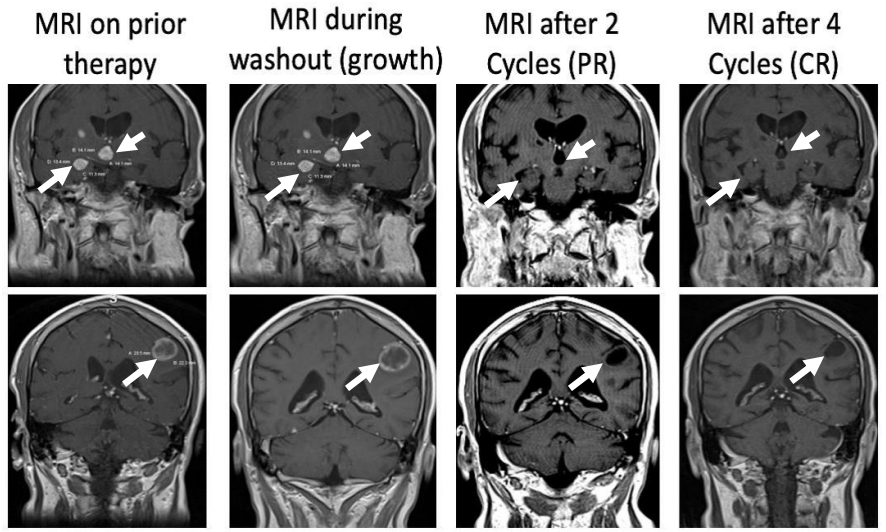
Clinical Activity in Areas of High Unmet Need in 1801 Part 1 and 2

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 (>5.0 years as of February 1, 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 biomarker enrichment to improve the probability of success**



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/Gemcitabine/ nab-paclitaxel	Metastatic Pancreatic Cancer (mPDAC)	15.3 months (Part 3A) 12.2 months (Part 3B)
Elraglusib Monotherapy	Refractory, Metastatic Melanoma	9.1 months
Elraglusib/Irinotecan	Refractory, metastatic Colorectal	6.9 months

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

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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 months[1]

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

1. Van Mater and Wagner. Onco Targets Ther. 2019;12:2279-2288.
Durer S, Gasalberti DP, Shaikh H. Ewing Sarcoma. StatPearls Publishing; 2024 Jan- https://www.ncbi.nlm.nih.gov/books/NBK559183/

