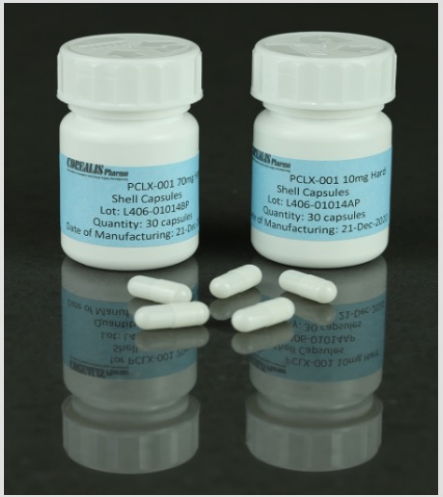
PACYLEX

ACCELERATING THE PACE OF CANCER CARE



Zelenirstat; first-in-class daily oral treatment for blood and solid tumor cancers in Phase 2

DECEMBER 2023

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Zelenirstat: first-in-class compound that inhibits myristoylation

Myristoylation is a fatty acid modification of certain proteins in critical cell functions.

Inhibition of myristoylation kills cancer cells at concentrations that don't affect normal cells (**selective lethality**).

Zelenirstat inhibits myristoylation:

- blocks both enzymes responsible for myristoylation,
- Part of Library of 503 compounds with PCLX-002, backup with extensive preclinical data

In animal cancer models, **zelenirstat**

- **regresses lymphoma and leukemia tumors,**
- **eliminates leukemic stem cells** from bone marrow,
- **Inhibits growth of solid tumors** (lung, breast)

In cancer patients refractory and/or relapsed to a median of 4 prior lines of therapy**, zelenirstat:**

- Is **safe and well tolerated at daily oral doses up to 210mg,**
- **Improved Progression free and overall survival** observed in Phase 1 **solid tumor patients** comparing 210mg to lower doses,
- **210mg dose advanced to Phase 2**

Seeks $55M USD Series B **to fund Phase 1/2a and 2b in pts with AML, and Phase 2a in pts with solid tumor cancers**

Billion dollar exit potential with history after successful **Phase 2**

Orphan and Fast Track received for **AML**

Synergy likely with other cancer therapies

- observed *in vitro* with venetoclax

Experienced **team >20 yr average** in **Pharma industry experience** in drug development and commercial strategy

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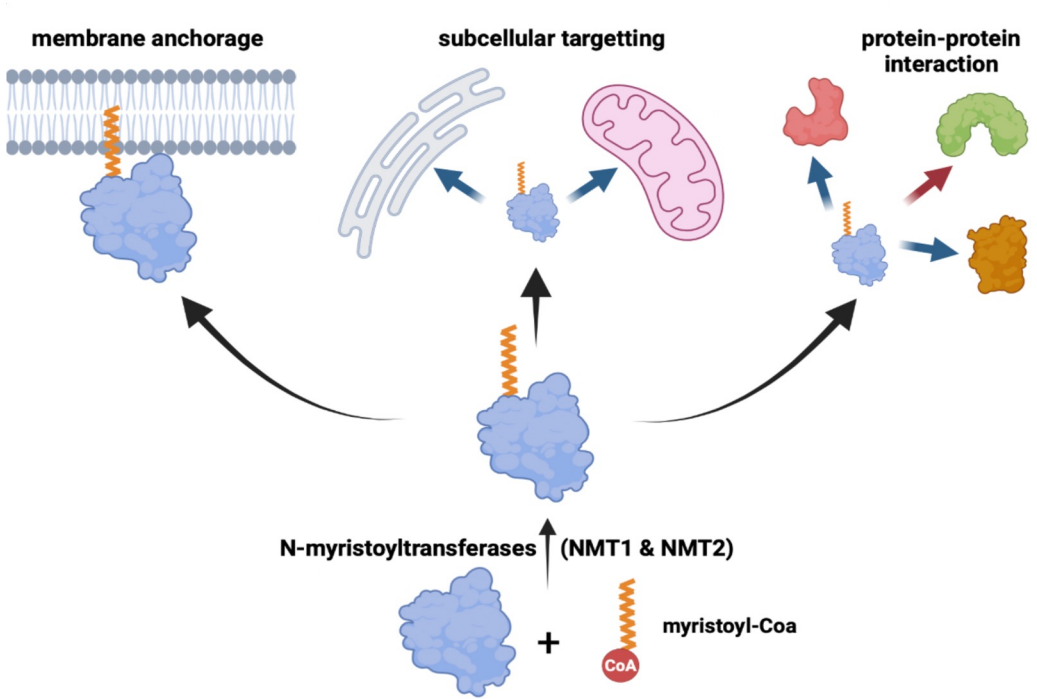
TARGET: Myristoylation is key to membrane binding of proteins involved in cancer signaling and other key functions

- **Myristoylation** is the addition of 14 carbon saturated fatty acid myristate to N-terminal glycine proteins, mediated by two **N-myristoyl-transferases (NMT), NMT1 and NMT2.**
- **Myristoylated proteins bind membranes** where they interact with other proteins in critical cell functions.
- Myristoylation is **essential for cancer cell prosurvival and proliferation signaling, energy production in mitochondria, and angiogenesis**, critical to cancer cell proliferation and survival.
- **Zelenirstat** is an **N-myristoyltransferase (NMT) inhibitor** which blocks both enzymes responsible for myristoylation.
- Inhibition of myristoylation kills cancer cells at concentrations that don't affect normal cells (**selective lethality**).



