Pancreatic Cancer and Small Cell Lung Cancer Program Updates

SEPTEMBER 26, 2023

Forward-looking statements

CERTAIN STATEMENTS IN THIS PRESENTATION ARE FORWARD-LOOKING within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of words such as "anticipate," "believe," "forecast," "estimated" and "intend" or other similar terms or expressions that concern our expectations, strategy, plans or intentions. These forward-looking statements are based on our current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, our need for additional financing; our ability to continue as a going concern; clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results; our clinical trials may be suspended or discontinued due to unexpected side effects or other safety risks that could preclude approval of our product candidates; our clinical trials may encounter delays in initiation or enrollment that impact the cost and timing of the trial readout; risks related to business interruptions, including the outbreak of COVID-19 coronavirus, which could seriously harm our financial condition and increase our costs and expenses; uncertainties of government or third-party payer reimbursement; dependence on key personnel; limited experience in marketing and sales; substantial competition; uncertainties of patent protection and litigation; dependence upon third parties; regulatory, and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. There are no guarantees that any of our technology or products will be utilized or prove to be commercially successful. Additionally, there are no guarantees that future clinical trials will be completed or successful or that any precision medicine therapeutics will receive regulatory approval for any indication or prove to be commercially successful. Investors should read the risk factors set forth in our Form 10-K for the year ended December 31, 2022, and other periodic reports filed with the Securities and Exchange Commission. While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and we do not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances.

Highlights of today's mPDAC and SCLC program update

Metastatic Pancreatic Ductal Adenocarcinoma (mPDAC)

1. **CRDF-001 trial**
   - Onvansertib, in combination with 2nd line standard-of-care, generated an efficacy signal and was well-tolerated
2. **Biomarker discovery investigator-initiated trial**
   - Onvansertib monotherapy generated an efficacy biomarker response
   - Onvansertib inhibited hypoxia-response pathway in treatment-responsive patient
3. **First-line investigator-initiated trial planned**

Small Cell Lung Cancer (SCLC)

Monotherapy investigator-initiated trial

- Confirmed PR in first seven patients in onvansertib monotherapy trial

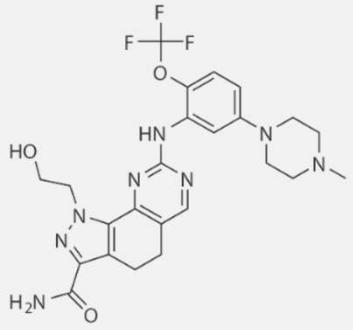
Onvansertib specifically targets PLK1, a well-established cancer target

Onvansertib

First oral, well-tolerated PLK1-selective inhibitor

PROPERTIES

- Small molecule
- Oral dosing
- 24-hour half-life



SPECIFICITY

Exquisitely specific for PLK1

ENZYME	IC_{50} (μM)
PLK1	**0.002**
PLK2	>10
PLK3	>10
CK2	0.4
FLT3	0.4
CDK1/CycB	>10
42 other kinases and >140 in the Millipore panel	>10

Our pipeline opens many attractive opportunities for onvansertib

	Line of Therapy	Trial	IIT*	Ph2	Ph3	Combination with:
mCRC (RAS-mut)	1st line	Ph 2 (w/Pfizer)		randomized		FOLFIRI/bev and FOLFOX/bev
	2nd line	Ph 1b/2		completed		FOLFIRI/bev
mPDAC	2nd line	Ph 2				Nal-IRI/leucovorin/ 5-FU
	1st line	Ph 2	OHSU Knight Cancer Institute			Gemzar®/Abraxane®
SCLC	2nd line	Ph 2	UPMC LIFE CHANGING MEDICINE			None (monotherapy)
TNBC	2nd line	Ph 2	Dana-Farber Cancer Institute			Paclitaxel

* For investigator-initiated trials (IITs) only, the investigator's institution is provided.

