CPD100

Opportunity to Invest in a Novel Hypoxia-Activated Therapy

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- Key inventor on 38 issued US Patents

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- Multiple senior roles at Novartis

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Executive Summary

CPD100: First-in-Class Hypoxia-Activated Therapy for *Locoregional* Therapy

- CPD100 is a novel, patent protected, polymorph B formulation prodrug of vinblastine
  - Selectively activated in hypoxic microenvironments, thereby sparing healthy tissue
  - Polymorph B is a more stable form of CPD100, allowing more favorable, lower cost storage conditions
  - Top priority is to develop CPD100 for locoregional administration in benign conditions with abnormal angiogenesis
  - Lead indication is wet age-related macular degeneration, where abnormal angiogenesis is a major feature of the disease
- Expect to complete IND-enabling studies in 2026 to support first-in-human (FIH) trial in wet age-related macular degeneration (AMD) in 2027
  - Innovative & cost-effective clinical strategy to achieve early value inflection points

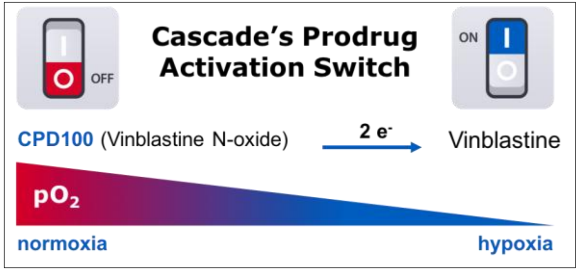
CPD100Li: First-in-Class Hypoxia-Activated Therapy for *Systemic* Therapy

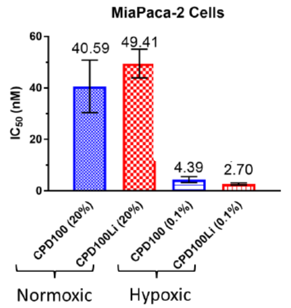
- In parallel we are developing CPD100Li – a liposomal formulation for systemic administration in oncology
- Hypoxia is a common feature in many cancers
- In addition to directly killing tumor cells, CPD100Li may also reverse the immunosuppressive microenvironment, thereby enhancing response to therapy
- Expect to start FIH study with CPD100Li in solid tumors in 2028

CPD100

CPD100 is vinblastine N-oxide for locoregional administration

- Starting material for CPD100 synthesis is vinblastine, an established IV chemotherapy
  - Blocks cell division by inhibiting tubulin in cells
- We then create a prodrug of vinblastine: Vinblastine-N-oxide *(= CPD100)*
  - Vinblastine-N-oxide can be activated to regenerate vinblastine
  - This activation occurs preferentially under hypoxic conditions
  - Vinblastine-N-oxide is therefore a prodrug for hypoxic diseases such as wet AMD





