IMMUNOMET
THERAPEUTICS

Developing Novel Cancer Drugs by Targeting Metabolism

BIO International June 2026, San Diego
Presented by: Dean Welsch, CEO

The case in **five key points**

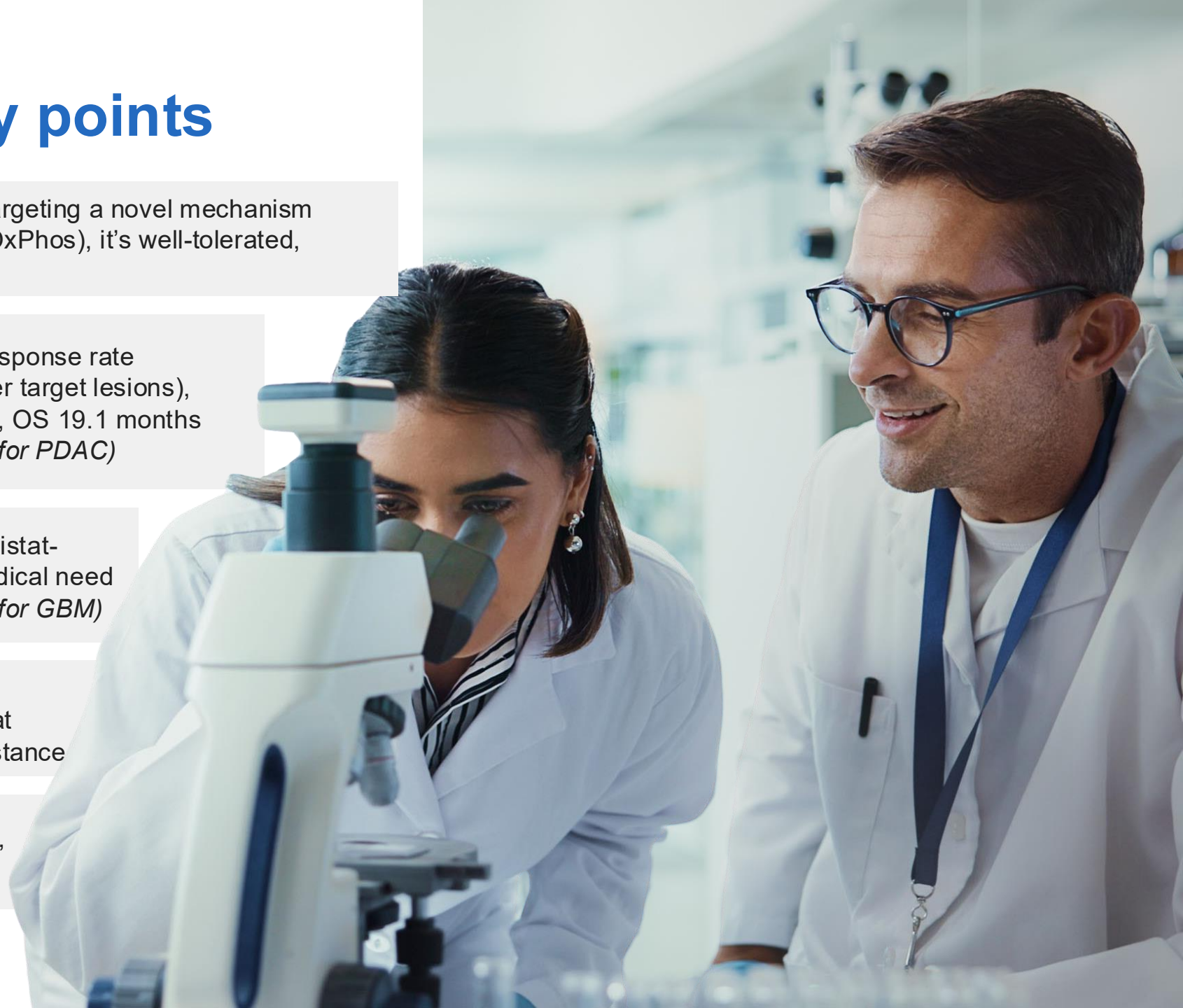
1. **Lixumistat:** a best-in-class inhibitor targeting a novel mechanism of action, oxidative phosphorylation (OxPhos), it's well-tolerated, and Phase 2 ready

2. **POC Data in PDAC patients:** 50% response rate (including one patient with a CR in liver target lesions), 83% disease control, PFS 6.2 months, OS 19.1 months *(Lixumistat Orphan Drug Designation for PDAC)*

3. **GBM:** novel biomarker identifies lixumistat-sensitive patients with high unmet medical need *(Lixumistat Orphan Drug Designation for GBM)*