Onvansertib's MOA targets large patient populations with unmet need

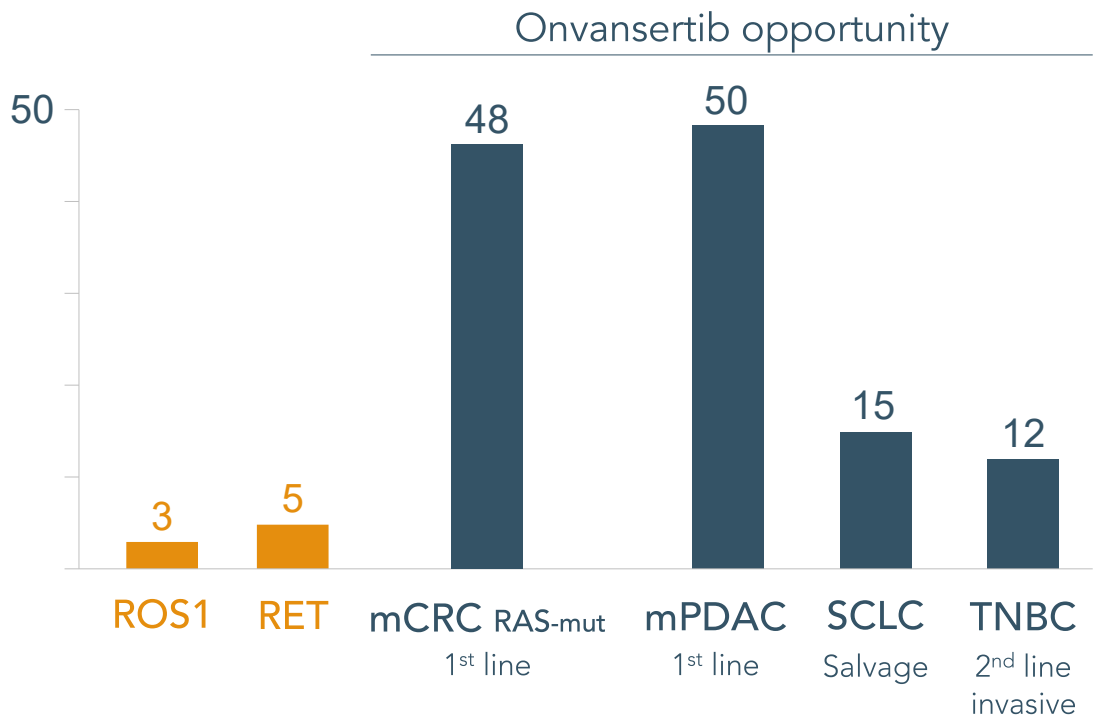
Targets with oncogenic alterations

- ROS1
- RET
- KRAS G12C
- EGFR
- TRK

Targets without oncogenic alterations

- **PLK1**
- PARP
- CDK4/6
- PD1/PDL1
- VEGF

Annual eligible U.S. patients ('000s)*



* ROS1 estimated eligible patients presented in Turning Point Therapeutics' corporate presentation May 2022 slide 6 (NSCLC disease incidence in the US of 140k of which 2% of patients harbor ROS1 translocation). RET estimated eligible patients presented in Loxo Oncology's corporate presentation January 2018 disclosed on Form 8-K (Jan 8, 2018).

mCRC estimated population includes 1st line, KRAS- and NRAS-mutated cancers. mPDAC estimated population includes 1st line PDAC patients. SCLC estimated population includes SCLC salvage patients. TNBC estimated population includes invasive, 2nd line TNBC patients.

Metastatic Pancreatic Ductal Adenocarcinoma (mPDAC)

Small Cell Lung Cancer (SCLC)

Data from two mPDAC trials provides a path forward in 1st line setting

mPDAC
CRDF-001 Ph 2 Second-Line Trial

- Combination with Nal-irinotecan/leucovorin/5-FU

mPDAC
Biomarker Discovery Trial (IIT)

- Patients have 10 days of onvansertib monotherapy with pre- and post-therapy biopsies and bloodwork

Path forward: Move to 1st line mPDAC

- New IIT combining onvansertib with SoC (Gemzar/Abraxane)

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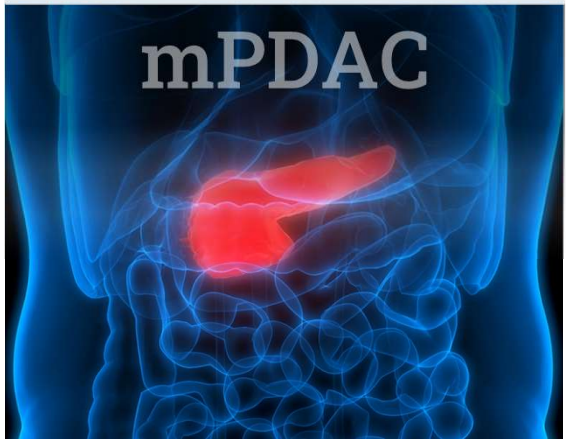
CRDF-001 mPDAC 2nd line Ph2 trial combines onvansertib with SoC

ENROLLMENT CRITERIA

2nd line refractory patients

Measurable tumor by RECIST 1.1



OBJECTIVE

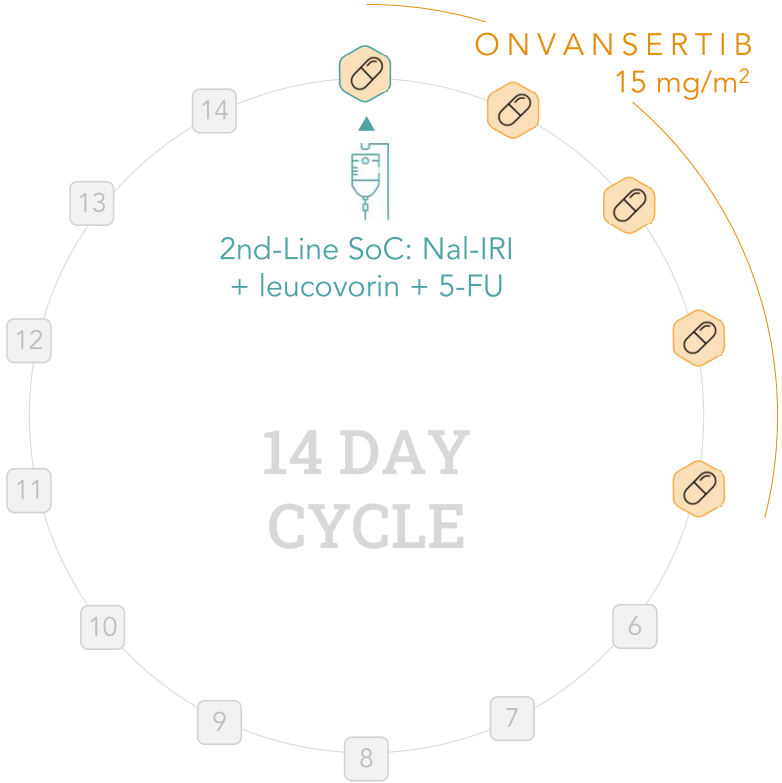
To determine the efficacy and safety of onvansertib when added to standard of care