Shah VM et al., 2017; Shah VM et al., 2022

Vinblastine in Non-Cytotoxic Doses Inhibits Normal Endothelial Cells

Could be useful to treat benign conditions with abnormal angiogenesis

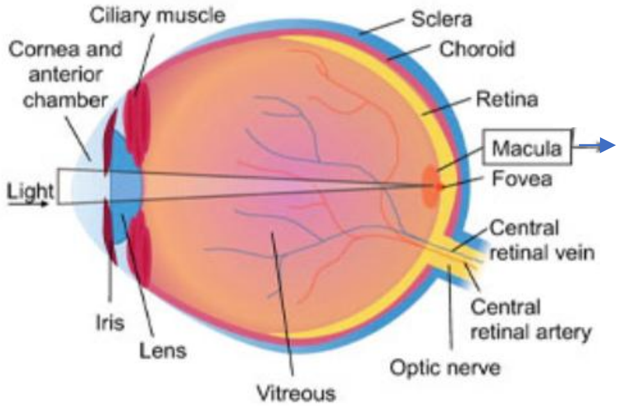
HUVEC morphogenesis on Matrigel

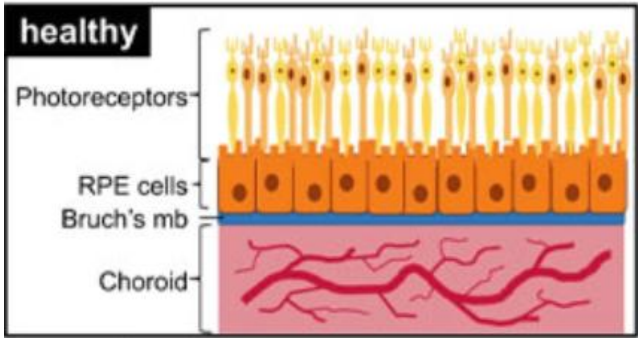
Low vinblastine doses halt proliferation of human umbilical vein endothelial cells (HUVEC), but not that of fibroblasts

Vacca A, Blood 1999

Wet Age-Related Macular Degeneration (AMD) is a Commercially Attractive Example of a Benign Condition with Hypoxia & Abnormal Angiogenesis

The macula is an oval-shaped pigmented area in the center of the retina which is responsible for the central, high-resolution color vision





Adapted from [Macular Degeneration](#) *(accessed 9/27/2025)*

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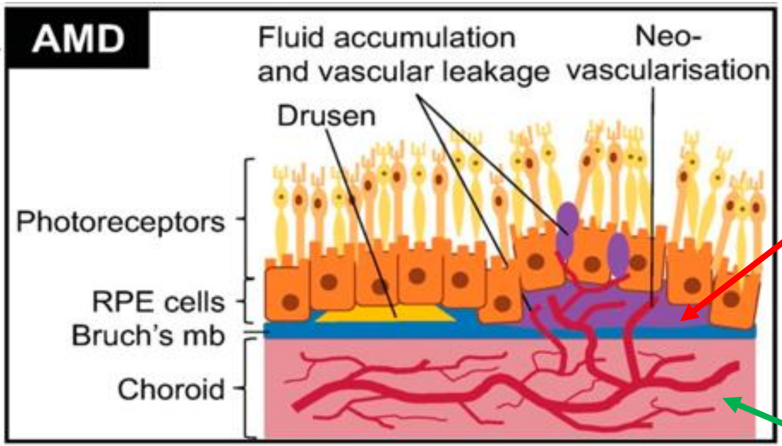


HIF-1: Hypoxia-inducible factor 1
VEGF:Vascular endothelial growth factor
Ang-2:Angiopoietin-2

Hypoxic microenvironment
elevated HIF-1, VEGF & Ang-2 induce abnormal angiogenesis

New blood vessels
leading to subretinal fluid accumulation

Central vision loss

CPD100 suprachoroidal injection:

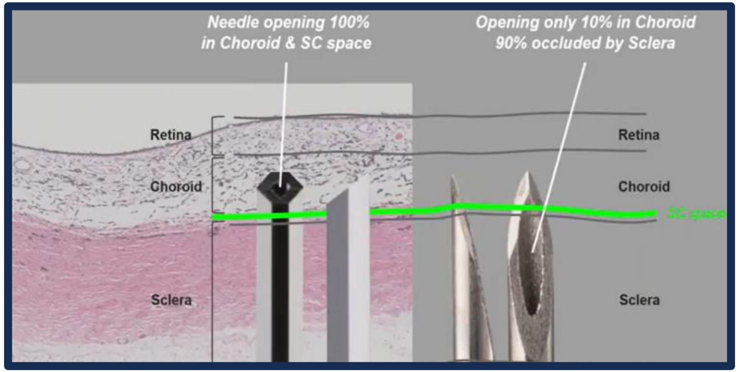
- Selectively and quickly halts aberrant angiogenesis
- Endothelial cells extremely sensitive to vinblastine
- Avoids intravitreal morbidity
- Could improve vision quickly

Adapted from [Macular Degeneration](#) (accessed 9/27/2025)

HIF-1: Hypoxia-inducible factor 1 VEGF: Vascular endothelial growth factor Ang-2: Angiopoietin-2

Suprachoroidal Administration of CPD100 for Wet AMD Could Improve the Efficacy & Safety of Locoregional Therapy

