ACTUATE THERAPEUTICS

STIFEL 2023 Targeted Oncology Days

Daniel M. Schmitt, President & CEO

April 26, 2023

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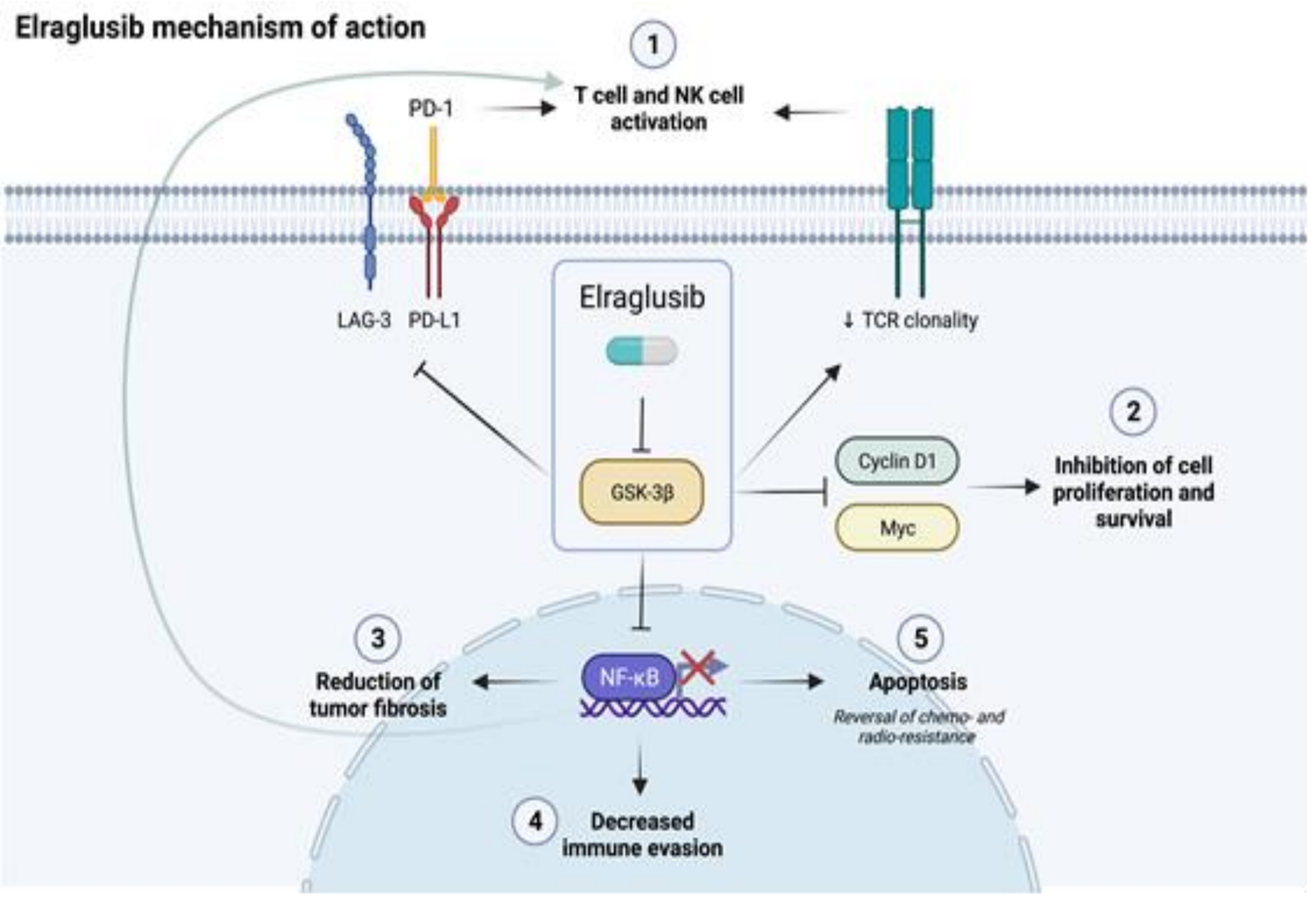
Company Highlights

- ✓ **Clinical stage oncology focused company in multiple advanced cancer phase 2 trials**
- ✓ **Clinical responses (CRs/PRs) and Disease Control across multiple cancer histologies with elraglusib (9-ING-41) IV as single agent and in combination**
- ✓ **Survival benefit in key diseases including PDAC, melanoma, lung cancer, colorectal cancer, and carbo/paclitaxel failures in multiple refractory cancer histologies**
- ✓ **Best in class GSK-3 inhibitor with novel, multimodal MOA**
- ✓ **Oral versions of elraglusib will enter clinic in 2022**
  - **First potential orally dosed I/O agent (amenable for consolidation and maintenance use)**
- ✓ **Blockbuster market potential with broad composition of matter IP protection**
  - **Orphan Drug and Fast Track Designations could accelerate path to registration**

Multimodal MOA Distinguishes Elraglusib from Other Glycogen Synthase Kinase (GSK-3) Inhibitors

Immunomodulatory effects, inhibition of cancer cell proliferation and survival, regulation of epithelial-mesenchymal transition (EMT) and fibrosis in multiple cellular compartments contribute to antitumor effects in progressive and metastatic disease[1]

