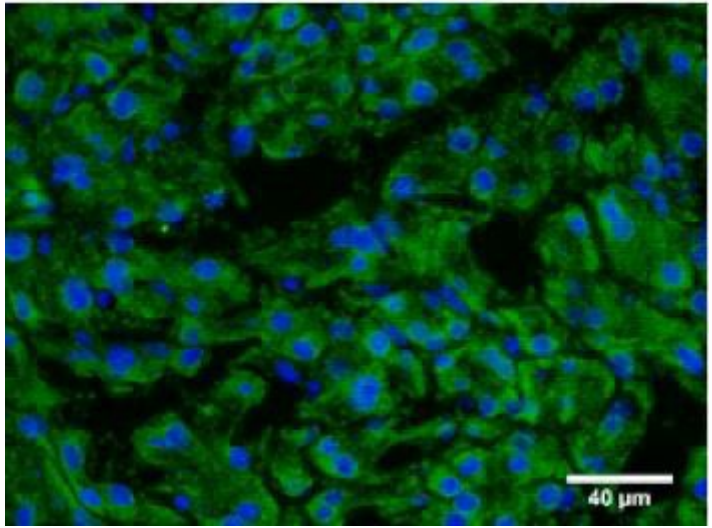
CPD 100Li - A Novel Targeting Prodrug For Oncology

Executive Summary

- Cascade's lead molecule, ***CPD100Li***, demonstrates remarkable preclinical results in multiple cancers, and in particular, ***Pancreatic Cancer***.
- Our compound is effective in ***combination therapy*** with both ***immuno-oncology (I/O)*** and ***chemotherapeutic*** agents.
- We are transitioning into the IND (Investigational New Drug) phase of development and are ***scaling up manufacturing***.
- Securing market exclusivity after the drug is introduced into the clinics, we have obtained ***Orphan Drug Designation (ODD) from the FDA for the treatment of Pancreatic Cancer.***
- Our current offer is a ***$3M convertible note.***
- These funds will support advancing the compound to IND status and support the attainment of critical milestones -- enhancing engagement with potential strategic partners.

Pancreatic Cancer

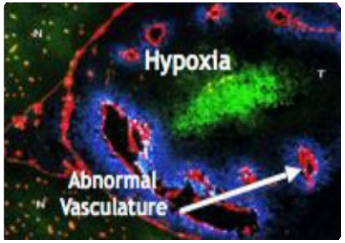
- Pancreatic Cancer is the second leading cause of death from cancer. It is a significant unmet medical need with 5-year survival < 5%
- Patient incidence in major markets (US/EU) is well over 50,000 cases/year
- Market potential for a new entrant with improved efficacy and safety compared to the current standard of care is estimated to be > $1 Billion
- Current standard of care (chemotherapy) is largely ineffective, despite multiple attempts with various agents and combination therapies
- Exceptional preclinical data with CPD100Li in Pancreatic cancer model warrants continued investment
- Pancreatic Cancer creates a very “hypoxic” tumor microenvironment (TME)



*pancreatic tumor regions of hypoxia in green

THE PROBLEM/OPPORTUNITY:

Hypoxia – What is it, and why is it important?



- Hypoxia (Hypo = Less/Low, Oxia = Oxygen), i.e. low oxygen concentration, is a ***common feature of a solid tumor's microenvironment***.
- Effectively, the tumor "outgrows" its blood supply resulting in a below normal oxygen tension/concentration and leads to a more acidic region surrounding and within the tumor.
- High Acidity and Low Oxygen tension create a hostile environment surrounding the tumor that is ***highly toxic to many compounds and drugs***, reducing effective drug penetration and efficacy.
- This TME (Tumor Microenvironment) negatively impacts the effects of chemo or immuno-oncology (I/O) treatments.
- And…was the topic of the 2019 Nobel Prize!!!

JCI The Journal of Clinical Investigation

The 2019 Nobel Prize honors fundamental discoveries in hypoxia response

Javid Moslehi, W. Kimryn Rathmell

J Clin Invest. 2020;130(1):4-6. https://doi.org/10.1172/JCI134813.

Hypoxia – What is it, and why is it important?

- Hypoxia provides ***multiple targeting opportunities***:
  - ✓ Prodrugs designed to accumulate in ***hypoxic tumor*** compartments.
  - ✓ Develop ***"hypoxia biomarkers"*** for optimizing patient selection.