- Suprachoroidal injection is a commercially approved route of administration for treating ophthalmic diseases
- A silicon microneedle is used for the delivery of drugs to the suprachoroidal space[1]
- Studies in animal models (rabbits, pigs and non-human primates) have demonstrated safe and effective delivery of compounds to the back of the eye[2]
- Clinical Phase 1 data have also shown safety and tolerability of the suprachoroidal injection in wet AMD
- Preclinical proof-of-concept studies with CPD100 – both *in vitro* and *in vivo* – are being planned



[1] Uneedle Inc, 2025; [2] Powered Research 2025

Quick, Cost Effective, and Low Risk Cell Viability Analysis Will Determine Further Investment in CPD100 for Wet AMD

- *In vitro and in vivo POC studies* to be completed in1Q2026
- IND-enabling studies kick-off 3Q2026
- First-in-human study in wet AMD in 2027

Objectives for Nanolive's Imaging Platform for Cell Viability Analysis

- Confirm that CPD100:
  - is more cytotoxic to endothelial cells cultured under hypoxia than in normoxia
  - is more cytotoxic to endothelial cells than to retina or epithelial cells cultured under hypoxia
  - is more cytotoxic to endothelial cells than vinblastine under hypoxic conditions
- Evaluate conversion rate of CPD100 to vinblastine under hypoxia versus normoxia

https://www.nanolive.com

CPD100 is an Attractive Commercial Opportunity for Wet Age-Related Macular Degeneration

2019 estimates for AMD prevalence in the USA:

~20 million in population ≥ 40 years old

~ 10% (2 million) with wet AMD

Current Standard of Care

Intravitreal antiangiogenic therapy:

Eylea® ($9.5 B global in 2024)
Lucentis®, Beovu®, etc.

Benefits

Endothelial cells are very sensitive to vinblastine micro-doses

Validated suprachoroidal administration

Avoids intravitreal morbidity

Potential market share in mid 2030s

≥ 20%

Additional indications are retinal vascular conditions where VEGF-driven leakage and neovascularization are central, including diabetic macular degeneration, diabetic macular edema, diabetic retinopathy & macular edema following retinal vein occlusion

VEGF is the Dominant Target for Wet AMD Pipeline (CPD100 Opportunity for Differentiation)

Product	Company	Phase	MOA / Target(s)	Modality	Delivery Route
6 Approved Products: Eylea, Vabysmo, Beovu, Lucentis, Susvimo, Conbercept	Regeneron, Bayer, Genentech, Novartis, Chengdu Kanghong	Marketed	VEGF-A + Ang-2 bispecific, VEGF-A inhibitor, VEGF trap (VEGF-A/B + PlGF), Anti-VEGF mAb fragment, Anti-VEGF mAb fragment, VEGF trap (VEGF-A/B + PlGF) aflibercept biosimilar	Biologic	5 Intravitrial, 1 surgical implant
OPT-302	Opthea	Phase 3	Trap VEGF-C & VEGF-D	Biologic / fusion protein	Intravitreal
RC28-E	RemeGen	Phase 3	Dual decoy receptor (VEGF + FGF2)	Biologic / fusion protein	Intravitreal
IBI302 (Efdamrofusp alfa)	Innovent / IBI	Phase 3	Bispecific fusion (VEGF + complement)	Biologic / fusion protein	Intravitreal
KSI-301 / Tarcocimab	Kodiak Sciences	Phase 3	Ab conjugate (VEGF ± IL-6)	Biologic ABC / conjugate	Intravitreal
RGX-314	Regenxbio / AbbVie	Phase 2 / 3	Anti-VEGF (AAV gene)	Gene therapy	Subretinal & Suprachoroidal
Ixoberogene soroparvovec	Lilly (via Adverum)	Phase 2 / 3	Encoded aflibercept (anti-VEGF)	Gene therapy	Intravitreal
4D-150	4D Molecular Tx	Phase 2 / 3	AAV-delivered sustained anti-VEGF + anti-VEGF-C	Gene therapy	Intravitreal
AM712	AffaMed	Phase 1	Fusion protein (VEGF + Ang-2)	Biologic / fusion protein	Intravitreal
AR-14034	Aerie Pharma	Phase 1 / 2	Anti-VEGF 1,2,3 (axitinib)	Small molecule tyrosine kinase inhibitor	Implant inserted locally Sustained release
VAN-2401/KH658	Chengdu Origen and Vanotech	Phase 1	Anti-VEGF (AAV gene)	Gene therapy	Suprachoroidal
OCU200	Ocugen	Phase 1	Fusion protein: Tumstatin (anti-VEGF) & transferrin	Fusion protein	Intravitreal
AIV007	Aiviva	Phase 1	Levantinib / VEFG1-3	Small molecule	Intravitreal single injection
AXT107	AsclepiX	Discontinued	Multi-target: VEGF-A/C, Tie2 activator	Peptide biologic	Suprachoroidal