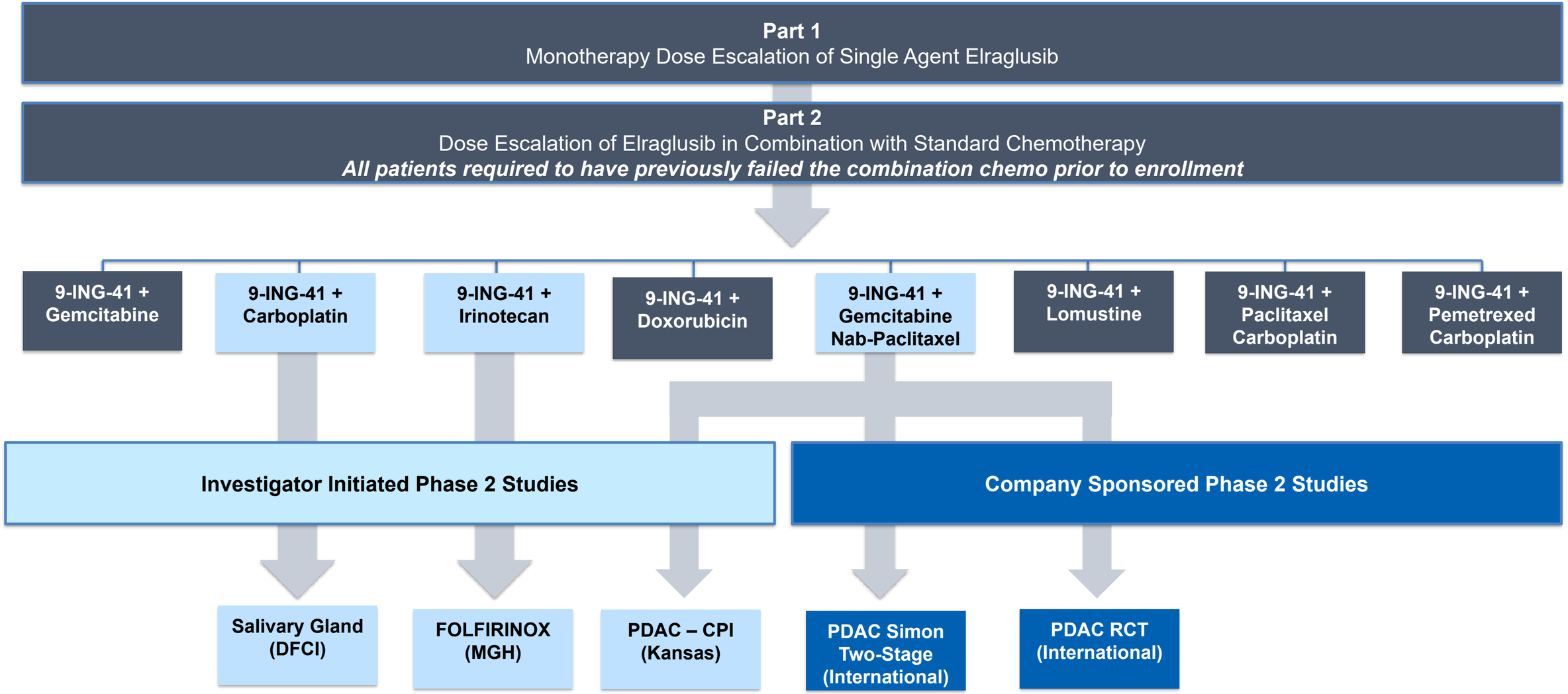
- Elraglusib is a reversible, ATP-competitive inhibitor of GSK-3β
- GSK-3β contributes to tumor progression in many treatment naive and refractory/resistant tumors
  - Pleiotropic effects as signaling adaptor are regulated by different substrates in different cell types
  - Supported by emerging biomarker studies in patient samples obtained in the 1801 trial
- Elraglusib downregulates well-credentialed molecular pathways that lead to chemotherapy and drug resistance
  - NF-κB 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"



(1) Source: Molecular Pathways, 2017; DOI: 10.1158/1078-0432.CCR-15-2240.

Clinical Study 1801 - Phase 1/2 Study Design

Part 3 – Seamless Initiation of Phase 2 Efficacy Studies Based on Part 1 and 2 Results



Complete Response in Melanoma
First Clinical Evidence of Immune Modulator Effects of Elraglusib

First objective response reported in cohort 4 (5 mg/kg) in a patient with metastatic melanoma

- 55 year old male diagnosed with metastatic melanoma in 2018
- Widely metastasized to the brain, lungs, bones, muscles, stomach, lymph nodes, pancreas and adrenal glands. Over 25 lesions in the brain, some larger ones causing headaches and seizures
- Failed all FDA-approved standard therapies, including immunotherapy and BRAF / MEK inhibitor

After 6 Weeks on elraglusib:

- PET scan showed excellent response to therapy with near complete resolution of all tumors and only residual focus of uptake in the stomach; no new lesions

After 12 Weeks on elraglusib:

- Brain MRI showed 8 cystic lesions with no change in size; no new lesions – complete response (CR) by RANO criteria
- PET scan showed no areas of residual uptake and resolution of uptake in the stomach – complete metabolic response (“CMR”)

Further response data:

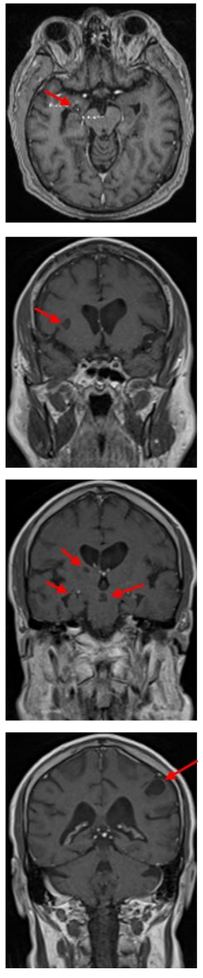
- By RECIST 1.1, durable CR based on target lesions but continued variability in nodes and non-target lesions by PET/CT consistent with other immune modulators which has been durable through most recent scan (8/4/2022)

Durable CR ongoing (~3.8 years as of 2/3/2023)