PRIMARY ENDPOINT

ORR (RECIST 1.1)

SECONDARY ENDPOINT

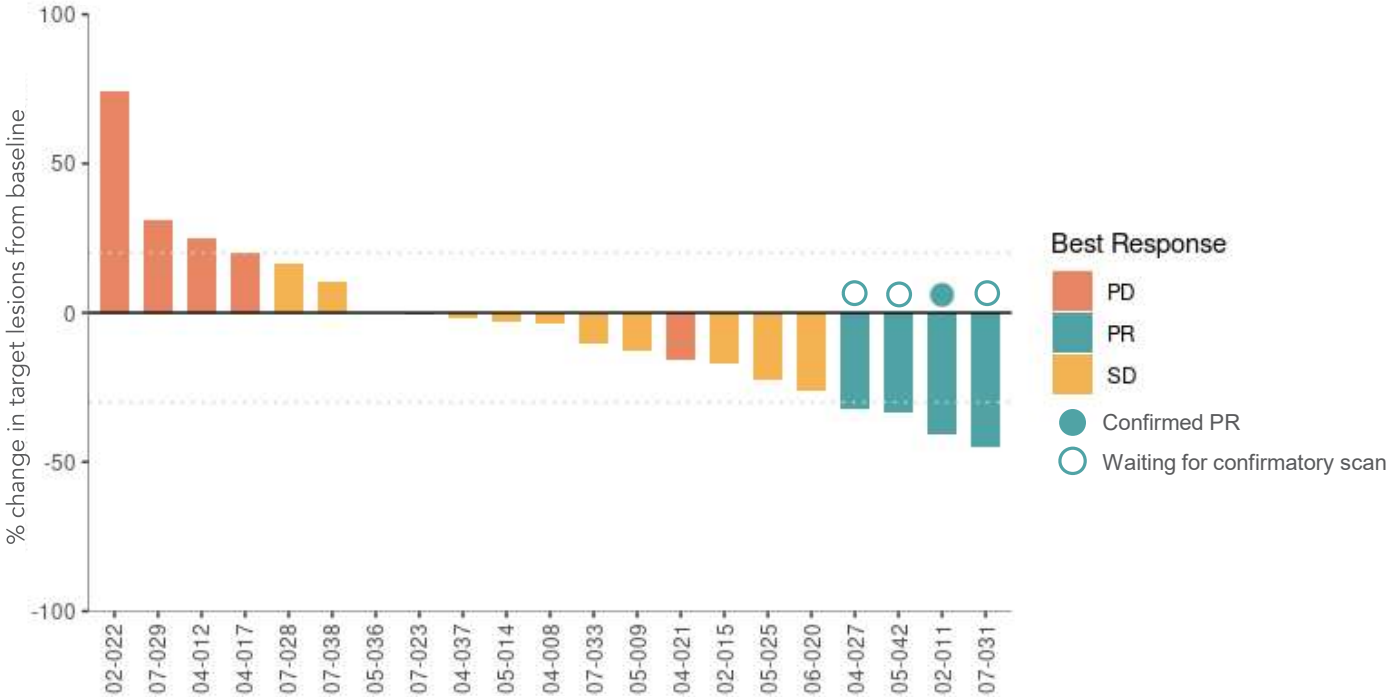
Disease Control Rate (DCR)



Onvansertib+SoC has higher efficacy than 2nd line historical controls

Best Radiographic Response – 21 evaluable patients (as of September 13, 2023)*

		Historical controls[1]	
	CRDF-001	2nd line mPDAC	1st line mPDAC
ORR	19% (4/21)	7.7%	23%