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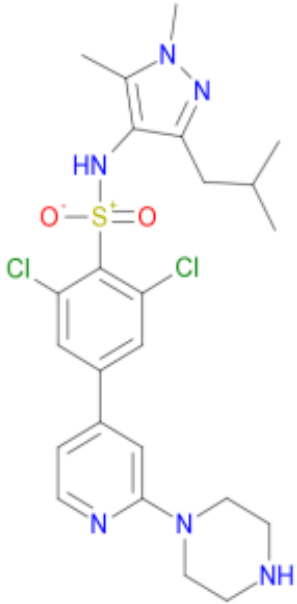
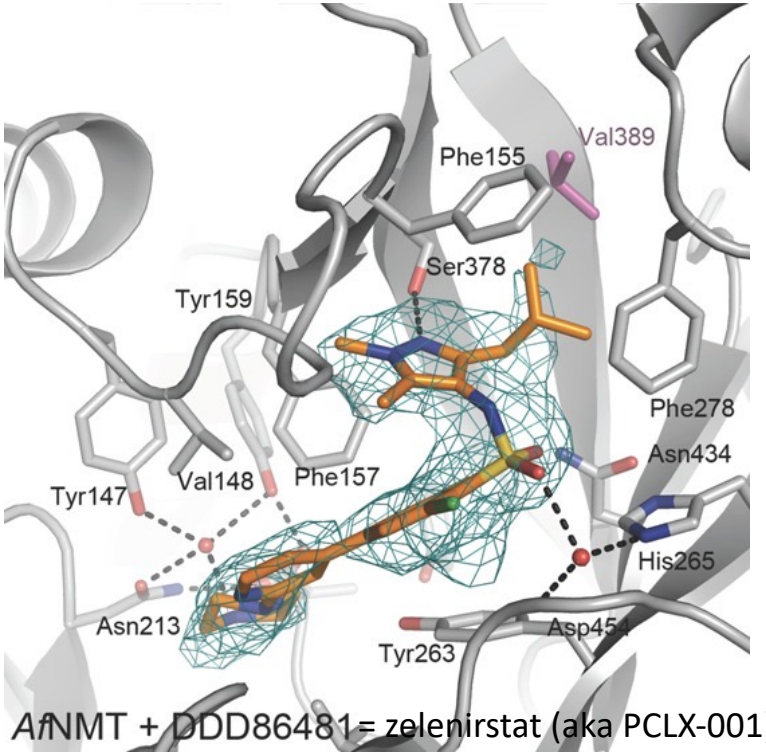
Zelenirstat is a small molecule N-myristoyltransferase inhibitor (NMTi) which binds in the active site, inhibiting myristoylation

Zelenirstat Structure
($C_{24}H_{30}Cl_2N_6O_2S$)



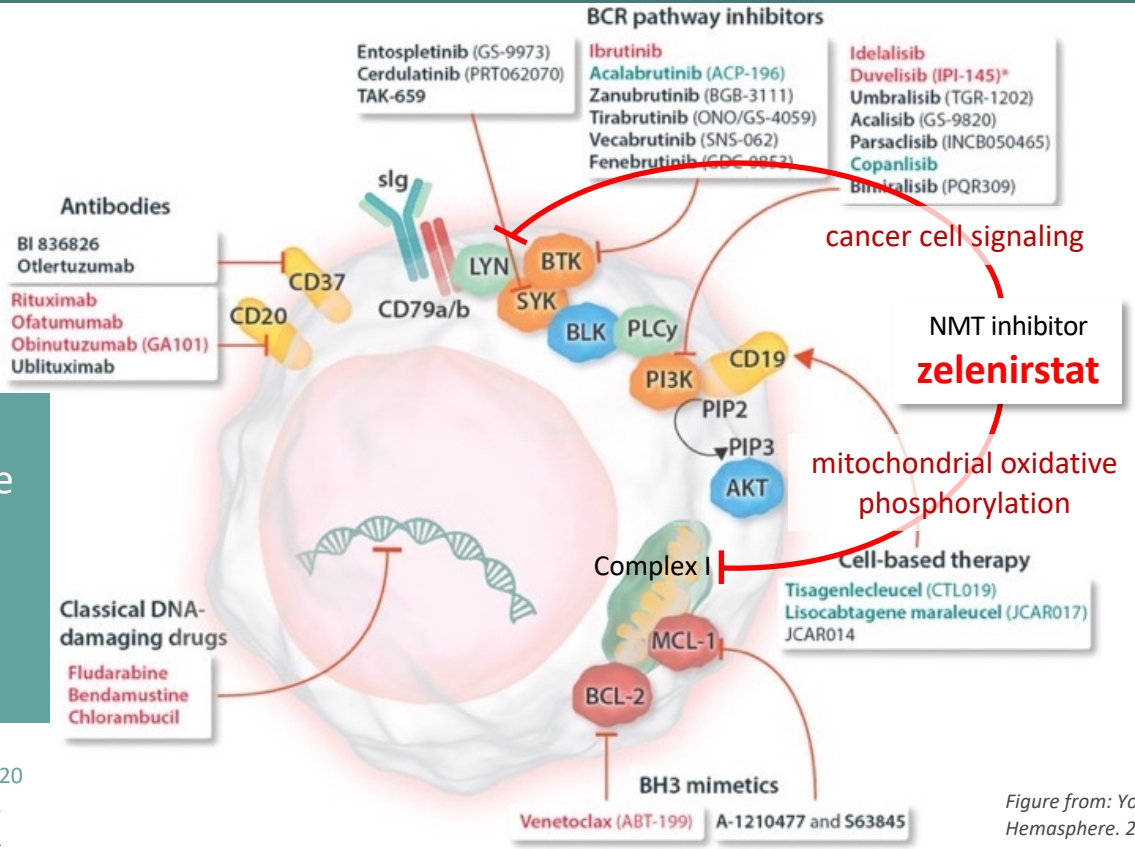
Active site of NMT in complex with zelenirstat