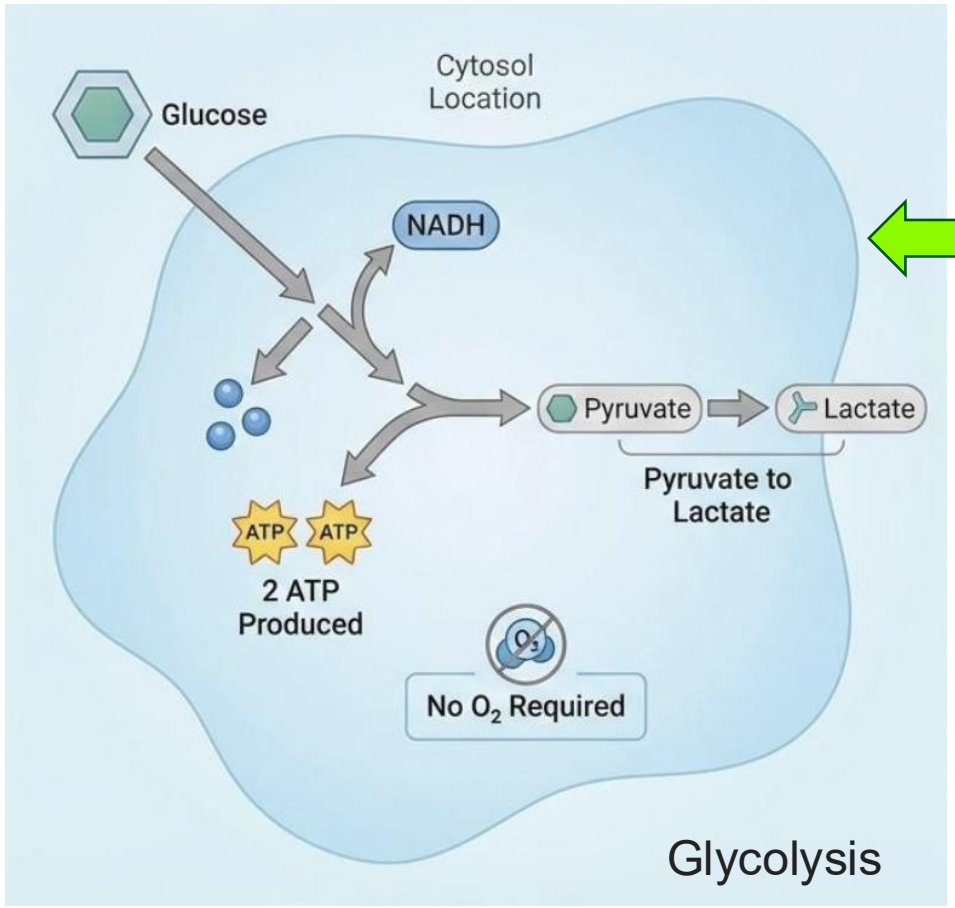
4. **Pan-cancer potential:** OxPhos is a therapeutic target with potential to treat cancers with intrinsic or acquired resistance

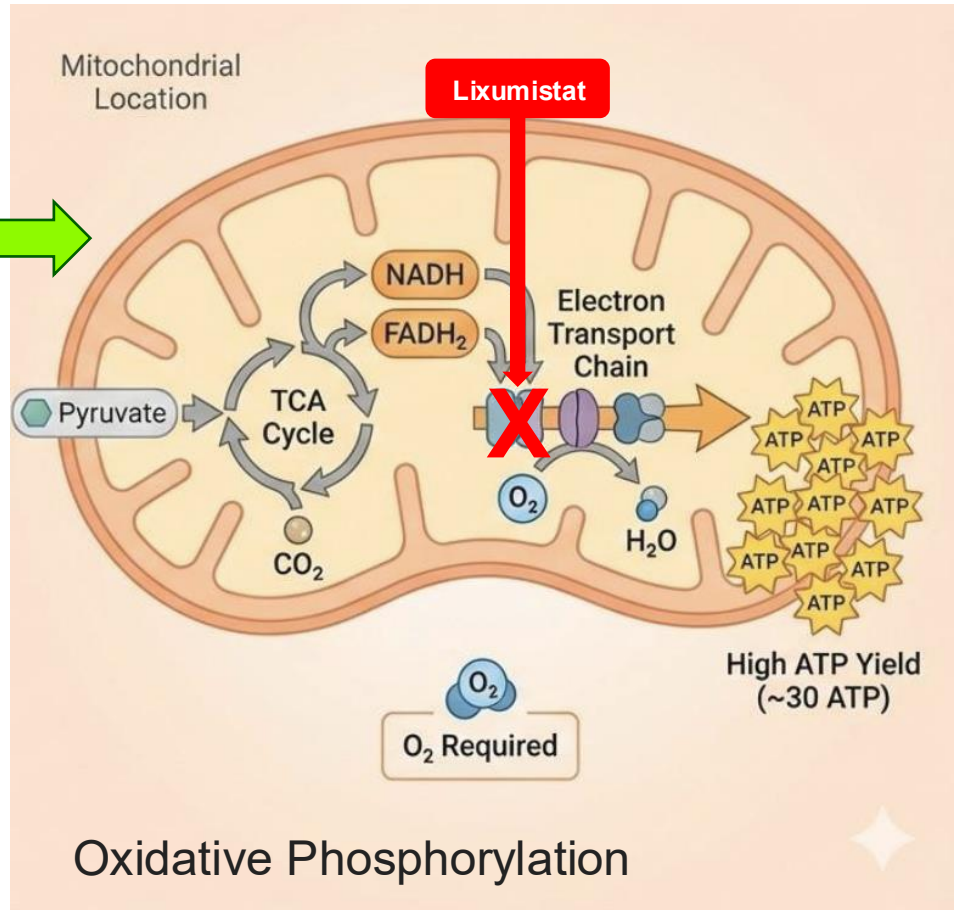
5. **KOL-enabled studies:** MD Anderson, Glioblastoma Therapeutics Network



ImmunoMet Therapeutics **Oncology**

Liximistat targets Oxidative Phosphorylation, a unique metabolic target





Lixumistat is best-in-class OxPhos inhibitor
A selective, well-tolerated, Phase 2 ready asset

Clinical experience

Ph 1 dose escalation in unselected cancer patients
(Published – Janku et al., Inv New Drugs, 2022)

Ph 1 dose-escalation in healthy subjects
(demonstrated on-target activity)