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Suprachoroidal Injection is Clinically and Commercially Validated

Product	Company	Phase	Indication	MOA / Target(s)	Modality	SC Injector Originator
Xipere	Bauch & Lomb (US) Artic Vision (AP) Artic/Santen (China)	Marketed	Macular edema	Corticosteroid, triamcinolone	Generic small molecule	Clearside Biomedical
Bel-sar	Aura	Phase 3	Choroidal melanoma	HPV virus-like particles conjugated to a light-activated cytotoxic payload	Viral-like toxin conjugate	Clearside Biomedical
RGX-314	Regenxbio / AbbVie	Phase 2 / 3	Wet AMD & diabetic retinopathy	Anti-VEGF (AAV gene)	Gene therapy	Clearside Biomedical
CLS-AX	Clearside Biomed	Phase 2b Planning Ph 3	Wet AMD	Pan-VEGFR TKI (Axitinib)	Small molecule TKI suspension	Clearside Biomedical
Avoralstat	Biocryst	IND enabling	Diabetic macular edema	Plasma Kallikrein Inhibitor	Small molecule	Clearside Biomedical
AXT107	AsclepiX Tx	Discontinued	Wet AMD	Multi-target: VEGF-A/C, Tie2 activator	Peptide biologic	Uneedle

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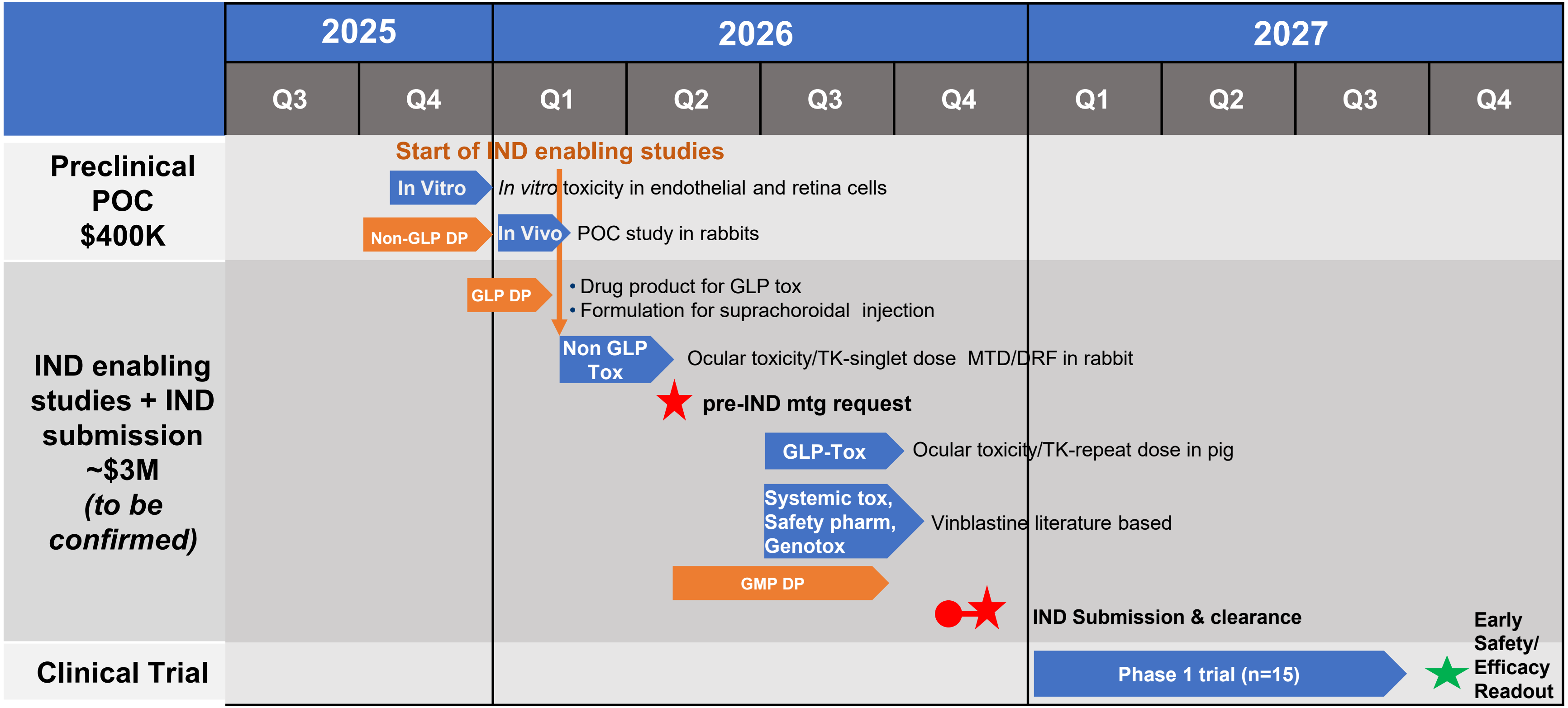
CPD100 Development in Wet AMD Could Lead to IND Filing in 2026, with Early Clinical Readout in 2027