*Af*NMT + DDD86481= zelenirstat (aka PCLX-001)

Fang *et al. ACS Chemical Biol.* (2015)

MOA: NMT inhibition disrupts prosurvival signal initiation and oxidative phosphorylation in cancer cells



Beauchamp, et al., *Nature Communications* 2020, 11:5348

Gamma, et al. *EHA* Library. 06/08/2023; 386294; P465

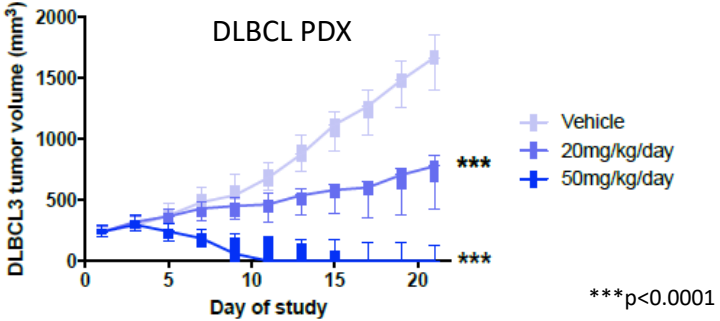
It also disrupts Src-family kinase signaling in angiogenesis inhibiting solid tumors

Pain, et al. *Cancer Res* 1 April 2023; 83 (7_Supplement): 3620

Figure from: Yosifov et al. Hemasphere. 2019 Apr;3(2):e175.

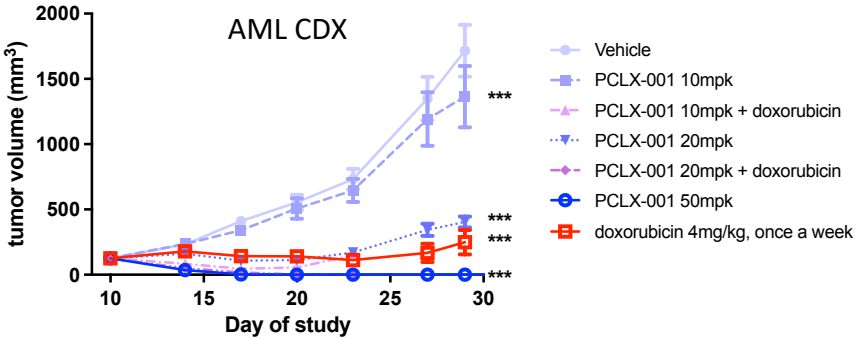
Zelenirstat (PCLX-001) regresses blood cancer xenografts and inhibits solid tumor xenografts in mouse models of cancers

Zelenirstat regresses tumors in lymphoma and leukemia



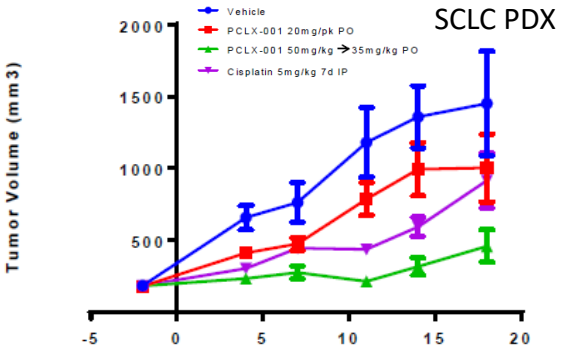
***p<0.0001

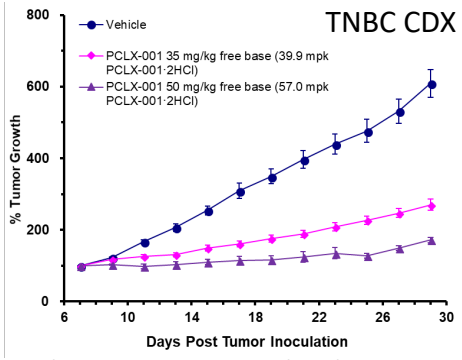
Beauchamp, et al., Nature Communications 2020, 11:5348



Mackey, et al. *Cancer Res* 1 July 2019; 79 (13_Supplement): 3043.

Zelenirstat inhibits solid tumors (lung and breast)