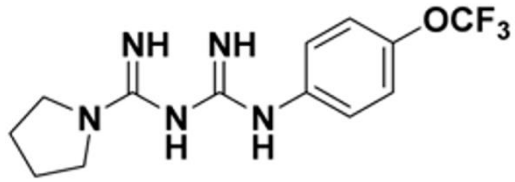
Ph 1 food effect in healthy subjects
(No effect of food on PK)

Ph 1b Pancreatic Ductal Adenocarcinoma
(clinical efficacy at safe dose)

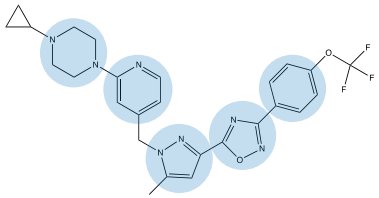
Window-of-Opportunity & Ph 2 GBM (planned)
(BBB penetration, PD, clinical efficacy)

Excellent drug-like properties

- ✓ Straightforward small molecule synthesis, very stable
- ✓ Excellent solubility, selectivity, distribution, and PK (PO, QD)
- ✓ On-target activity – enzyme, cellular, in vivo (preclin & clinical)
- ✓ Demonstrated in vivo anti-cancer activity
- ✓ Toxicity profile supports development



Differentiated from OxPhos inhibitors that failed due to safety in Phase 1



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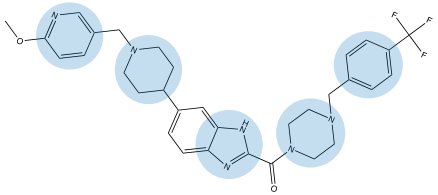

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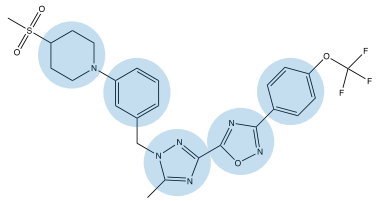


IACS-010759

Reported early demonstration of neurotoxicity

Intellectual property

ImmunoMet holds patents on both the compound composition of matter and the method of use – lixumistat is fully owned by ImmunoMet Therapeutics

Patents are held in the US and major world markets, providing broad geographic coverage

ImmunoMet has complete freedom to operate with its compounds

Pancreatic ductal adenocarcinoma (PDAC) scientific and medical rationale

PDAC is:

- a highly aggressive malignancy
- currently the third-leading cause of cancer mortality in the US, and is projected to become the second
- there exists an urgent need for highly effective therapeutic strategies

The poor prognosis is largely due to late-stage diagnosis:

- 50% of patients present with metastases
- 30-35% present in a locally advanced, unresectable stage

Conventional chemotherapy regimens:

- FOLFIRINOX and Gemcitabine-Nab-Paclitaxel (Gem+NP)
- are difficult to tolerate
- provide modest survival benefits, mPFS ~6 months and OS rate of < 50% at one year

Pancreatic tumor cells, once thought to rely primarily on glycolysis, exhibit metabolic heterogeneity, with **oxidative phosphorylation (OxPhos) playing a critical role in driving treatment (or acquired) resistance** and serving as a potentially promising therapeutic target.

Lixumistat is:

- a small-molecule biguanide that inhibits the first and rate-limiting step of the OxPhos pathway
- an inhibitor of the growth/proliferation of gemcitabine-treated PDAC tumor cells

ImmunoMet Therapeutics **Oncology**

Lixumistat for PDAC Patients

Clinical trial (NCT05497778)

Protocol title

A Phase 1b Study of Gemcitabine and Nab-paclitaxel in Combination with lixumistat in Patients with Advanced Pancreatic Cancer

Principal investigators

This study was conducted under the direction of Principal Investigator Dr. Shubham Pant at the M.D. Anderson Cancer Center.

Status

Completed, with 18 patients treated. Dose escalation include 12 patients (7 at 400 mg and 5 at 800 mg) and 6 treated in the dose-expansion cohort (400 mg). The median age at screening was 68 years, 61% of patients were female. KRAS and TP53 alterations were reported in 89%, and 61% of patients, respectively.

Clinical Study Design

Dose Escalation Phase
(N=12)

SOC: Gemcitabine + nab-paclitaxel
+
Lixumistat: 400mg or 800mg

Cohort Expansion Phase:
(7 Dose Esc rollover + 6, N=13)

Gemcitabine + nab-paclitaxel + Lixumistat at RP2D determined in Dose Escalation Phase (400 mg)

Endpoints:
Primary – Safety, Tolerability
Secondary – ORR, PFS, OS

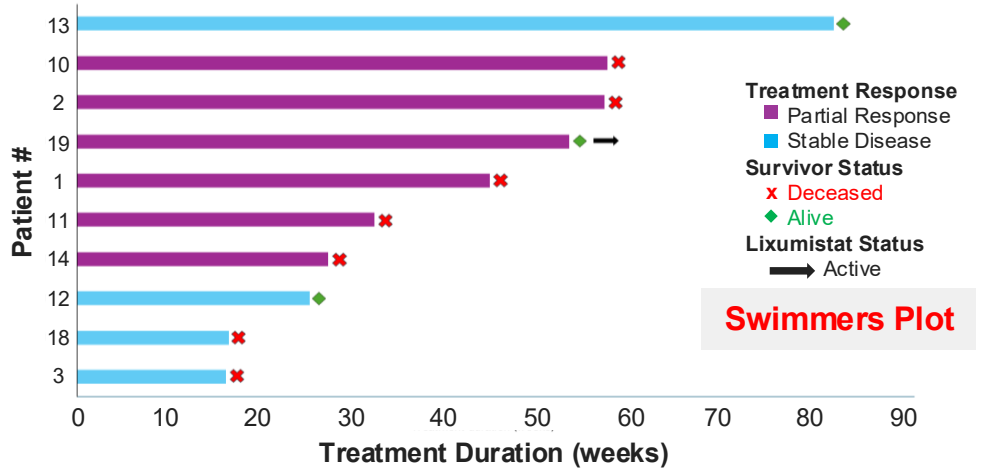
Comparator arm will be derived from existing MDACC data from patients with similar profiles to those enrolled in this study