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

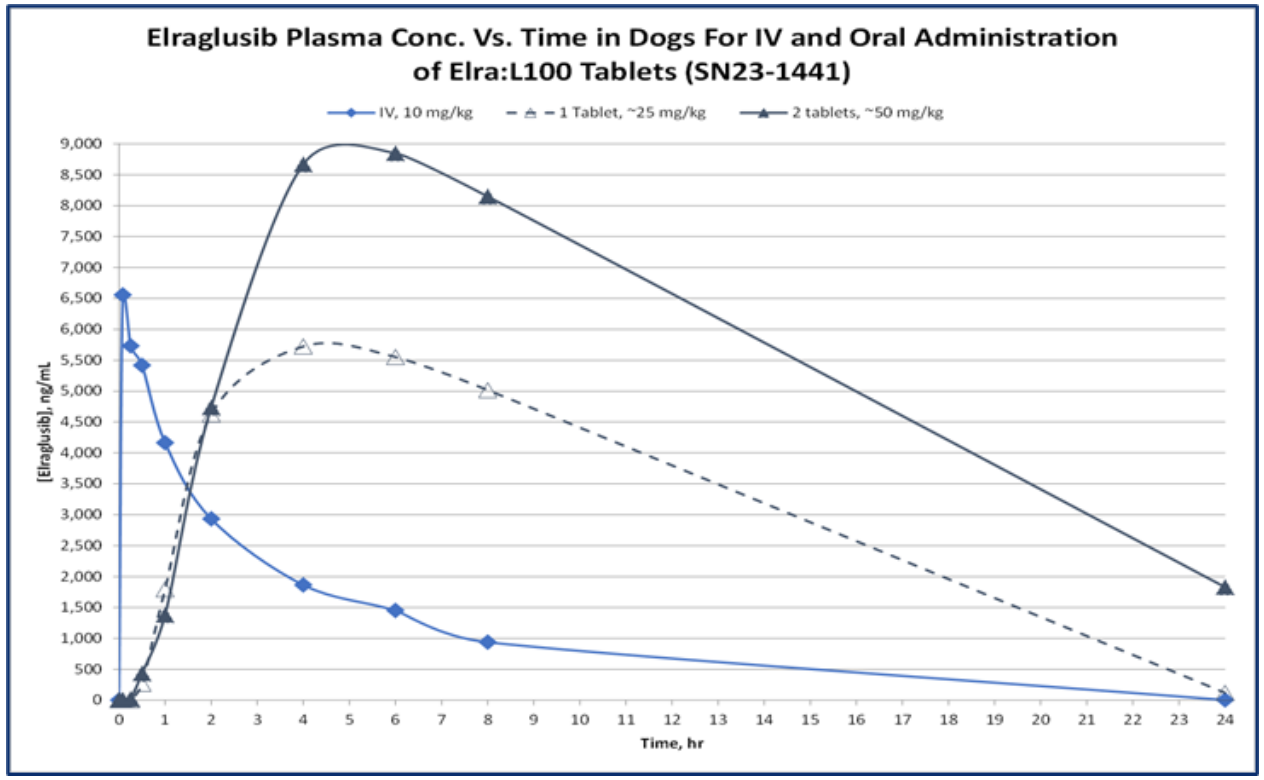
4/8 patients remain alive

CMR: Complete Metabolic Response, CR: Complete Response, PR: Partial Response, DSRCT: Desmoplastic Small Round Cell Tumor, SD: Stable Disease PD: Progressive Disease, BOR: Best Overall Response, FDG-PET: Fluorodeoxyglucose -Positron Emission Tomography

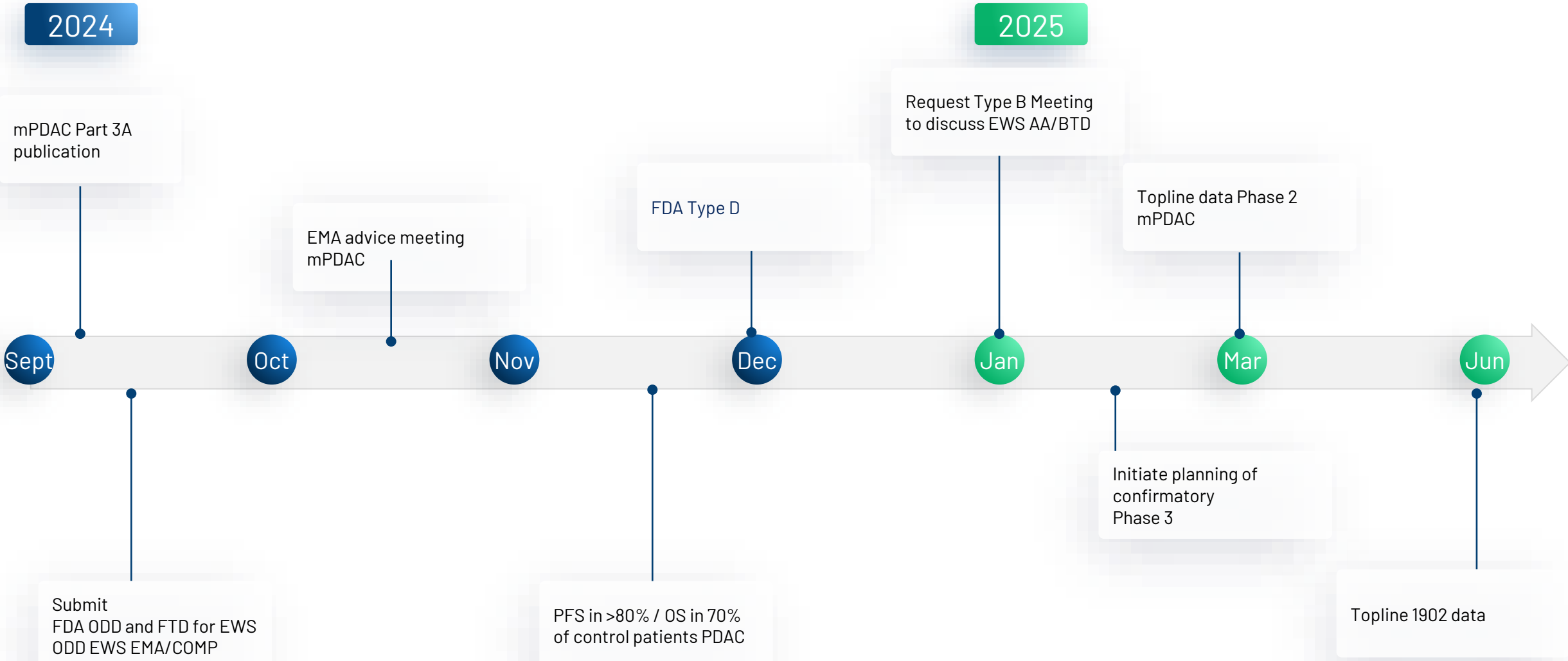
Elraglusib Oral Formulations Provide Similar Drug Exposures to IV

- 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

Elraglusib Arithmetic Mean Concentration-Time Profiles



Key Near Term Anticipated Development Plans and Milestones



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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

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-kB 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, Rare Pediatric) with registration path clinical trials underway and in development
Seasoned Leadership Team	Distinguished leadership and recognized world leading scientific advisory team

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The Passion to Pursue More