- Pancreatic Cancer's extremely low oxygen levels presents a prime target for a ***focused, and highly activated*** chemotherapeutic warhead

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The 2019 Nobel Prize honors fundamental discoveries in hypoxia response

*Oxygen Levels (pO2 in mmHg) using electrode probes		
Tumor Type	Normal Tissue	Tumor Tissue
Pancreas	57	2
Brain	26	13
Lung	N/A	16
Breast	52	10
Cervix	42	9

*Compilation of studies: 2000+ cancer patients. Reviewed in Vaupel, P. *et al.*, Antioxidants & Redox Signaling, *9*: 1221, 2007

THE SOLUTION:

A ProDrug that targets the Hypoxic Tumor Microenvironment (TME) increasing the effectiveness of standard chemotherapeutic and Immuno-Oncology treatments

CPD100Li

Cascade PRODRUG™

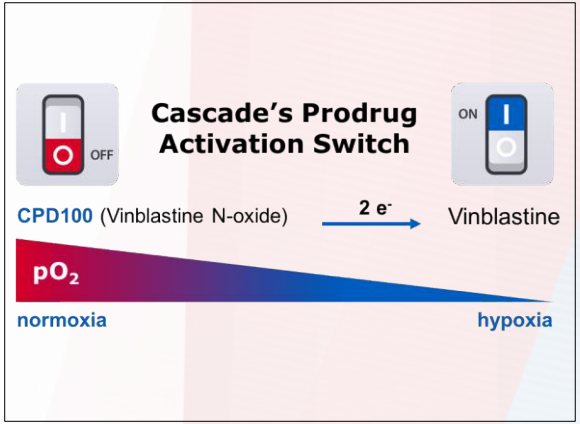
THE SOLUTION:

CPD100Li

- A Prodrug that is ***activated selectively in hypoxic regions*** of tumor

- It is formulated in ***liposomes*** to optimize pharmacokinetics (PK) and safety

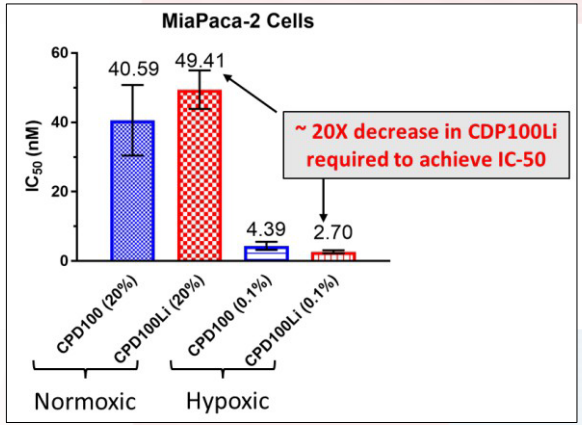
- Mechanism of Action (MOA) is via the warhead molecule, vinblastine, a ***tubulin inhibitor*** which blocks tumor cell division



THE SOLUTION:

CPD100Li

- ***Increased activity against tumor cell cultures exposed to hypoxic conditions***
- Targeting of tumor hypoxia results in higher therapeutic index:
  - ✓ Less normal tissue toxicity = ***Fewer systemic side effects***
  - ✓ Higher MTDs (Maximum Tolerated Dose) in vivo = ***Increased Efficacy***
  - ✓ Selective accumulation of activated cytotoxic drug in hypoxic tumor tissue = ***Targeted Warhead***
  - ✓ Enriched hypoxic tumor cell killing = ***Increased Accuracy*** and Efficacy
- Alters the TME (Tumor Microenvironment) - ***eliminating the tumor associated cells*** supporting the cancerous growth, metastasis & immunosuppression