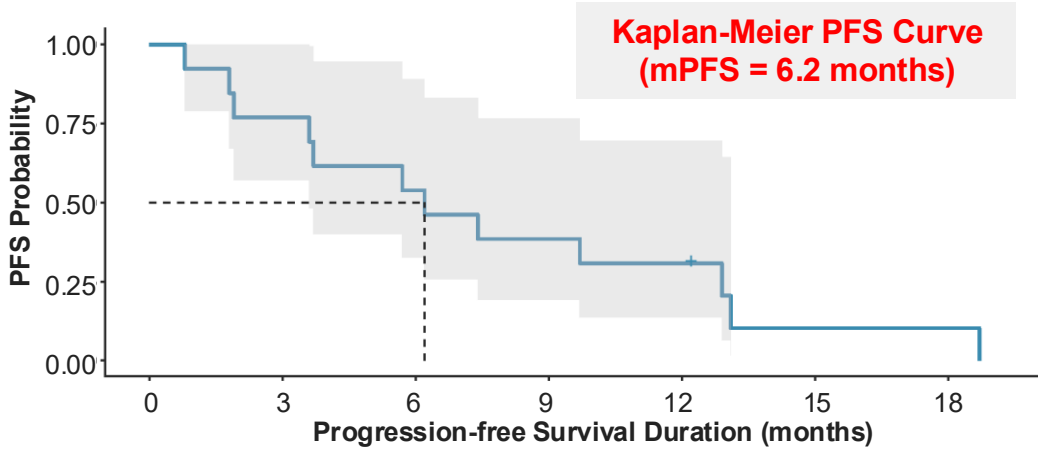
PDAC study data are very encouraging:

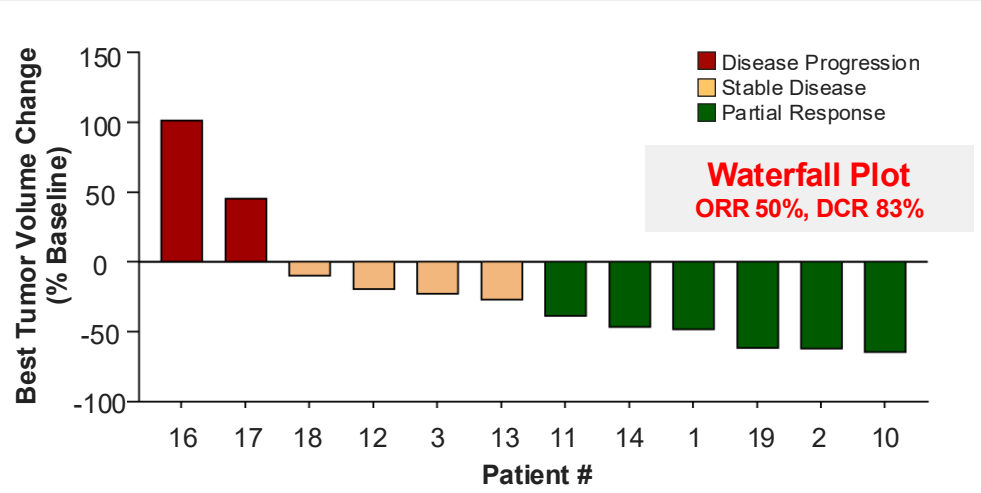
50% clinical response rate, 83% disease control rate, progression-free survival 6.2 months and overall survival 19.1 months

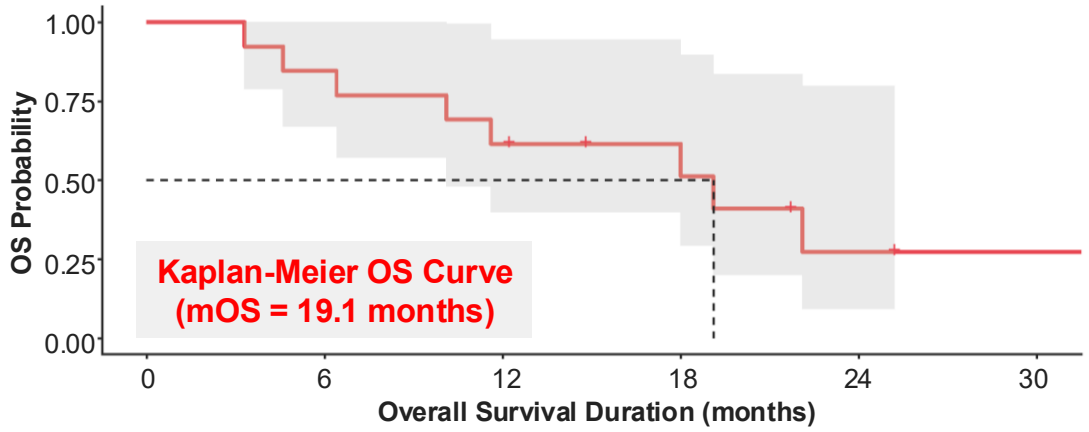
ImmunoMet Therapeutics Oncology

Liximistat for PDAC patients, study results of liximistat treatment at RP2D (400 mg, PO, QD)









ImmunoMet Therapeutics **Oncology**

Lixumistat for PDAC Patients, Study Conclusions

The clinical results demonstrate that 400 mg daily oral dosing of lixumistat, in combination with gemcitabine and nab-paclitaxel (GA), is safe, well tolerated, and was selected as the RP2D.