12 weeks on elraglusib

Complete Metabolic Response

CR; Cystic Lesions

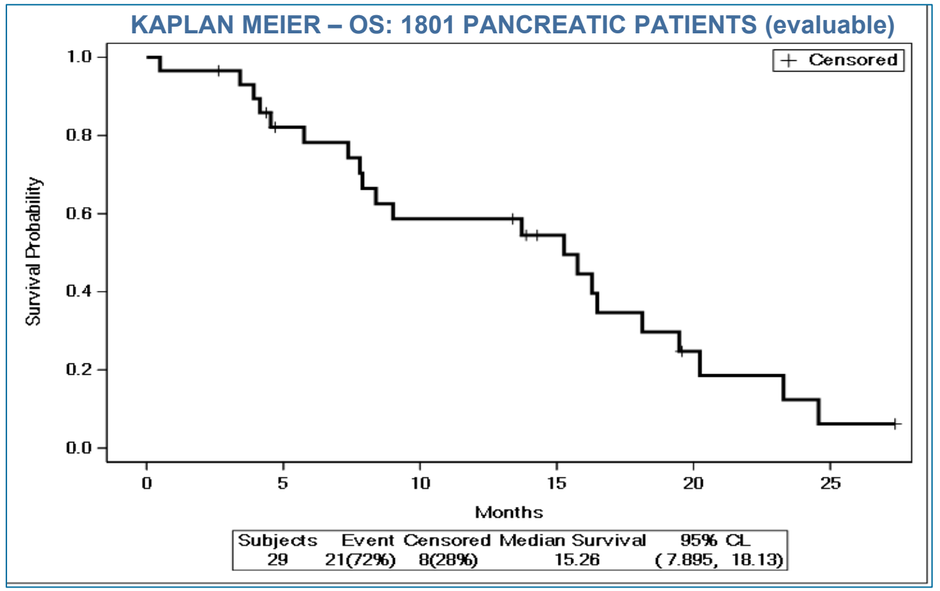


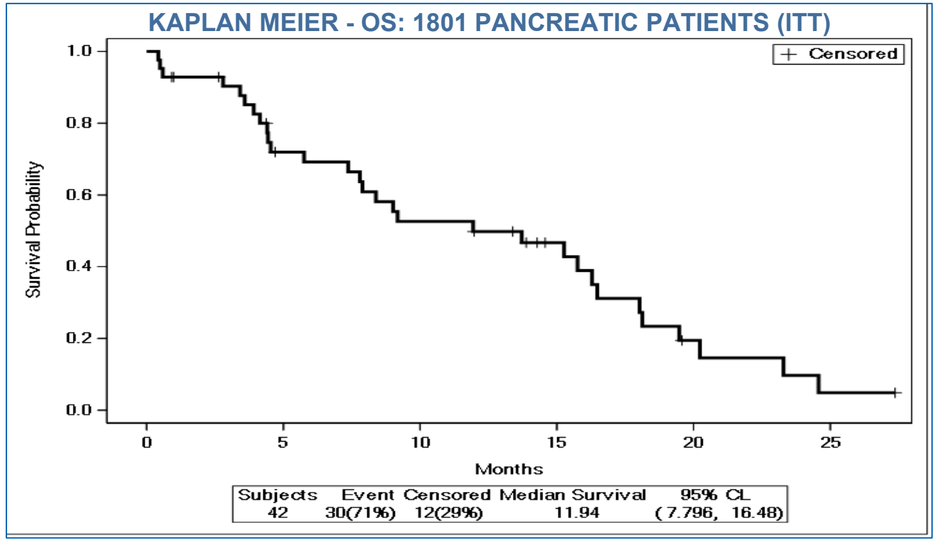
1801 Arm A – Preliminary OS Analysis

- ✓ **Disease control in 1801 Parts 1 and 2 and in PDAC Part 3 suggests immune modulator activity**
  - Typical Phase 1 population associated with rapid progression and short overall survival
  - Traditional response criteria do not predict for observed prolonged survival
  - Higher than expected number of long-term survivors
- ✓ **Finalizing data for ASCO2023 and manuscript submission**

Histology	Avg previous lines of Tx	mOS (1081)[1]	mOS (literature)
Pancreatic (PDAC)	0 (1st line)	15.3 months	8-9 months
Metastatic melanoma	3	9.9 months	3-4 months
1801 carboplatin combinations	3	10.4 months[2]	~4 months
Lung cancer (NSCLC)	2	12.8 months	~4 months
Metastatic CRC[3]	6	> 7.0 months	<2 months
Ovarian	4	7.0 months	ND

[1]mITT population [2]Therapeutic range ≥5 mpk [3] majority RAS mutated





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Draft unaudited data as of 3/08/23.

Phase 2 Clinical RCT in First Line Treatment of Metastatic PDAC

Randomized Control Trial compares Gem/Abraxane versus combination with elraglusib