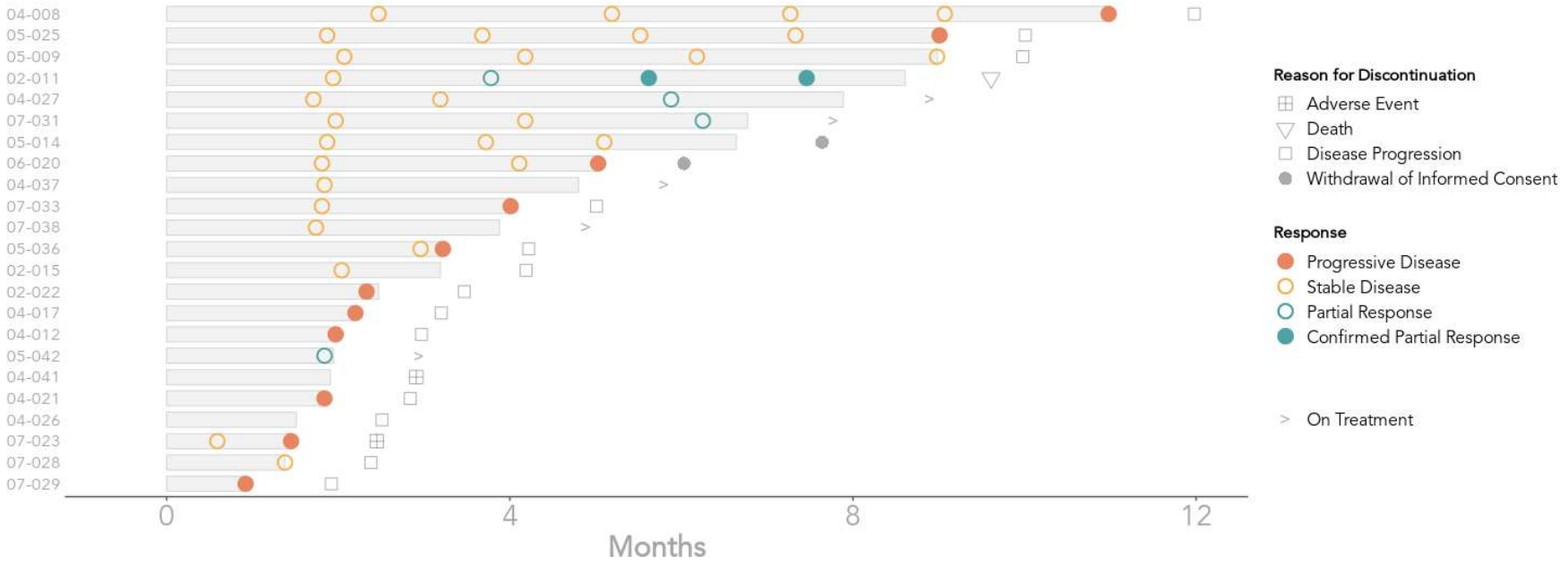


* Radiographic response determined per RECIST 1.1. Waterfall plot and table reflect interim data as of September 13, 2023 from an ongoing trial and unlocked database. For ORR analysis, there are two patients excluded (04-026 and 04-041) that had two cycles of treatment but left the trial before their first post-baseline scan.

1. FDA insert for Onivyde (Nal-IRI): https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207793lbl.pdf; 387: 545–57. Von Hoff et al., N Engl J Med 2013; 369:1691-703.

Stable disease patients have converted to partial responses over time

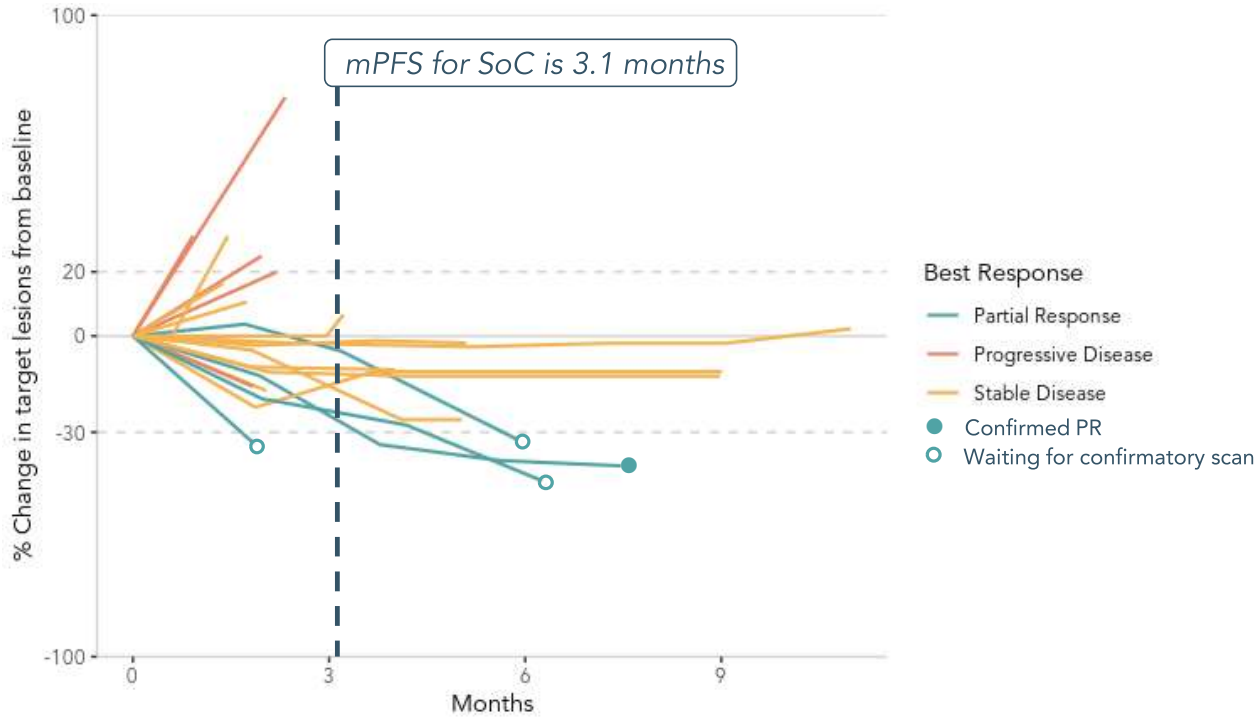
Swimmer plot – 23 evaluable patients (as of September 13, 2023)*



* Swimmer plot reflects interim data as of September 13, 2023 from an ongoing trial and unlocked database. For the swimmer plot, there are two patients included (04-026 and 04-041) that had two cycles of treatment but left the trial before their first post-baseline scan.