The study provides evidence of antitumor activity in patients with advanced PDAC vs GA (published), respectively: **ORR 50% vs 23%, DCR 83%, PFS 6.2 vs 5.5 months, OS 19.1 vs 8.5 months).**

Recent RAS inhibitor (daraxonrasib) Phase 3 data in previously treated metastatic pancreatic cancer patient (>91% with KRAS mutation) vs chemo: **ORR 33% vs 11%, PFS 7.2 vs 3.6 months, OS 13.2 vs 6.7 months.** Daraxonrasib received Breakthrough Therapy designation and daraxonrasib is available through an Expanded Access Program.

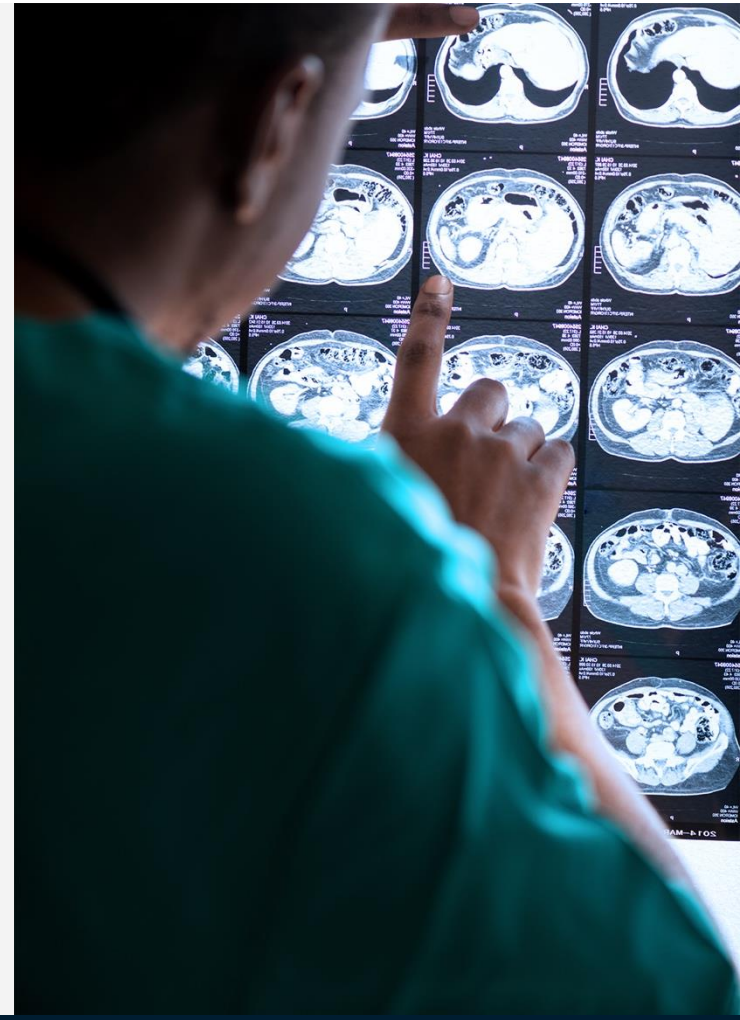
Overall, the findings with lixumistat strongly support continued clinical investigation of OxPhos inhibition as a strategy to overcome metabolic resistance mechanisms that limit the efficacy of standard chemotherapy in PDAC.

GBM: 20 years without a new standard of care

GBM is the most common & aggressive malignant brain tumor, 48% of all malignant CNS cases, and has an incidence of 3.21 per 100,000 population; 25% of $2.5-3 billion WW market, or ~$700 million

SoC treatment for newly diagnosed GBM consists of surgical resection, then radiotherapy & chemotherapy with temozolomide, this has been SoC for 20 years

Tumors consistently recur, and median OS remains poor at 14-18 months, with 40% and 17% survival in the first and second years post-diagnosis, and <7% of GBM patients survive longer than 5 years



Treatment challenges include **tumor heterogeneity**, localization in the brain, resistance to conventional therapy, limited capacity of the brain to repair itself, migration of malignant cells to adjacent brain tissue, variable tumor blood supply, and tumor capillary leakage, resulting in peritumoral edema

Molecular alterations in GBM include changes in IDH, EGFR, FGFR, and H3F3A (all potential therapeutic targets), MGMT methylation status has predictive value for response to temozolomide

Biomarker-informed Precision Medicine is expected to identify the next therapeutics for GBM

ImmunoMet Therapeutics' OxPhos inhibitor **Lixumistat is active/selective** in MTC subtype of GBM patient samples

Analysis of GBM Patient-derived Cellular Subtypes

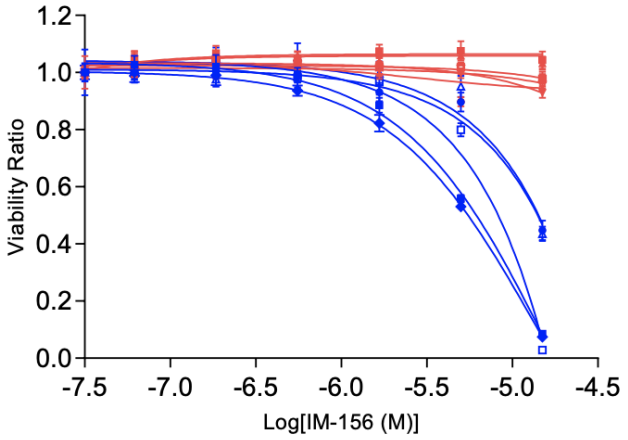
Identification of OxPhos inhibitor GBM Subtype