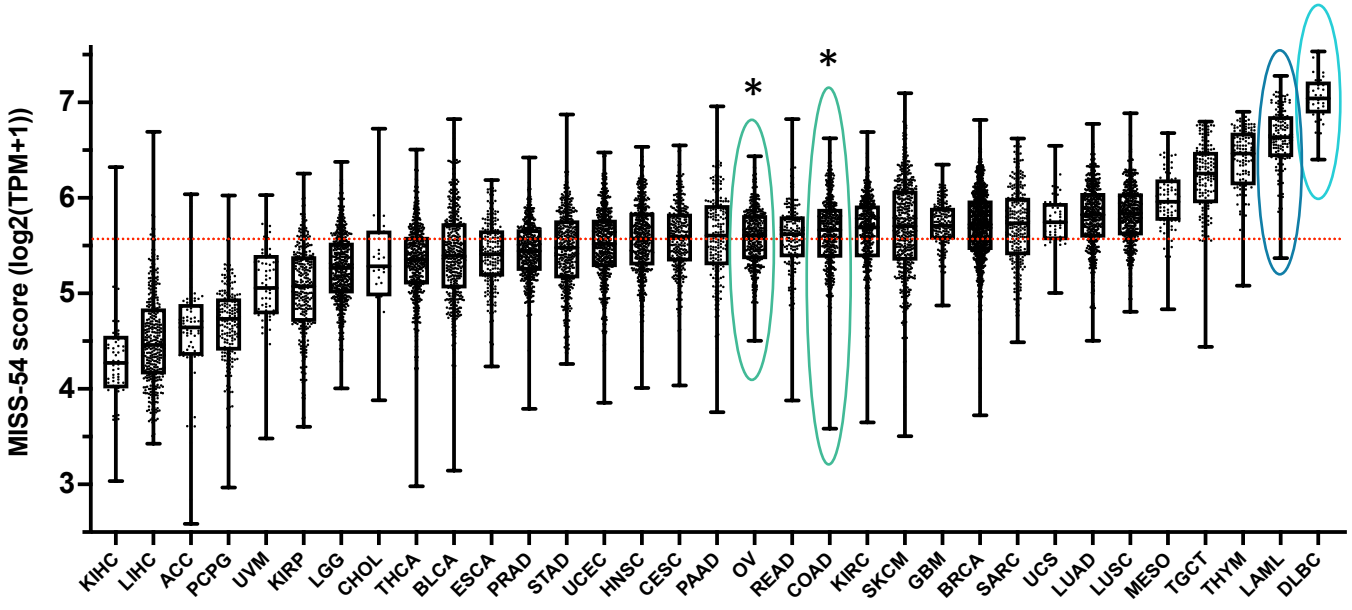


Mackey, et al. *Breast Cancer Research and Treatment*, 2021

DLBCL – Diffuse Large B-cell Lymphoma, AML – Acute Myeloid Leukemia, SCLC – Small Cell Lung Cancer, TNBC – Triple Negative Breast Cancer, PDX – patient derived xenograft, CDX – cell line derived xenograft

Gene expression signature predicts cancers most sensitive to zelenirstat

Myristoylation inhibition sensitivity signature predicts cancers and patients susceptible to respond to myristoylation inhibition treatment



Gene expression signature identifies DLBCL and AML among the most zelenirstat-sensitive blood cancers, and colorectal and ovarian cancers (represented in long-term Phase 1 patients) among the most zelenirstat-sensitive solid tumor cancers. Cervix, Lung, testis, thymus, uterus, and Head and Neck are also predicted to be sensitive to zelenirstat treatment. Would also be expected to be used to ID sensitive patients within each cancer type.

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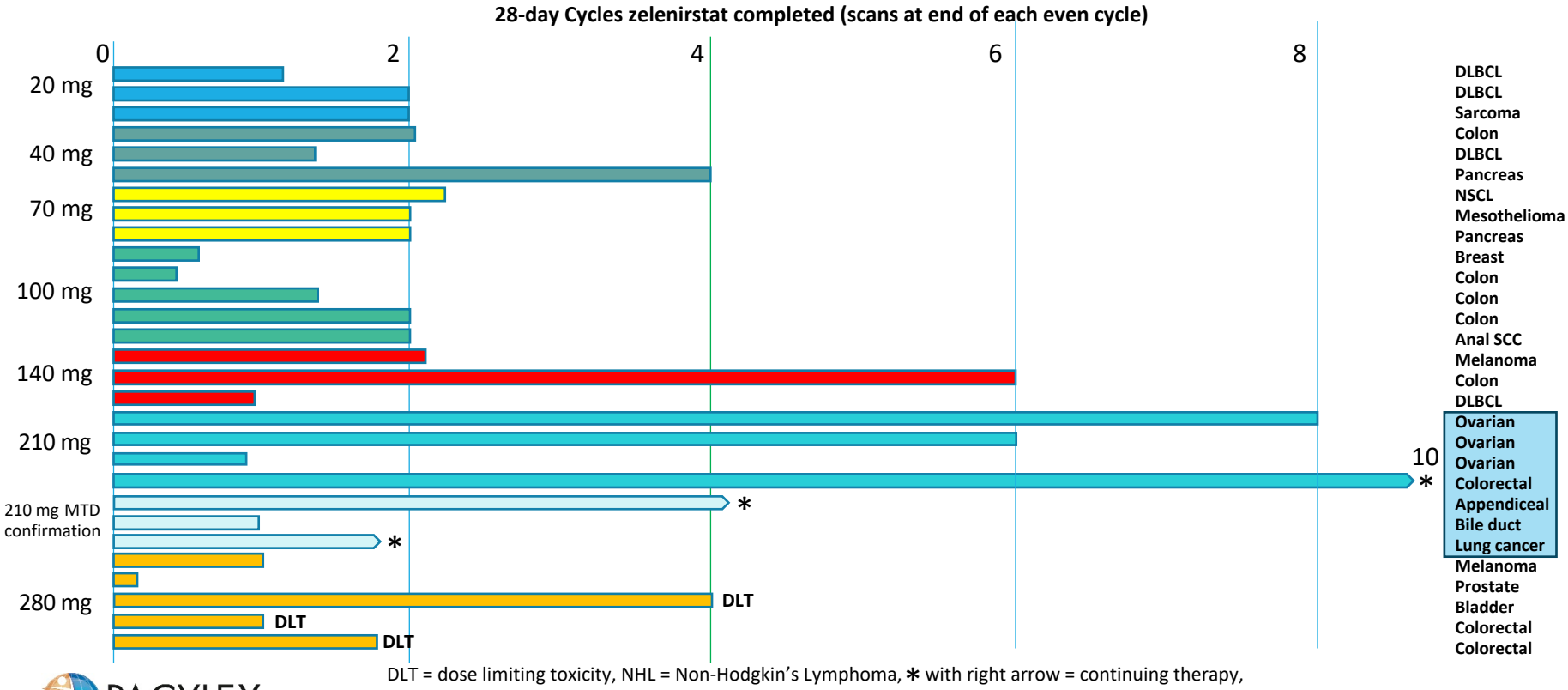
Beauchamp, E, et al. Cancer Res 2023;83(7_Suppl):Abstract nr 1662.