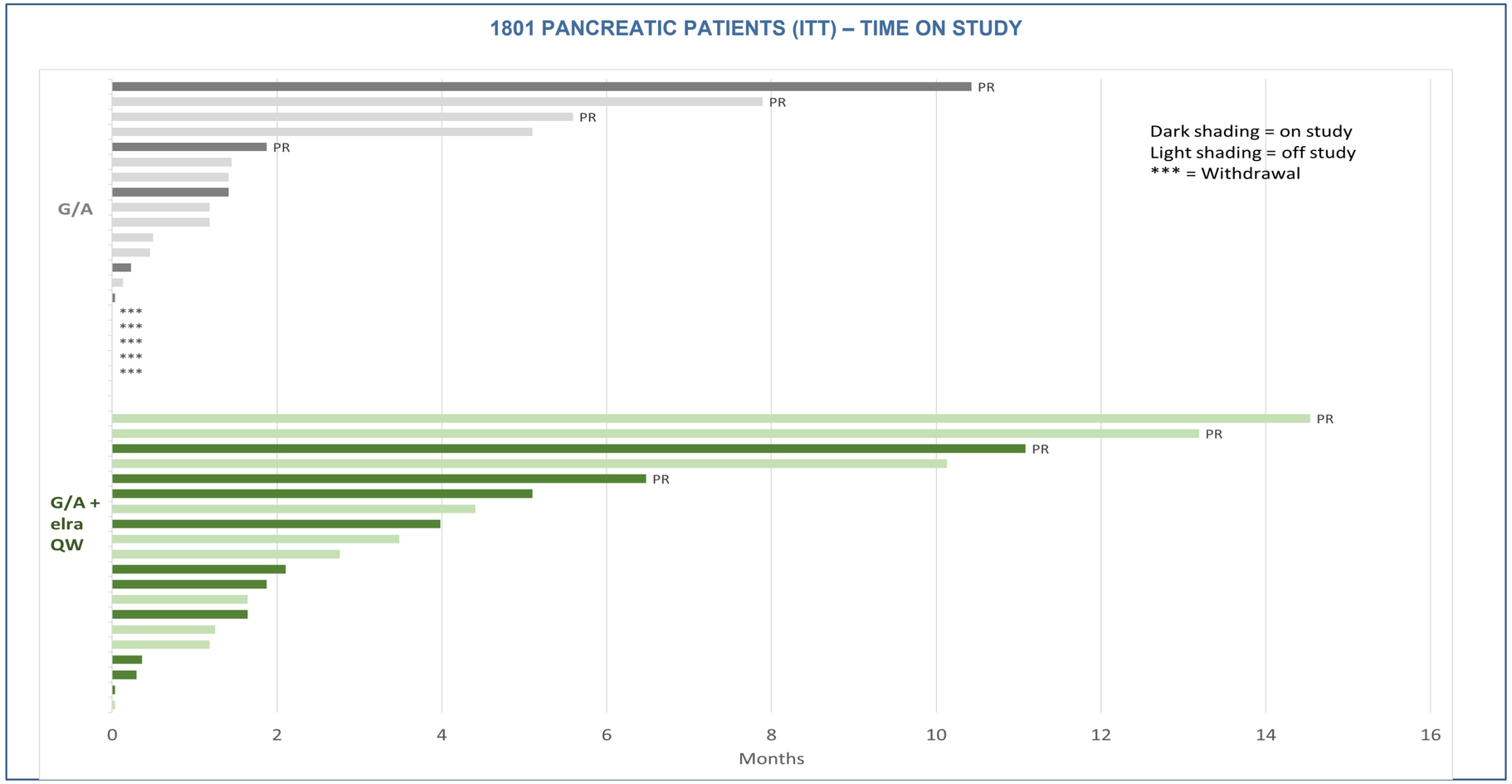
Run-in: Elraglusib schedule determined by a randomized three arm run-in that compared:
Gem-Abraxane (GnP)
QW elraglusib + GnP
BIW elraglusib + GnP

RCT Continuation:
Combination QW elraglusib+GnP vs GnP (2:1 randomization)

Primary endpoint:
1 year survival
Secondary endpoints:
ORR, DOR, PFS, mOS

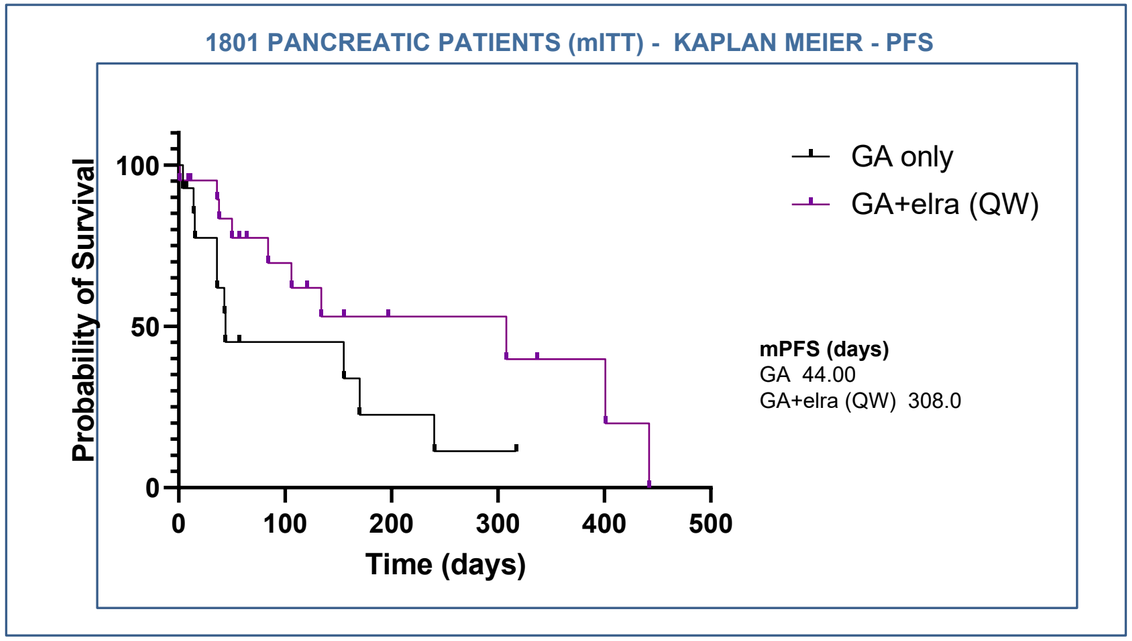
Total enrollment:
Approximately 232 subjects
α 0.05 with 80% power