GBM patient samples

Precision medicine characterization of tumor

Four sub-types identified

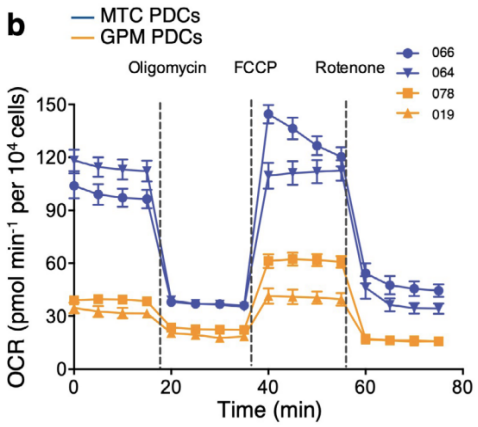
- **MTC** Mitochondrial
- **GPM** Glycolytic/ Plurimetabolic
- **PPR** Proliferative/ Progenitor
- **NEU** Neuronal



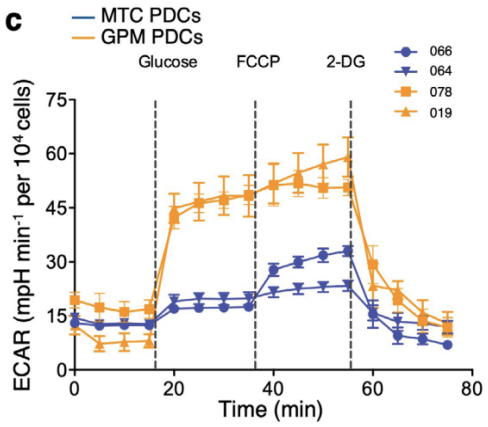
OxPhos inhibitor lixumistat selective for MTC subtype

Metabolic Activity*

Oxidative Phosphorylation



Glycolysis



MTC Subtype: OxPhos > Glycolytic **GPM Subtype:** Glycolytic > OxPhos

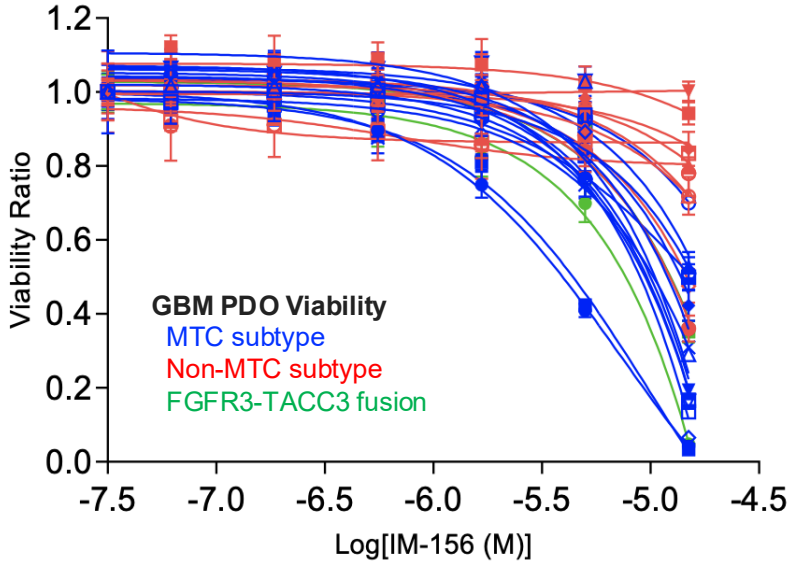
*Garofano et al., Nature Cancer (2021) 2: 141

Lixumistat is an OxPhos Inhibitor Selective for MTC Subtype in GBM Patient-derived Cells

We know which patients may respond – before treatment begins

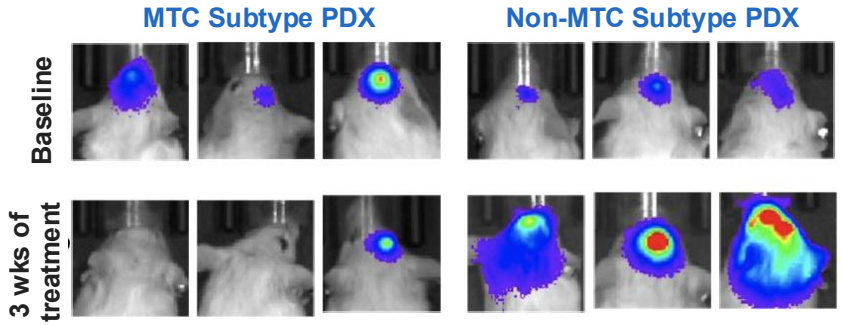
A novel pathway biomarker was discovered that identified a subset of GBM patients whose tumor growth and proliferation were OxPhos-dependent, the mitochondrial (MTC) subtype.

Lixumistat selectively inhibited viability of GBM patient-derived organoids (PDOs) of the MTC subtype, with minor or no activity against other GBM subtypes.