Patients receiving 210mg zelenirstat in Phase I dose escalation study responded and remained on study treatment much longer



DLT = dose limiting toxicity, NHL = Non-Hodgkin's Lymphoma, * with right arrow = continuing therapy,

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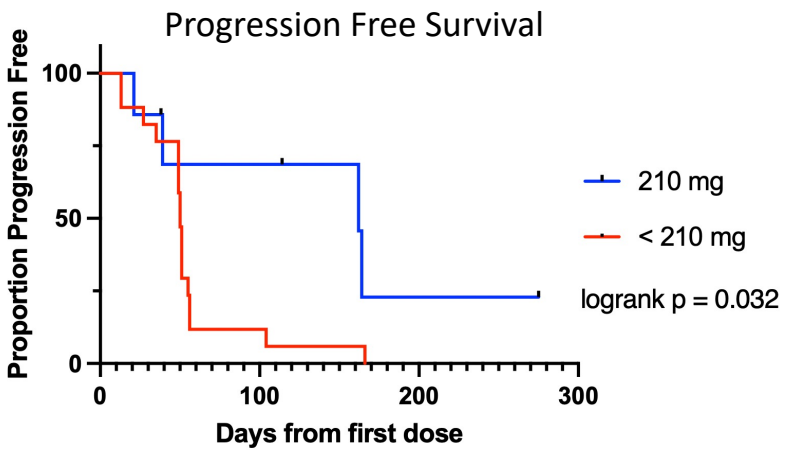
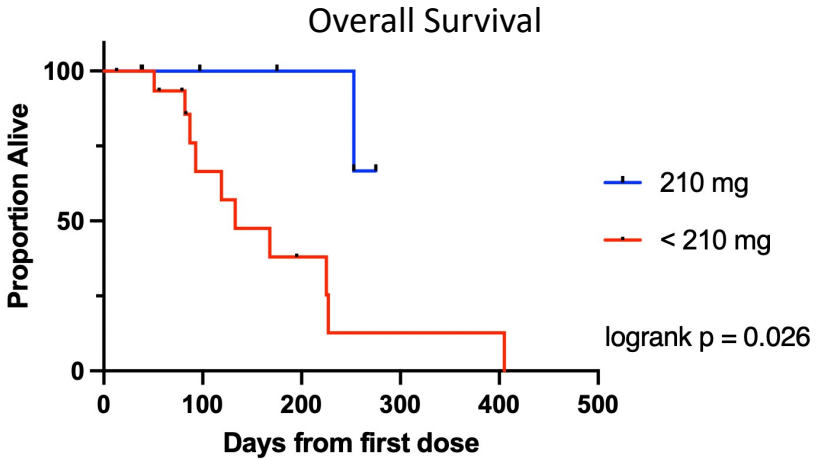
Safety results: No dose limiting toxicities in patients receiving 210mg or less in Phase 1 study; a minority of patients experience GI adverse events

- No dose limiting toxicities identified from 20mg to 210 mg: compliance >90%
  - 280 mg cohort had three patients with first cycle GI Dose Limiting Toxicities
    - grade 3 dehydration (1); grade 3 biliary tract stenosis requiring hospitalization and antibiotics (1); grade 3 diverticulitis (1)
- For patients 20mg-210 mg
  - Grade 1-2 GI adverse events (AEs) most frequently reported at 20mg-210 mg
    - decreased appetite (11/24 patients = 46%)
    - nausea – responsive to standard antiemetics grade 1 and 2 (10/24 patients = 42%)
    - diarrhea – grade 1-2 self limited or responsive to therapy (10/24 patients = 42%)
    - vomiting – grade 1-2 responsive to standard antiemetics (9/24 patients = 37%)
  - Grade 1-2 fatigue in 11 patients (46%)
  - Grade 2 thrombocytopenia (75 to 100 × 10^9/L), transient, in 3 patients (12%) with baseline grade 1
  - No neutropenia, no febrile neutropenia, no neutropenic fever
  - No QT prolongation or arrhythmia
  - No zelenirstat related renal, neurologic or skin AEs; no worsening of baseline neuropathy

Zelenirstat 210 mg monotherapy resulted in a benefit in both Progression Free Survival and Overall Survival in Phase 1

Compared 210mg zelenirstat (n=7), the recommended Phase 2 dose versus < 210mg (n=17)
PCLX-001-01 Phase 1 dose escalation study:





Post-hoc Progression-Free Survival analysis indicates patients at the Phase 2a dose of 210 mg have experienced significantly less progression (p = 0.032)

Progressive disease: first occurrence of radiologic RECIST 2.0 or investigator-assessed disease progression.