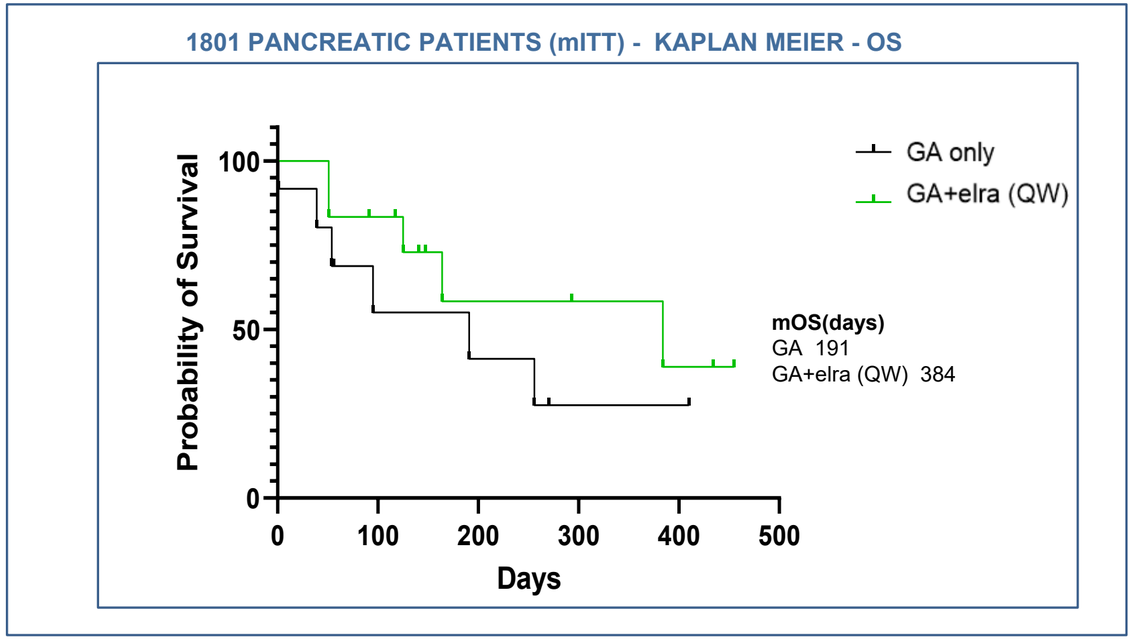
Trial open and enrolling



Phase 2 Clinical RCT in First Line Treatment of Metastatic PDAC

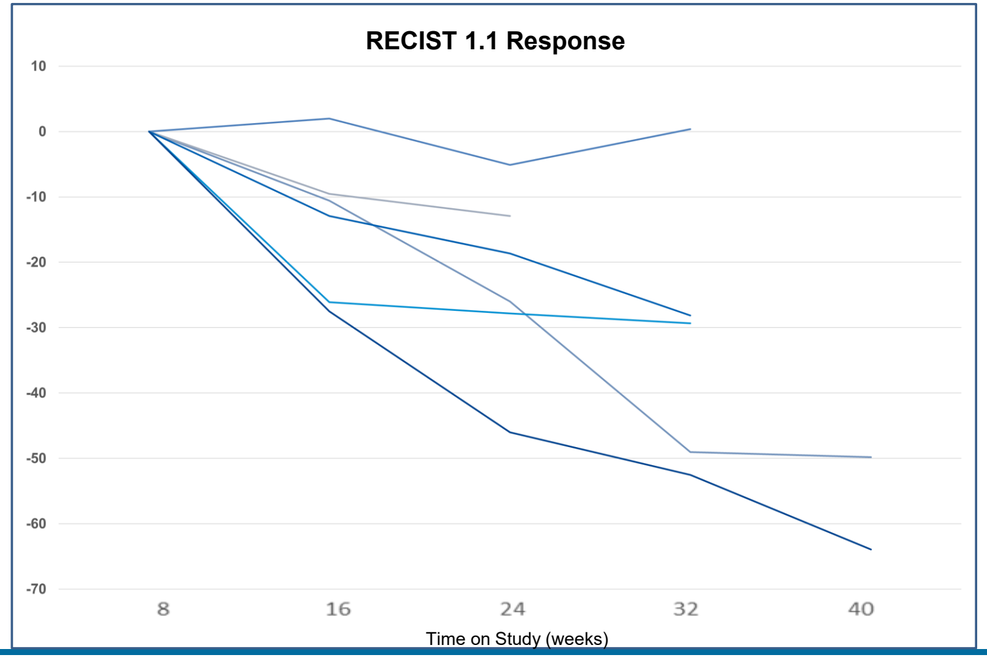
Open Label Randomized Control Trial compares Gem/Abraxane versus combination with elraglusib