Patient responses to onvansertib+SoC can deepen over time

Spider plot – 21 evaluable patients (as of September 13, 2023)*

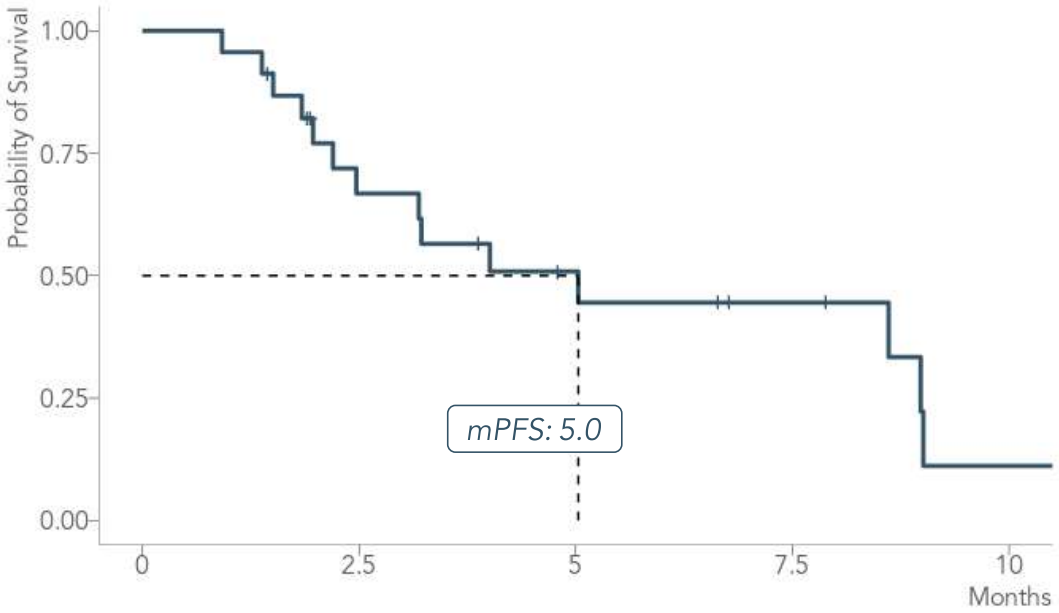


* Spider plot reflect interim data as of September 13, 2023 from an ongoing trial and unlocked database. For ORR analysis, there are two patients excluded (04-026 and 04-041) that had two cycles of treatment but left the trial before their first post-baseline scan.

Onvansertib+SoC has longer median PFS than 2nd line historical controls

Progression-free survival – 23 evaluable patients (as of September 13, 2023)*

	CRDF-001	Historical controls[1]	
		2nd line mPDAC	1st line mPDAC
mPFS	5.0 mos	3.1 mos	5.5 mos
16 week progression-free[2]	56%	Not available	48%



* Onvansertib mPFS are interim data as of September 13, 2023 from an ongoing trial and unlocked database. For PFS analysis, there are two patients included (04-026 and 04-041) that had two cycles of treatment but left the trial before their first post-baseline scan.

1. FDA insert for Onivyde (Nal-IRI): https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207793lbl.pdf ; 387: 545–57. Von Hoff et al., N Engl J Med 2013; 369:1691-703.
2. Probability of being progression-free at 16 weeks using KM survival analysis. Data not available for 2nd line

Data from two mPDAC trials provides a path forward in 1st line setting

mPDAC
CRDF-001 Ph 2 Second-Line Trial

- Combination with Nal-irinotecan/leucovorin/5-FU

mPDAC
Biomarker Discovery Trial (IIT)

- Patients have 10 days of onvansertib monotherapy with pre- and post-therapy biopsies and bloodwork

Path forward: Move to 1st line mPDAC

- New IIT combining onvansertib with SoC (Gemzar/Abraxane)

mPDAC Biomarker Discovery trial evaluates onvansertib monotherapy

Investigator-initiated trial at OHSU Knight Cancer Center

ENROLLMENT CRITERIA

Patients with metastatic pancreatic cancer (any line)

OBJECTIVES

Responsive biomarkers

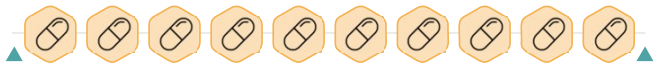
- To demonstrate pancreatic tumor response to onvansertib monotherapy by measuring Ki67 and CA 19-9

Predictive biomarkers

- Use multi-omic analyses to identify predictive biomarkers of pancreatic tumor response to onvansertib

ONVANSERTIB
MONOTHERAPY

(12mg/m^2 QD, 10 days)



Pre-treatment biopsy & research blood

Post-treatment biopsy & research blood

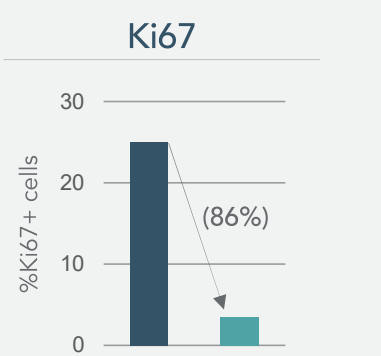
Obtain biopsies / bloodwork before and after 10 days of onvansertib monotherapy to conduct extensive multi-omic analyses

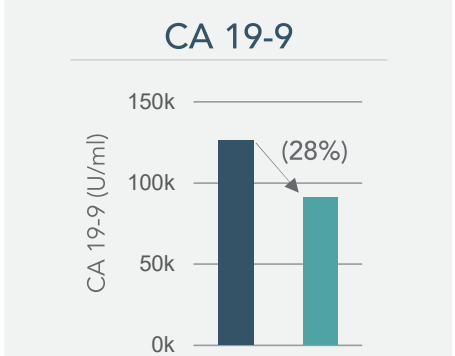
Onvansertib monotherapy decreased tumor proliferation and CA19-9