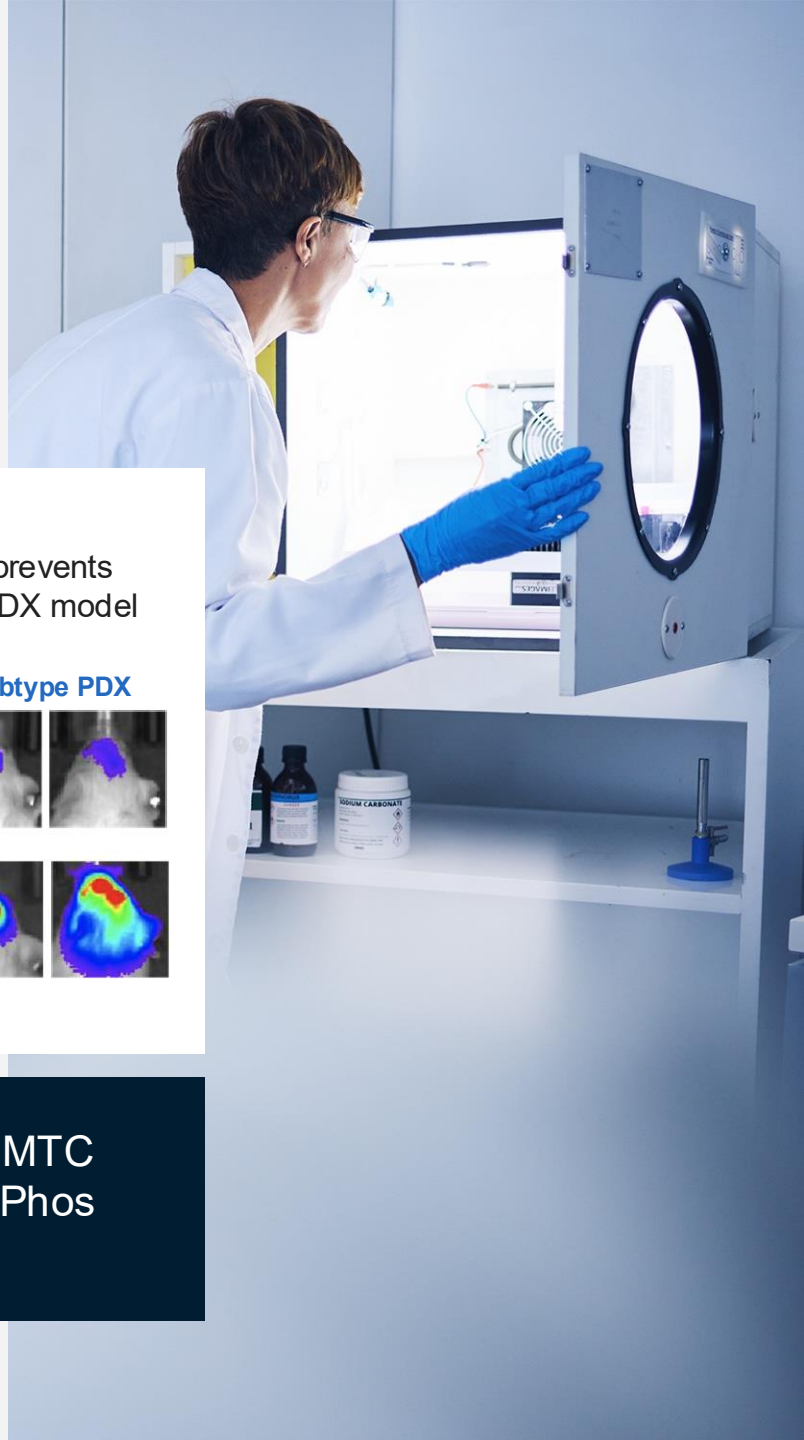


* Lixumistat also reduced viability of a GBM PDO harboring the FGFR3-TACC3 gene fusion, the most recurrent gene fusion across all human tumors

OxPhos inhibitor (IACS-010759) selectively prevents growth of MTC GBM subtype in vivo using PDX model



Hypothesis: GBM patients of the MTC subtype will be sensitive to the OxPhos inhibitor lixumistat



Clinical development plan
Overview

Window-of-Opportunity study of Lixumistat in patients with newly diagnosed GBM

Goal: Data to support Phase 2 study

Outcomes

- Measure lixumistat in target tissue
- Demonstrate pharmacodynamic effect in target tissue

Study timing

- 1st patient dosed 3Q'26, last pt dosed 4Q'26

Patients/treatment: (10 total)

- Newly diagnosed GBM patients, subtype- independent
- 5 pts at 400 mg then 5 pts at 600 mg 4 once-daily oral doses per patient

High likelihood of success

- Lixumistat crosses BBB in preclinical speies
- Metformin (another biguanide) crosses BBB in humans
- Doses selected have PD effects in the skin of healthy subjects

Multicenter, randomized, Phase 2 study of the OxPhos Inhibitor Lixumistat Plus SoC versus SoC in patients with newly diagnosed IDH-WT Glioblastoma, Mitochondrial Subtype

Goal: Data demonstrate SoC+lixumistat superior to SoC in biomarker-selected GBM patients

Outcomes

- Objective Response Rate (ORR), Progression-free Survival (PFS), Overall Survival (OS)
- Validation of biomarker to identify additional OxPhos-dependent tumors

Study timing

- 1st patient dosed 2-3Q'27, last pt dosing initiated 4Q'28 (1.5 yrs), end of study 4Q'29 (2.5 yrs)

Patients/Treatment: (60 total, 40 SoC+lixumistat + 20 SoC)

- Newly diagnosed GBM patients of the MTC subtype
- SoC+lixumistat: SoC (2:1)
- 400 or 600 mg once-daily (determined by WoO study) + SoC or placebo + SoC

Key features of the approach:

- High unmet medical need exists in GBM treatment
- Lixumistat targets OxPhos, identified as a key driver in subset of patients using human organoid assays
- Precision medicine-guided patient selection
- De-risked by Window-of-Opportunity study
- Efficacy beyond SoC would support an FDA Fast Track designation application

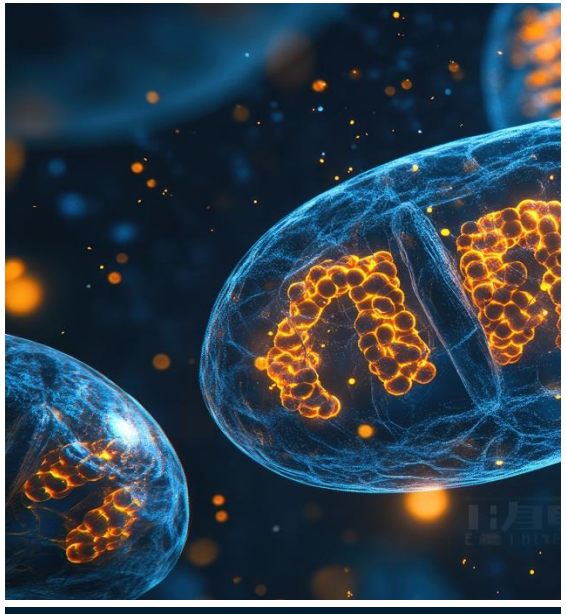
OxPhos biomarker defined, WoO to de-risk BBB penetration and then Phase 2 clinical efficacy study.

Lixumistat has Platform potential

Treating OxPhos-dependent intrinsic and acquired resistance

Intrinsic resistance

Cancers with OxPhos-dependent subtypes: **GBM**, Melanoma, Breast, Lung, Prostate, pan-cancer for FGFR3-TACC3 fusions, and metastasis



59% of cancer cases have no actionable target

Acquired resistance

Cancers that acquire resistance to therapy by upregulation of OxPhos

Pancreatic (PDAC) – to SoC and PD-1 blockade

Melanoma – to BRAFi/MEKi and checkpoint inhibitors

Lung - NSCLC to PD-1/PD-L1 inhibitors

Prostate – to androgen-deprivation

Ovarian – to PD-1/PD-L1 inhibitors

Gastrointestinal – to checkpoint inhibitors

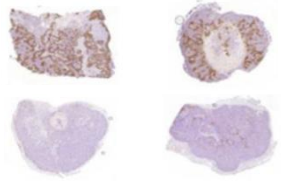
Breast – drug resistance associated with chemo- and targeted-therapies

Acquired resistance is due to metabolic switch to OxPhos.

ImmunoOncology sensitization

Inhibition of Tumor Microenvironment Hypoxia

Melanoma

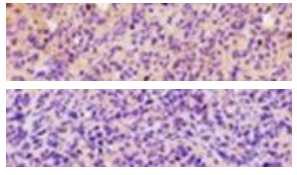


Vehicle

OxPhos Inh (IACS)

Clin Cancer Res (2019) 25:6429

Pancreatic cancer



Vehicle

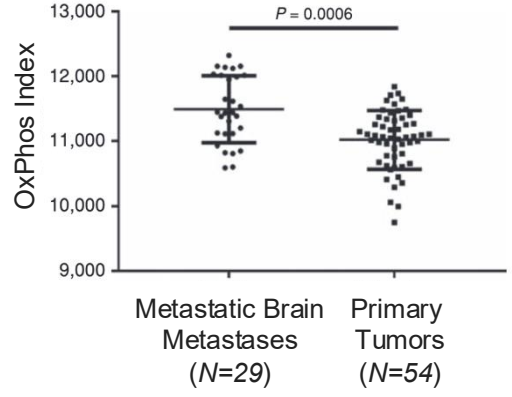
Lixumistat

Unpublished data

Tumor microenvironment hypoxia limits IO effectiveness

Metastatic brain tumors

OxPhos activity increased in brain melanoma metastases



Cancer Discov (2019) 9: 628

Brain metastases associated with increased OxPhos activity

ImmunoMet's success supported by collaborations

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Investigator-sponsored trial with Dr. S. Pant @ MD Anderson Cancer Center

"A Phase 1b Study of Gemcitabine and Nab-paclitaxel in Combination with IM156 in Patients with Advanced Pancreatic Cancer"

(clinical expertise & financial support for conduct of clinical trial)

GLIOBLASTOMA THERAPEUTICS NETWORK

– a collaboration of multi-institutional teams of scientists, clinicians, and innovators to advance promising therapies forward into pilot clinical studies in patients living with GBM

TEMPUS

An AI-enabled precision medicine company to develop novel OxPhos pathway activation biomarker

MIAMI MILLER SCHOOL of MEDICINE

Dr. A. Iavarone
Deputy-Directory
Sylvester Comp.
Cancer Center

Dr. M. de la Fuente
Chief, Neuro-Onc
Sylvester Comp.
Cancer Center

MAYO CLINIC

Dr. I Parney
Neurosurgeon
Mayo Clinic

STEP 01

- Complete ongoing PDAC study (‘26)
- Complete Window-of-Opportunity (’26) & initiate Phase 2 GBM study (’27)
- Prioritize additional opportunities

STEP 02

- Expand patient experience consistent with Regulatory registration path (‘27)

STEP 03

- Provide runway to partnering, exit, or next fundraising round (‘26/‘27)

STEP 04

- Current investors continue to express interest to invest

Partnering with ImmunoMet to **help cancer patients**

ImmunoMet Therapeutics is currently seeking strategic investors and collaborators to realize lixumistat’s full potential