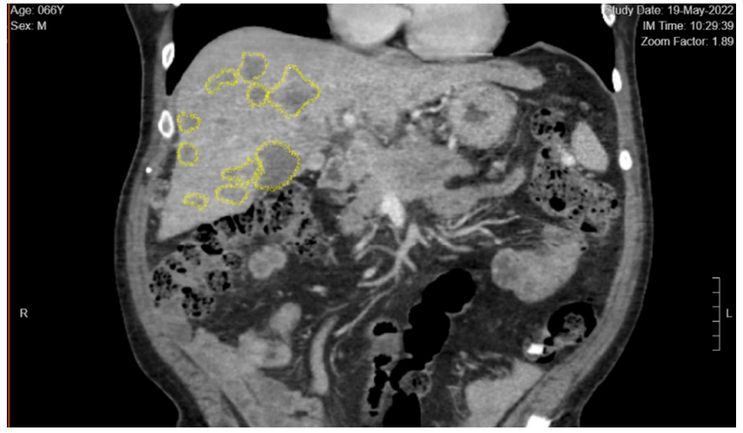


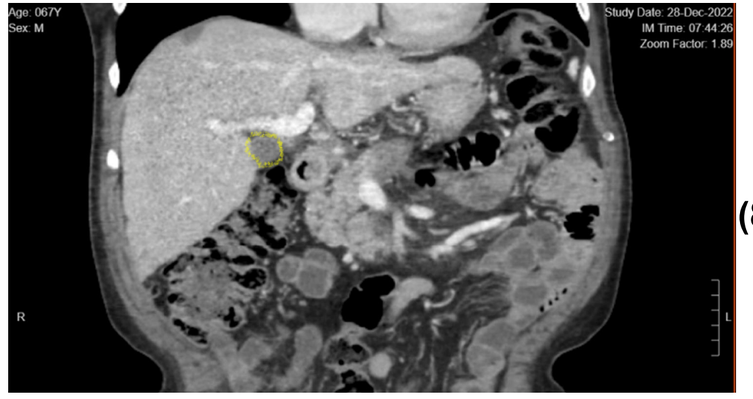
Elra + FOLFIRINOX in First Line PDAC-Initial Results from IIT Study

- Metastatic Pancreatic Cancer (1st line)
- FOLFIRINOX+losartan+elraglusib (RCT)
- IIT at Mass General / Fred Hutchinson (Lustgarten Foundation)
- Tox run-in recently completed (n=6). Patients characterized as having extensive aggressive metastatic disease.
- **NO DLTs. All patients have evidence of response: 2 PR, 2 near PR, 1 with >10% TB reduction, 1 SD (100% DCR)**
- Randomized enrollment across 4 arms just initiated, total of 16 patients enrolled.



Patient A-001

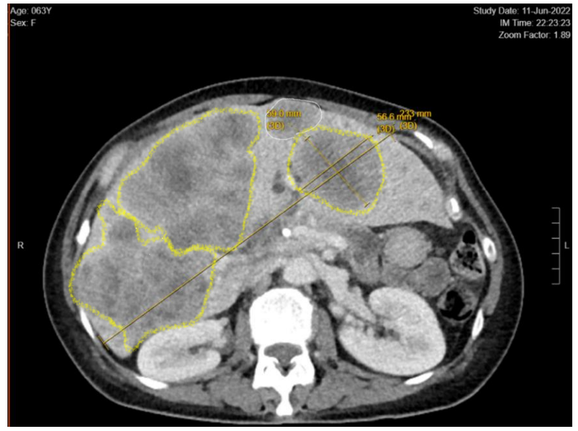


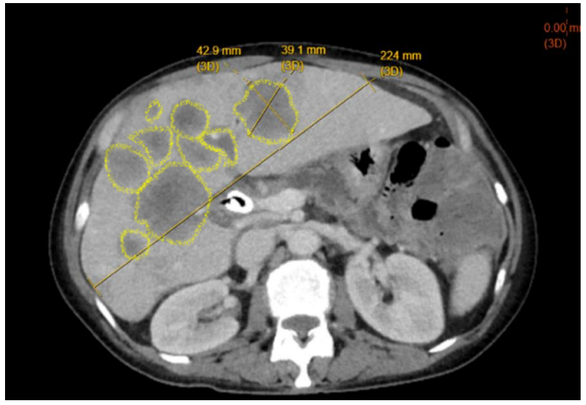


Baseline

Post Cycle 16 (8 months)