Biomarker Discovery Trial: Biomarker Response* – 2 patients (as of September 13, 2023)

- Ki67 is a well-established marker of tumor proliferation
- CA 19-9 is a clinically-used biomarker to monitor treatment response

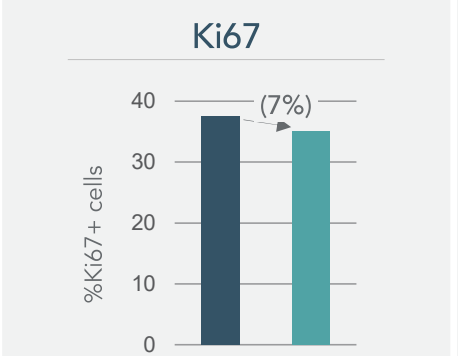
Patient 28 (tumor responder)

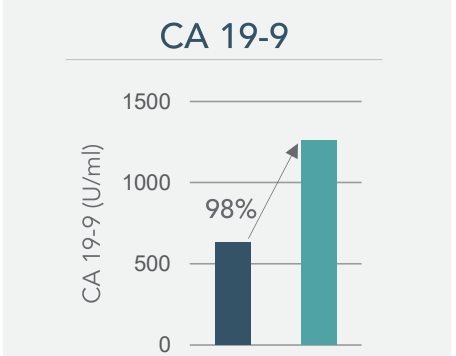




Mutation: KRAS G12V
1st line: Atezo/Bev + Gem/Nab → Response
2nd line: FOLFIRINOX → Progression
3rd line: Onvansertib monotherapy → CA19-9 Response

Patient 33 (tumor non-responder)





Mutation: KRAS Q61R
1st line: FOLFIRINOX → Response
2nd line: Onvansertib monotherapy → CA19-9 Progression

Pre-treatment Post-treatment

* Patient 28 and patient 33 had liver matastases and biopsies were taken pre- and post-onvansertib monotherapy treatment for ten days.

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CRDF-001 Ph 2 Second-Line Trial

- Combination with Nal-irinotecan/leucovorin/5-FU

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Biomarker Discovery Trial (IIT)

- Patients have 10 days of onvansertib monotherapy with pre- and post-therapy biopsies and bloodwork

Path forward: Move to 1st line mPDAC

- New IIT combining onvansertib with SoC (Gemzar/Abraxane)

Proposed mPDAC 1st line Ph2 trial combines onvansertib with SoC

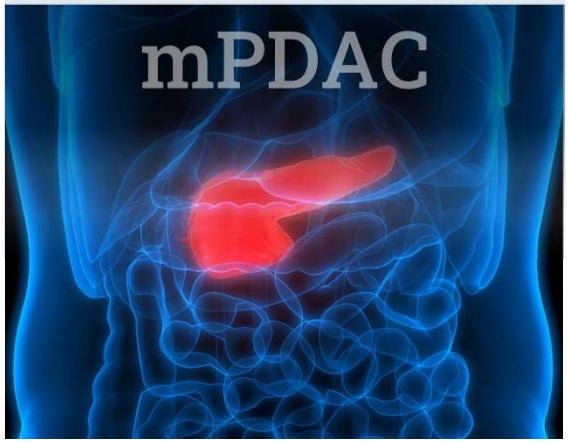
Proposed investigator-initiated trial with the OHSU Knight Cancer Institute

ENROLLMENT CRITERIA

First-line patients

Unresectable

Locally advanced or metastatic



TWO LEAD-IN COHORTS

Cohort 1

- 10-day lead-in with onvansertib monotherapy (30mg po daily)

Cohort 2

- No lead-in therapy

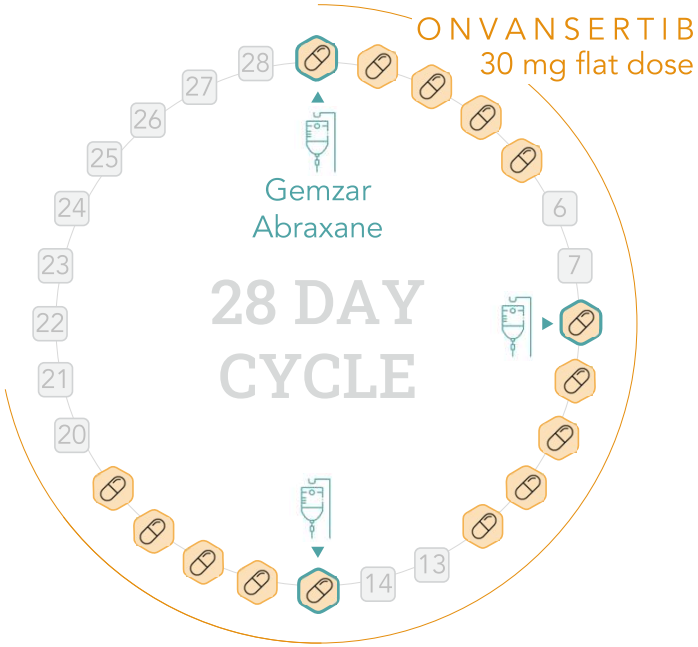
PRIMARY ENDPOINT

ORR, DCR at 16 weeks

SECONDARY ENDPOINTS

DoR, PFS, Safety

SUBSEQUENT CHEMO + ONVANSERTIB TREATMENT*



* If a DLT occurs at dose level 1; then omit day 8 chemo only, and continue with onvansertib 30mg dose; but if toxicity persists at day 15, then decrease onvansertib dose to 20mg daily