All censored patients continuing on PCLX-001 as of Dec 1st 2023

A post-hoc analysis of Overall Survival (all-cause death) indicates patients receiving the Phase 2a dose of 210 mg survived significantly longer (p=0.026)

Overall survival: death from any cause

Database review Dec 1st 2023

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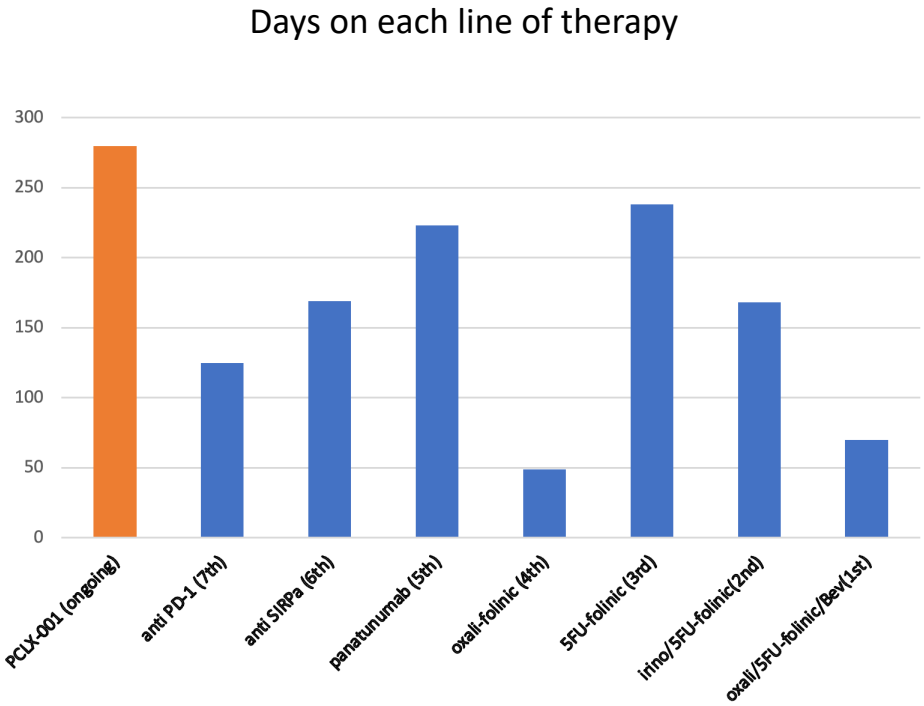
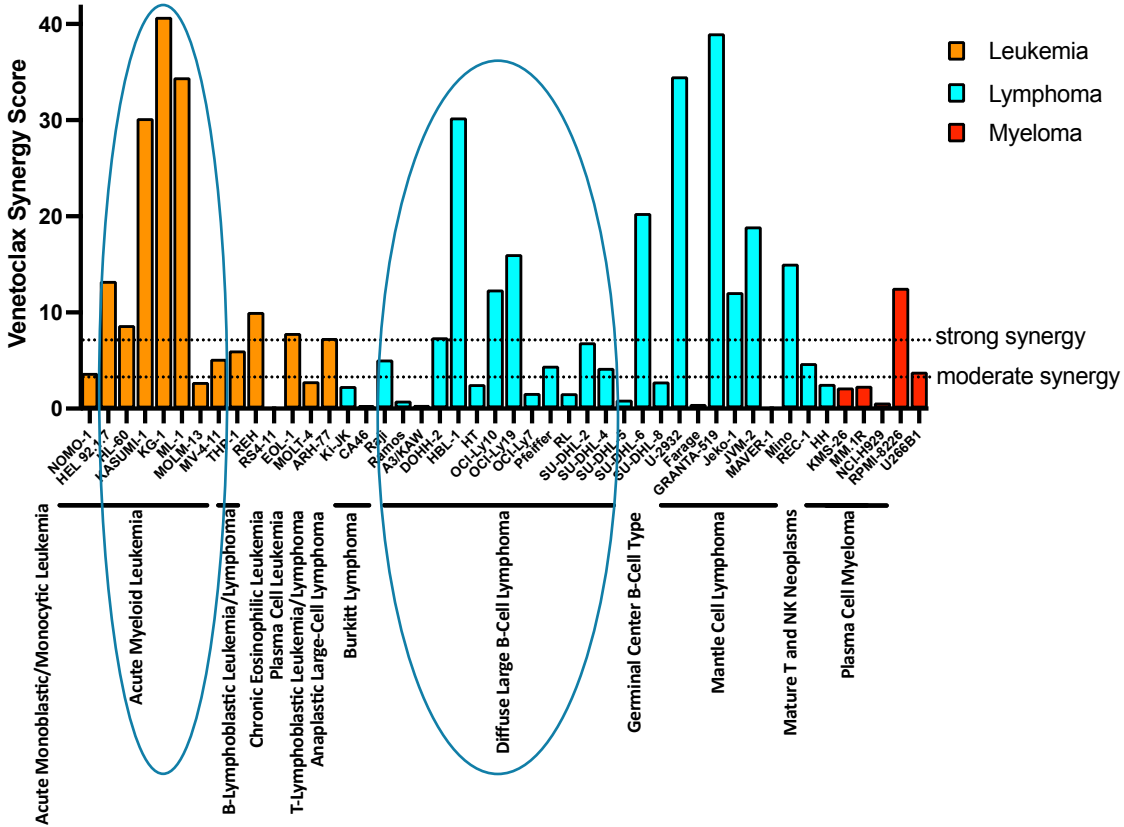
Patient with colorectal cancer in Cohort 6