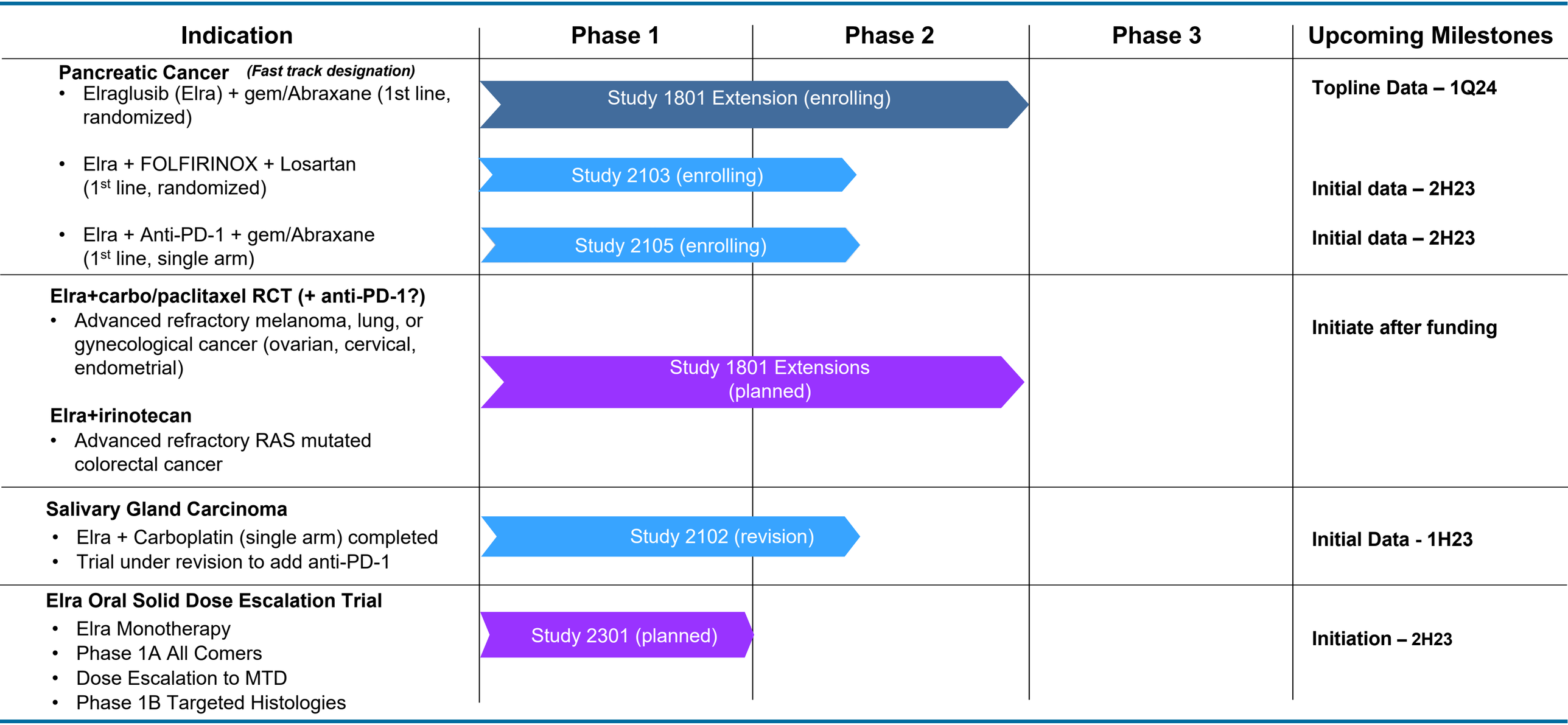
Patient A-003





Substantial Reduction in Liver Metastases (yellow outline)

Actuate Development Pipeline-Enrolling and Planned Studies



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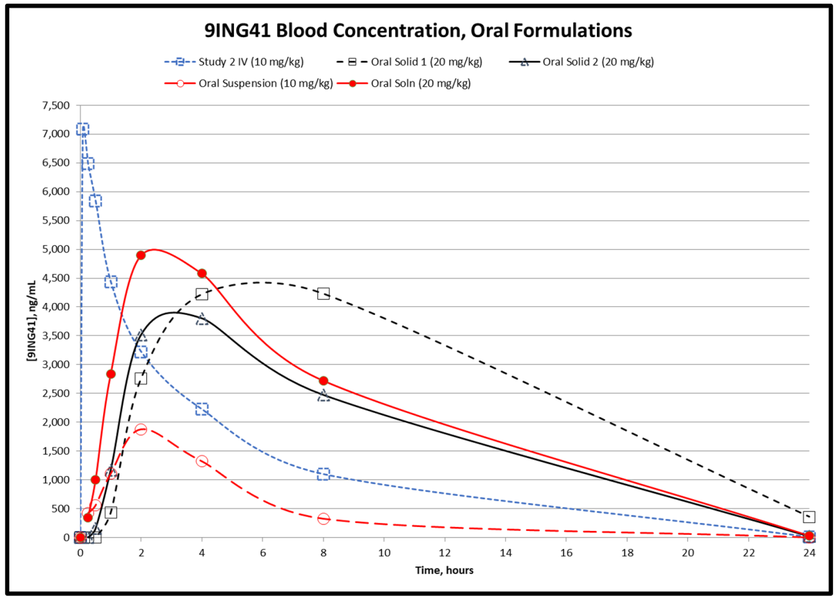
Note: As of October 31, 2022

Investigator Initiated Study Planned 1901-MF and 1902-refractory pediatric cancer studies are active, not recruiting

Elraglusib Oral Formulations – PK Profiles

Oral elraglusib formulations have been developed that provide similar drug exposures to current IV

- Several viable oral dosage forms will allow potential expansion into pediatric cancer indications and adult indications where standard of care is oral (e.g. myelofibrosis)
- Improve compliance and patient experience in indications where long DCR is observed
- Decreased cost of manufacturing at commercial scale
- Phase 1 Study in Healthy Volunteers recently completed
  - Oral Solution vs IV. >50% Bioavailability.
  - Exposure and pharmacodynamic effects exhibited in fed/fasted patients
- Clinical crossover bioequivalence study of Oral Solid scheduled for 2H24



	Plasma Concentration (AUC)	%BA	Normalized BA
IV 10 mg/kg	32,299	100%	100%
Oral Solid 1, 20 mg/kg	62,611	194%	97%
Oral Solid 2, 20 mg/kg	43,904	136%	68%
Oral Solution, 20 mg/kg	51,653	160%	80%
Oral Suspension, 10 mg/kg	11,161	35%	35%

Actuate Issued Patent Portfolio

International

- **9-ING-41 Polymorph I Composition of Matter:** Patent Issued (10/5/2021) US 11,136,334
- Patent Application No. PCT/US2018/046203, filed August 10, 2018
- **Expires August 10, 2038**, Potentially Eligible for Patent Term Extension (PTE)
- Claims directed to Polymorph I, compounds, pharmaceutical compositions, methods of preparing, and uses for treating cancers

- **9-ING-41 Polymorph II Composition of Matter:** Patent issued (8/9/2022): US 11,407,759
- International Patent Application No. PCT/US2018/056083, filed October 16, 2018
- **Expires October 16, 2038,** Potentially Eligible for Patent Term Extension (PTE)
- Claims directed to **Polymorph II**, compounds, pharmaceutical compositions, methods of preparing, and uses for treating cancers

United States

- US 8,207,216-licensed from UIC
- Claims directed to compounds, pharmaceutical compositions, and methods of use
- Expires March 16, 2028, Eligible for Patent Term Extension (PTE) (**March 16, 2033**)
- Pediatric Exclusivity: + 6 months

Europe

- EP 2125683 (Germany, France, United Kingdom, Italy, Spain)
- Claims directed to compounds, pharmaceutical compositions, and uses
- Expires December 19, 2027

Canada

- CA 2673368
- Claims directed to compounds, pharmaceutical compositions, and uses
- Expires December 19, 2027