CPD100Li Efficacy in Pancreatic Cancer Model

Human Panc-1 orthotopic model, Mono and Combo Therapy

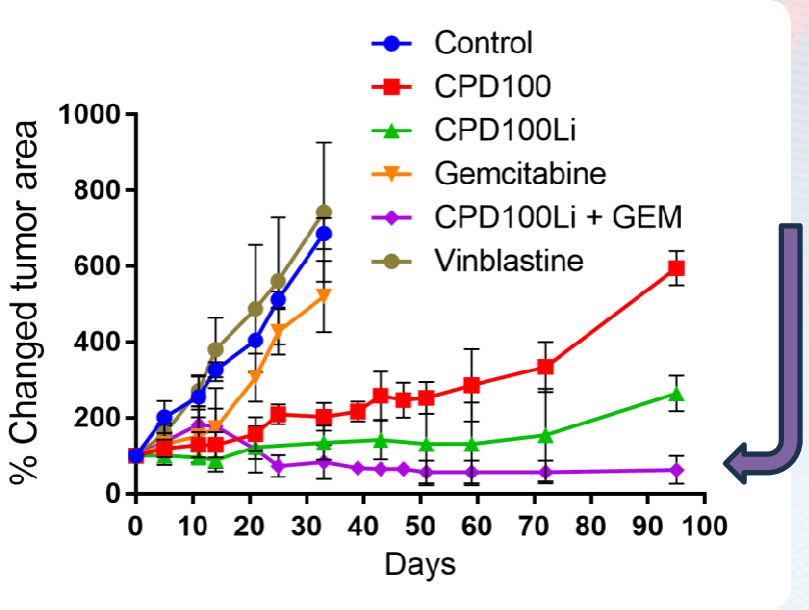
CPD100Li is ***active as monotherapy and in combination*** with gemcitabine (GEM) in Panc-1 model

Result:

- ***Strong synergy in combination with GEM***
- ***CPD100Li prodrug more active than vinblastine alone***

Dosing regimen:

- CPD100 and CPD100LI at 40mg/kg weekly for eight cycles
- GEM at 100 mg/kg biweekly six cycles
- Vinblastine at 5 mg/kg eight cycles
- CPD100LI at 40mg/kg weekly for eight cycles and GEM at 100 mg/kg biweekly six cycles



CPD100Li Efficacy in Human Lung Cancer Model

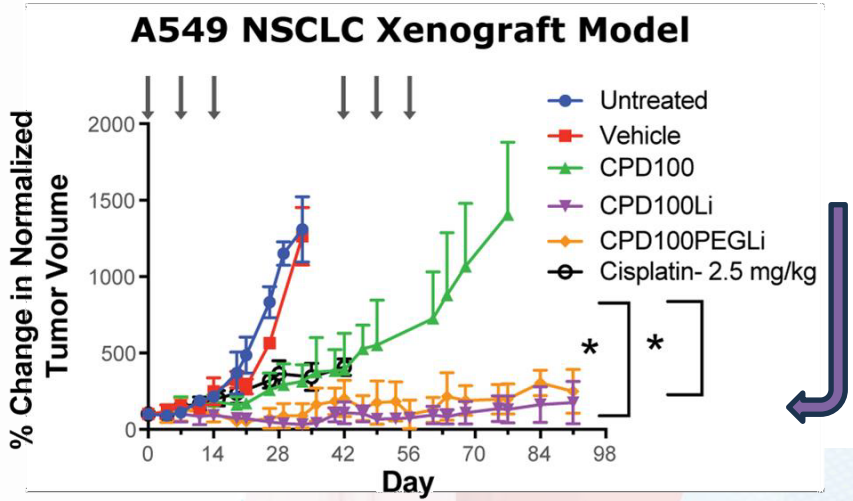
A549 NSCLC Xenograft, Mono Therapy

Result:

- ***Prolonged tumor growth inhibition with CPD100Li***

Dosing regimen:

- CPD100 dosed at 40 mg/kg (iv) in all on-treatment cohorts
- Cisplatin dosed at 2.5 mg/kg (MTD)