Metastatic Pancreatic Ductal Adenocarcinoma (mPDAC)

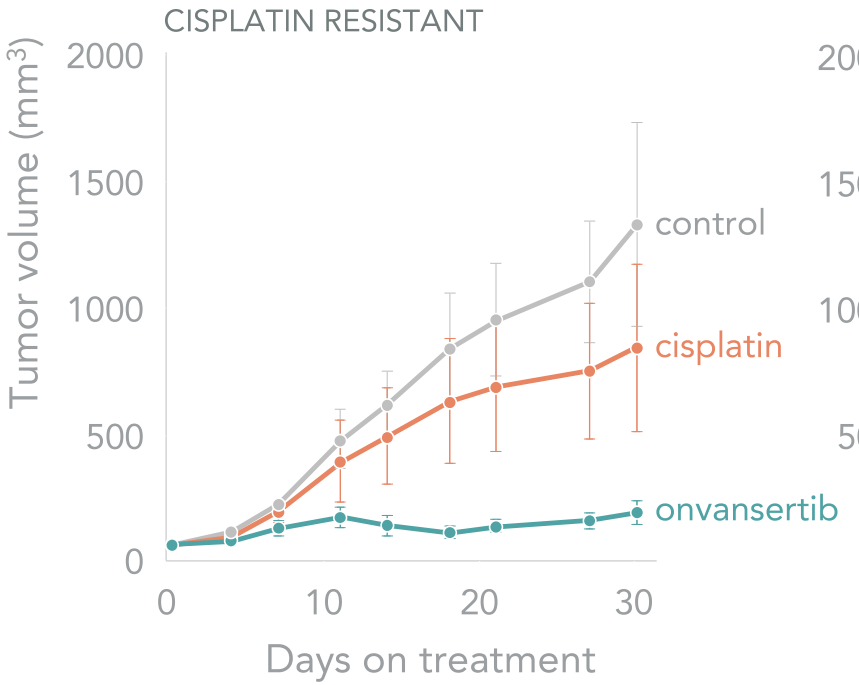
Small Cell Lung Cancer (SCLC)

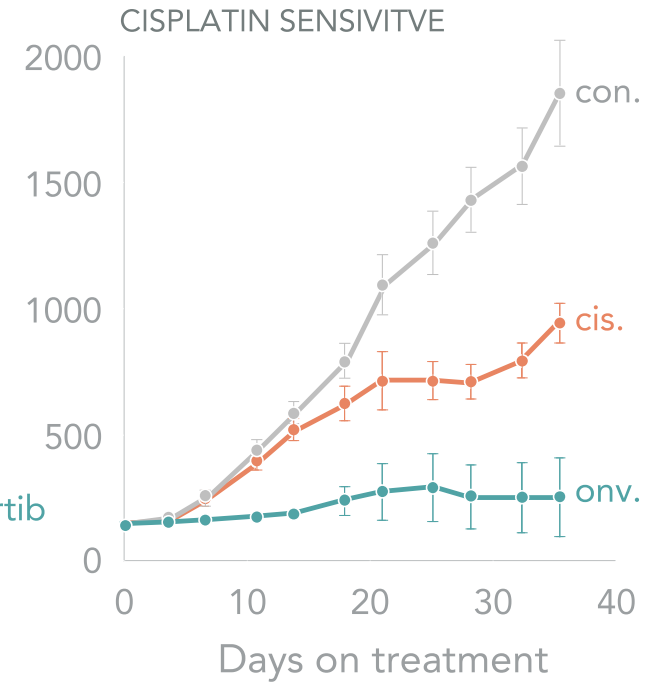
Onvansertib demonstrates single-agent activity in preclinical SCLC models

TRIAL RATIONALE

Onvansertib monotherapy showed significant tumor growth inhibition against platinum-sensitive and -resistant models

In vivo efficacy of onvansertib monotherapy (SCLC xenografts)*





* Mice were implanted with SCLC PDX and treated with vehicle, cisplatin 3mg/kg IP weekly, or onvansertib oral 60mg/kg 10 ON / 4 OFF

Trial design for onvansertib monotherapy in extensive stage SCLC

ENROLLMENT CRITERIA

Relapsed who have received ≤2 prior therapies

Single-arm trial
Stage 1: N=15
Stage 2: N=20

UPMC LIFE CHANGING MEDICINE

OBJECTIVE

To determine the efficacy and safety of onvansertib monotherapy

PRIMARY ENDPOINT

ORR (RECIST 1.1)

SECONDARY ENDPOINTS

Progression-Free Survival (PFS)
Overall Survival (OS)

Preliminary safety and efficacy for onvansertib monotherapy in SCLC

ENROLLMENT CRITERIA

Relapsed who have received ≤2 prior therapies

Single-arm trial
Stage 1: N=15
Stage 2: N=20

UPMC LIFE CHANGING MEDICINE

PRELIMINARY SAFETY (N=6)

IRB reviewed safety data for the first 6 patients. Post IRB review, the trial continues to enroll with no conditions.