Seasoned and Successful Executive Leadership

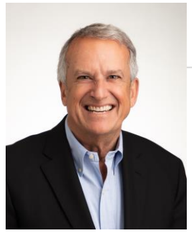
Experienced leadership team with demonstrated ability to develop and commercialize cancer drugs

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 12+ 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



Gilad S. Gordon, MD, MBA – Consulting Chief Medical Officer

- Experienced pharmaceutical executive with broad expertise in product development
- Consultant to various healthcare organizations from clients ranging from early-stage start-ups to Fortune 100 companies
- Largely focused in oncology
- 100+ peer-reviewed research publications
- Inviragen, Ligand, FeRx, Ribozyme, Spectrum

Richard Kenley – VP, Chemistry Manufacturing & Controls

- Expertise in small molecules, protein therapeutics, drug delivery, and manufacturing
- Fellow of the American Academy of Pharmaceutical Scientists
- 4 patents, and 60+ peer-reviewed research publications
- Gynazole, Zirgan, Synarel, Inductos, Symlin,Byetta

Actuate Therapeutics Summary

Best-in-Class Therapeutic Profile

Extensive pre-clinical demonstration of activity from multiple laboratories and positive clinical data in multiple cancer histologies

- Objective and clinical responses across a broad range of tumor types
- Initial validation of elraglusib's efficacy, safety, and tolerability

Significant Unmet Needs

Elraglusib alleviates therapeutic shortcomings in difficult-to-treat and refractory tumors

- First clinically actionable GSK-3β inhibitor in oncology

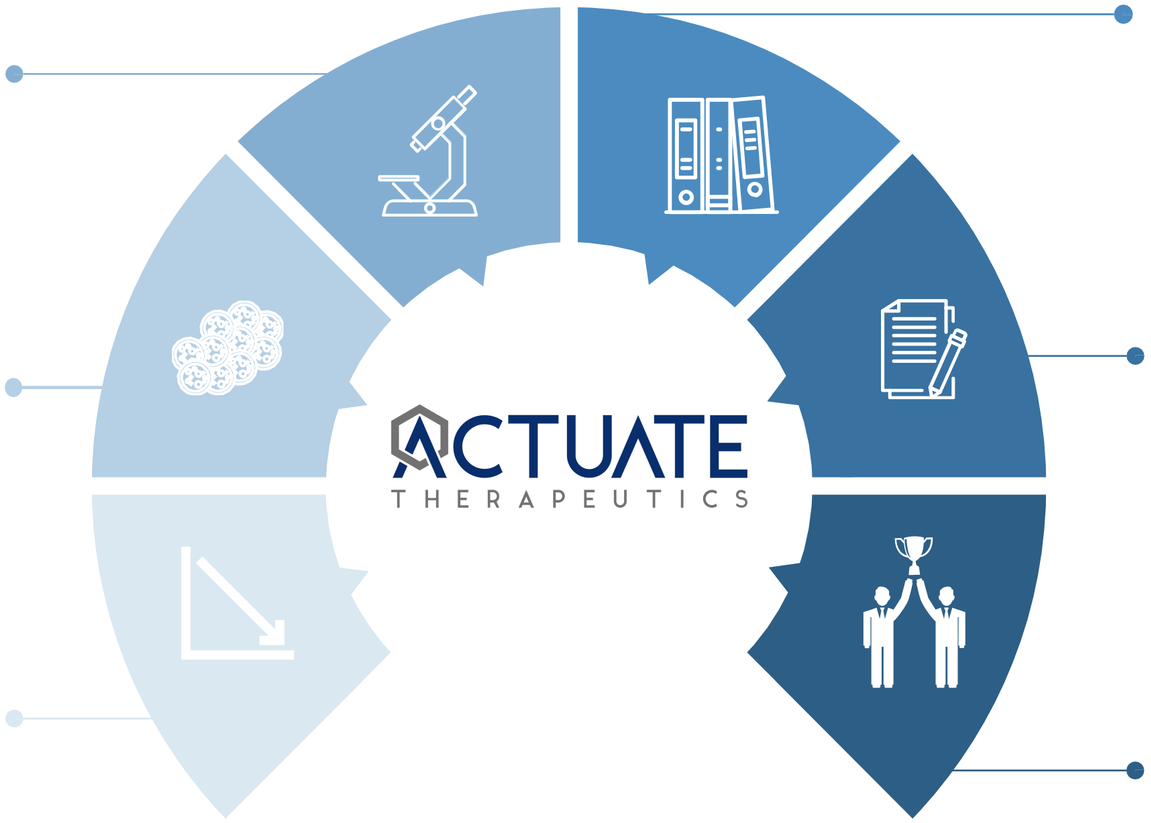
Complementary Mechanisms of Action

Elraglusib exerts its effects by mediating NF-κB pathway and DDR responses

- Known to mediate cancer cell survival and chemoresistance

Regulates antitumor immune response:

- T and NK differentiation, activation and expansion
- Mediator of validated immune check points like PD-1/PD-L1 and LAG-3



Robust IP Portfolio

Expansive, global patent portfolio

- Composition of matter and methods of use surrounding Elraglusib's formulation and addressable indications

Clearly Defined Regulatory Path

- Orphan drug designation
- Rare pediatric disease designations
- Fast Track Designation in PDAC

Multiple registration path clinical trials underway and in development:

- Randomized Phase 2 PDAC frontline G/A study
- Randomized Phase 2 metastatic melanoma 3rd line in ICI failures
- Randomized Phase 2 carbo/paclitaxel combination trial in 3rd line advanced cancer (TBD)
- Phase 2 Myelofibrosis trial
- Phase 1 Pediatric Cancer

Seasoned Leadership Team

Distinguished leadership and scientific advisory team

- Expertise spanning translational and clinical oncology, R&D, regulatory affairs and commercialization
- Direct leadership roles for development and registration of multiple oncology agents

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