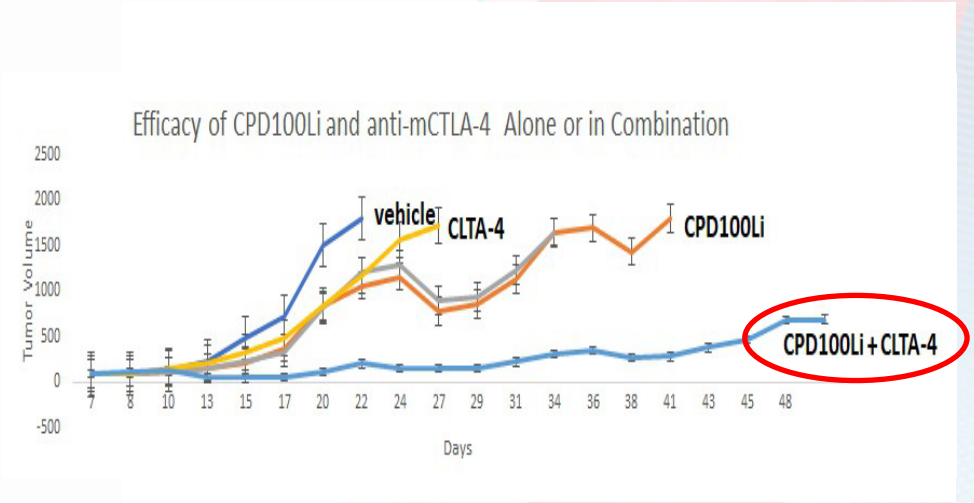


CPD100Li Efficacy in Syngeneic Colon Cancer Model

CT26.WT Murine Colon Carcinoma in Female BALB/c mice, Mono and Combo w/CTLA-4

Result:

- CPD100Li demonstrated ***strong synergistic response in combination with anti-CTLA-4***
  - Significant prolonged tumor growth inhibition vs CTLA-4 or CPD100Li alone
  - Effect on immunosuppressive cells support demonstrated synergy with anti-CTLA-4



Our Leadership Team

August J. Sick
Co-Founder|ProDrug Development

- Senior Executive for Invitrogen Corp
- Former President of Molecular Probes
- Key inventor on 35 issued US Patents

Allan Cochrane
Co-Founder|President

- Former President Epoch Pharmaceuticals
- Former COO Pacific Biometrics
- Adjunct Professor University of Oregon, Lundquist College of Business

John Nepute
Chief Financial Officer

- Former President Monaco Coach Corp
- Board Advisor Bit Cork
- Board of Directors Oakshire Brewing

Thomas Wuest, M.D.
Board Observer & Advisor

- CEO Ulcer Solutions, LLC
- Orthopedic Trauma Surgeon
- Former President Slocum Center for Orthopedics & Sports Medicine
- Former CMO Trillium Community Health Plan & Health Net of Oregon

Dr. David Regan
Director of Medical Affairs

- Oncology field veteran & expert
- Former President Association of Community Cancer Centers
- Member of Clinical Practice Comittee American Society of Medical Oncology

Eric Malek
Board Member|Chief Business Officer

- EDM Bio Consulting
- Former SVP Corporate Development Threshold Pharmaceuticals
- Previously, BiPar Sciences, Allos Therapeutics, Gilead Sciences, JNJ

Armen B. Shanafelt, PH.D.
Board Member

- ABShannafelt Advisory, LLC.
- Formally General Partner Lilly Ventures, Eli Lilly & Company, Roche Diagnostics corporation Bayer Corporation, DNAX Research Institute, Syva Company

Advisors

Adam Alani, PH.D. | Drug Delivery/Pharmacology R&D

John Keana, PH.D. | Chemistry R&D

Matthew Taylor, M.D. | Oncologist/Early Clinical trials

Christopher Klemm, PH.D. (Observer)

Pathway to Pre-IND Meeting & Use of Investor Funds

CMC

- Develop liposome formulation & pilot lot
- CPD100 DS GLP lot
- CDP100 DP GLP lot

Pharmacology

- Panc xenograft dose response
- CEREP off target screen

PK

- CYP Phenotyping & Induction
- Dog PK
- Rat PK
- PGP & PPB studies
- Bioanalytical method validation

Tox

- Rat DRF
- Dog DRF

Regulatory

- Pre-IND prep and meeting

Clinical

- Protocol Synopsis

PHARMA DIRECTIONS

Contract vendor providing development services

Pathway to and thru Pre-IND Meeting with FDA:	~ $2 M
G&A and Working Capital:	~ $1 M
TOTAL:	$3 M

Investment Terms and Rationale

- $3 Million Convertible Note
  - ***20% discount*** off Next Raise or ***$35M Market Valuation Cap***
  - ***Interest rate 9%***
- Mitigates valuation and investment risk for our investors
- Reserving $1.5 million, 50% of raise, for existing investors
- IND phase development significantly increases the value and likelihood of business development terms in favor of the company

Cascade PRODRUG™

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