- 63 year-old male with refractory metastatic colon cancer
- Seven prior lines of therapy
- Has now received 275 daily doses of zelenirstat 210 mg with only mild GI upset at the start, retains his hair, feeling well
- This treatment has controlled his cancer longer than any prior therapy
- 11% reduction in tumor sizes, 48% reduction in blood markers of cancer



In vitro data show zelenirstat is strongly synergistic with venetoclax

- In most hematologic cancer cell lines, zelenirstat (PLCX-001) is synergistic with venetoclax
- Many cell lines show strong synergy
- Additional synergy studies planned



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Pacylex pipeline extends beyond oncology indications

Product	Indication	Discovery		Preclinical		IND	Clinical			NDA
		In vitro	*In vivo*	Lead Op	GLP	(CTA-CAN)	Phase 1	Phase 2	Phase 3	
Zelenirstat	Non-Hodgkin Lymphoma (DLBCL)								n/a	2026
Zelenirstat	Solid tumors							2024	2025	2027
Zelenirstat	Acute Myeloid Leukemia (AML)						2023	2024	n/a	2026
Zelenirstat + venetoclax etc.	Acute Myeloid Leukemia (AML)							2024	n/a	2026
PCLX-002	Autoimmune					2024		2025	2026	2028

- B cell NHL Phase 2a expansion study started in 2023 at 4 clinical sites in Canada
- Solid tumor Phase 2a expansion study will start early Q1 2024
  - Phase 2a to ID solid tumors which respond best to zelenirstat will initiate study with 4 cancer types: breast, non-small cell lung (NSCLC), small-cell lung (SCLC), colorectal (CRC), and bladder cancers
- IND and IRB cleared Phase 1/2 AML dose escalation study at MD Anderson expected to start in late 2023; supported by DOD grant
  - Orphan and Fast Track designations granted for AML
- Additional cancer indications are planned

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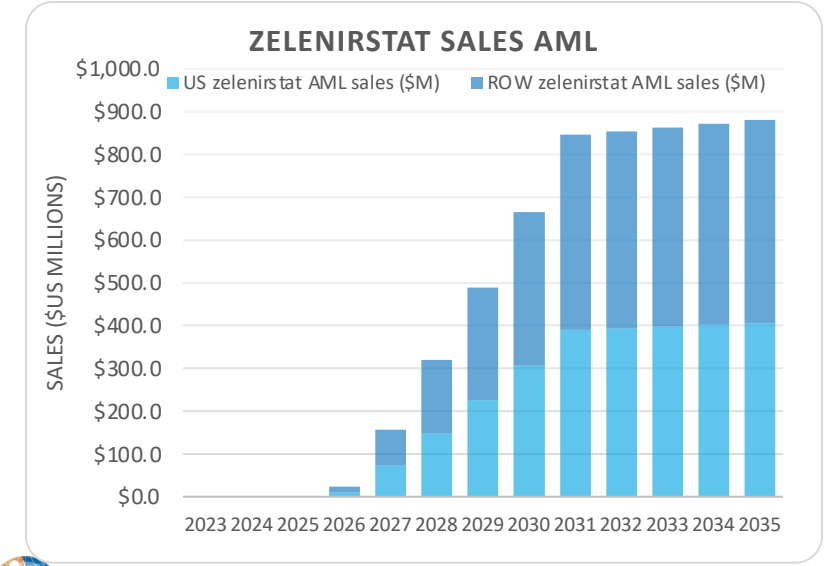
Zelenirstat is 10x more potent *in vitro* than B-cell receptor pathway inhibitor ibrutinib ($10B 2021) with similar market potential

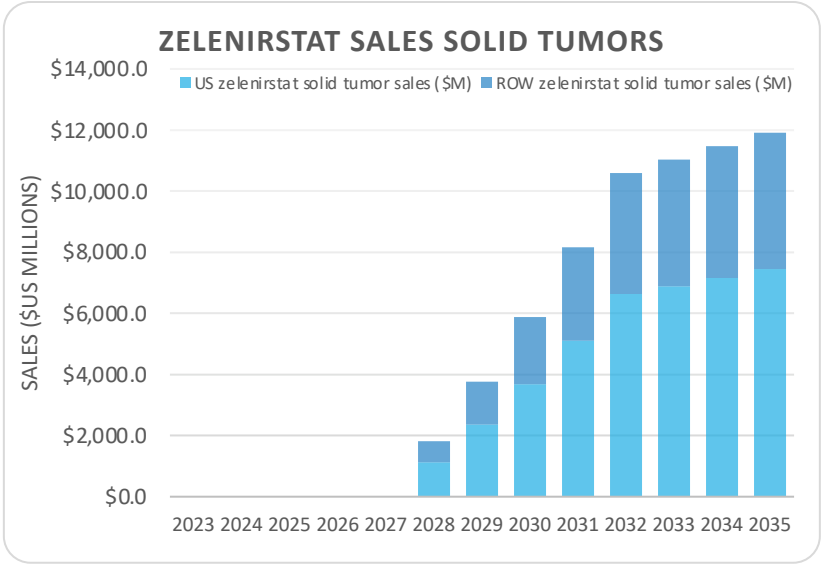
Market Assumptions Acute Myeloid Leukemia (AML)

- Initial indication (late 2026 launch; accelerated approval)
- 25% peak market share
- 6 months on treatment
- $10,000 per month price in the US
- ROW worth 117% of the US

Market Assumptions Solid Tumor (market potential for breast, lung cancers, and colorectal)