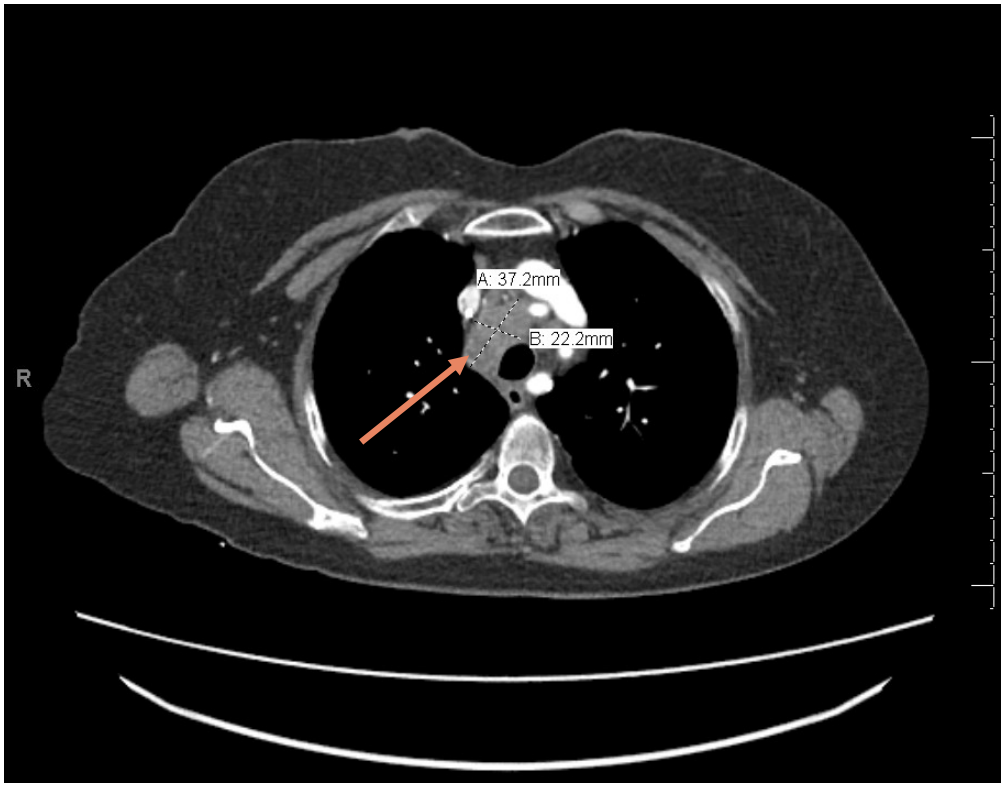
PRELIMINARY EFFICACY (N=7)

Best response	PR	SD	PD
# of patients	1 (confirmed)	3	3

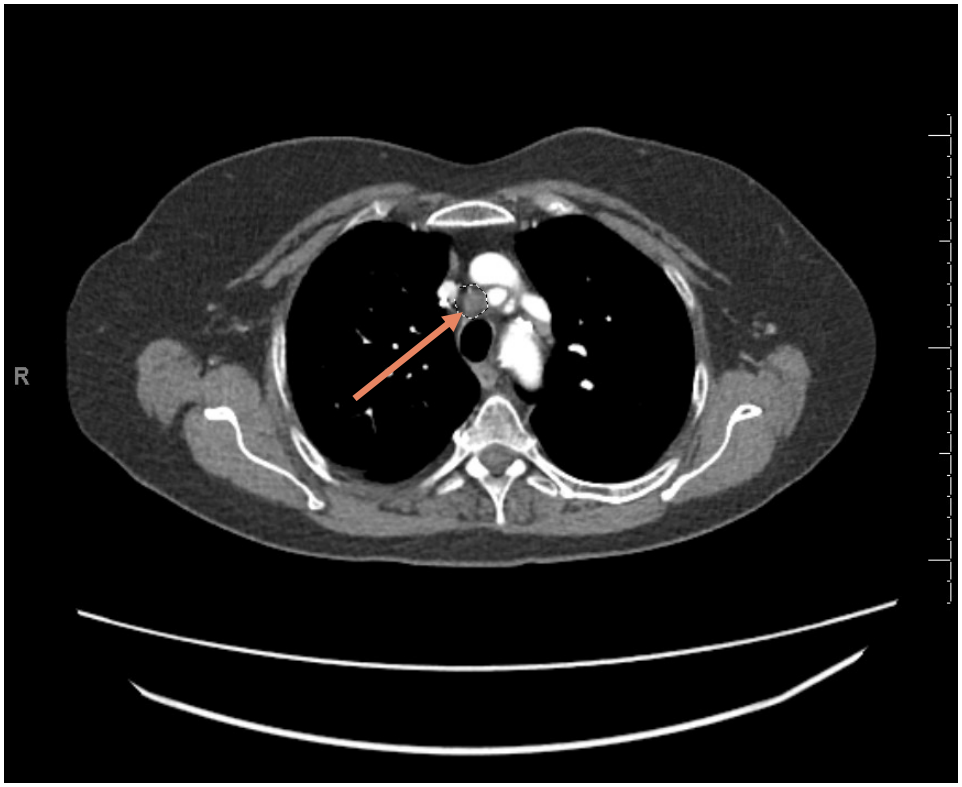
Disease control rate = 57% (4/7)

Radiographic scans for patient with a confirmed PR in SCLC IIT

Baseline Scan



Restaging after Cycle 2



We have multiple near-term clinical data read outs

June 30, 2023 cash and investments*	$89.4M
Net cash used in Operating Activities* (Rolling two-quarter period ending June 30, 2023)	$15.8M
Based on our current projections we expect that our capital resources are sufficient to fund our operations into 2025	

* Financial information above is derived from our unaudited financials in Form 10Q filed on 8/9/23.

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