- 2028 launch
- 10% peak market share
- 6 months on treatment
- $10,000 per month price in the US
- ROW worth 60% of the US





Sales continue beyond 2035; epidemiology and some market assumptions from GlobalData

Pacylex has made steady progress on zelenirstat development

	Seed 2019-20	Series A 2021	$55m Series B 2023-2024
Risk reduced	Clinical drug candidate verified	PCLX-001 safety and tolerability at target dose(s)*	PCLX-001 efficacy at recommended Phase 2 dose
Key milestones	✓GMP manufacturing ✓2-species toxicology ✓CTA cleared (Canadian IND) ✓In vivo POC published	✓Phase 1 dose escalation ✓Safety and tolerability, pharmacokinetics, drug exposure ✓Recommended Phase 2 dose (RP2D) ✓Regulatory milestones (Orphan, Fast Track, IND clearance) ✓First patient dosing of NMTi published	•Initiate Phase 1 dose escalation in AML •Phase 2a expansion cohorts in R/R AML and solid tumors •Phase 2 in R/R AML •Orphan and Fast Track for AML •Potential for AML accelerated approval, global partnering, or an exit

*based on *in vitro* and *in vivo* efficacy studies

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Zelenirstat has blockbuster exit potential in an area of pharma interest

- Zelenirstat is 10x as potent *in vitro* as B-cell receptor pathway inhibitor ibrutinib ($10B 2021)
- Pharma companies acquire B-cell receptor pathway inhibitors around Phase 2:

Acquirer	Acquired	BTKi Phase	Price	Date
Sanofi	Principia Biopharma	Phase 2b	$3.7B	Aug 2020
Merck	ArQule	Phase 2	$2.7B	Dec 2019
Eli Lilly	Loxo Oncology	Phase 1/2	$8B	Jan 2019
AZ	Acerta	Phase 2/3*	$6.8B	Feb 2016

*subsequently approved

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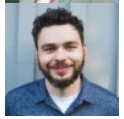
An experienced Pacylex team is in place to drive R&D

Michael Weickert, PhD – CEO, Director
30+ yrs Pharma; 5x startup CEO, 15 yrs public pharma; Former VP Auspex, Senior Program Executive, Nektar, Ligand, NCI/NIH

Luc Berthiaume, PhD – CSO, co-Founder, Director
World leader in protein fatty acylation; Founder of Eusera and Pacylex; 3 patents

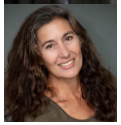
Ryan Heit, MSc, MBA – VP Ops, co-Founder
20+ companies in early-stage commercialization; founder/ co-founder of 4 companies; led deal screening for VA Angels



Erwan Beauchamp, PhD – Dir. Discovery Biol.
Protein fatty acylation expert for 15+ years; made seminal discovery of sensitivity of hematologic cancers to PCLX-001

Michele Libonati, MSc – COO
30+ yrs Pharma; Former SVP Program Strategy Leadership, Gilead Sciences, CEO Proneurotech, Lifecycle Leader OCREVUS, LUCENTIS, Rituxan, Raptiva (Genentech/Roche), Development Leader Intermezzo (Trancept), Tysabri (Elan Pharmaceuticals)

John Mackey, MD, FRCP – CMO, co-Founder, Director
Former Director of clinical trials at CCI and Director of TRIO (CRO); practicing oncologist, ~100 clinical trials, founder of 3 cos.



Annette Marcantonio – VP Clinical Operations
30+ yrs Pharma; Former VP Clinical Affairs at Neurogastrx, Aimmune, Sr. Dir. Clinical Ops at Alvine, Nektar, consultant at Genentech, Xenoport, Aviron.

Vanessa Grant - Counsel
Counsel with Norton Rose Fulbright - expertise in M&A, corporate governance, private equity and venture capital.

Outside Board Directors

Cindy Jacobs, MD, PhD – Board Director and Chair
CMO Achieve Life Sciences, CMO OncoGenex, Corixa, executive with Cytran, CellPro, Immunex (inventor and devel. Enbrel). On Board of Renown Pharma.

Mark Huson, PhD – Board Director
Professor of Finance and the Dianne and Irving Kipnes Chair in Finance and Development University of Alberta. is an expert in Corporate finance, Income trusts, Management science and Private enterprise.

Ajit Gill, – Board Director
CEO, Founder, and Director, Greenfire Bio, former CEO & President, Nektar Therapeutics, Auspex; VP and Gen Mgr Kodak's Interactive Systems; VP, Finance at TRW-Fujitsu

Nola Masterson, MSc, – Board Director
co-founder and former CEO Sequenom, Inc. (SQNM). Chair Emeritus California Life Science Institute, Boards: EpiCept Corporation, Nanostream, Inc., Omicia, Inc., Repros Therapeutics Inc. (RPRX, Chairman), EmbraceHer Innovations, Inc., Resonance-Med, and Lynx Bio.

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Pacylex is an extraordinary investment opportunity NOW

First-in-class, potent, oral therapy with safety and tolerability largely derisked

Orphan Drug and Fast Track Designations granted for AML

Progression free and overall survival advantage in Phase 1; Major value inflection; Phase 2 efficacy data, just ahead

Potential exit after Series B since Phase 2 data has been historic partner point

$55m Series B supports two indications in Phase 2, 1 for registration (AML)

Combination therapy in liquid and solid tumors, and expansion to autoimmune disorders create huge upside

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Contact Info:

Michael Weickert, PhD, CEO

michael.weickert@pacylex.com

650-218-1840