DP: Drug Product
MFG: Manufacturing
GLP: Good Laboratory Practice
POC: Proof of Concept
IND: Investigational New Drug Application
TK: Toxicokinetics

CPD100: Rationale for Wet AMD Indication

Rationale	Comment
Cascade current resources	• Most viable, cost efficient, timely pathway to value inflection
Lead candidate selected	• CPD100 (vinblastine N-oxide) will be lead in wet AMD
Hypoxia targeting MOA	• Reduced blood flow in choroidal layer of eye leads to chronic hypoxia • HIF activation & promotion of VEGF lead to abnormal blood vessel growth characterized by wet AMD
Low dose vinblastine effects on HUVEC cells	• Halts proliferation of HUVEC cells (anti-angiogenic effect) and not that of fibroblasts or other cells • CPD100 preferential activation in hypoxia should improve therapeutic index of vinblastine
Cost & timeline to clinic	• Phase 1 opportunity in 2027 for ~ $1 million (first cohort ~ 3-5 pts) and up to $3M total (~15 pts)
Significant market opportunity	• Multiple > $1 billion blockbuster products in wet AMD, US patient prevalence ~ 1.5 million
Opportunity for 1st in class MOA	• No hypoxia targeted therapies in clinic (marketed/clinical pipeline dominated by anti-VEGF therapies)
Suprachoroidal delivery	• Ideal for a microtubule inhibitor (local delivery at choroid, minimizing vitreous exposure & systemic tox) • Next generation micro-injection technology

HUVEC: Human umbilical vein endothelial cells used to evaluate anti-angiogenic effects

CPD100: Key Takeaways

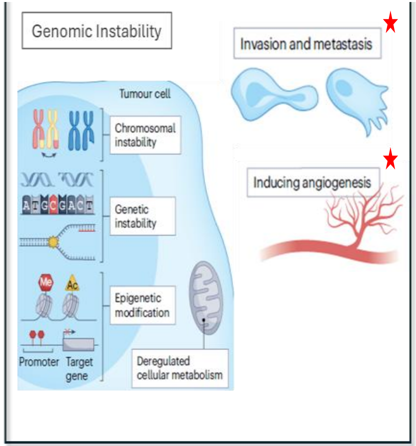
- CPD100 for suprachoroidal injection is a stable, polymorph B formulation prodrug of vinblastine
- CPD100 can be activated in hypoxic areas to regenerate vinblastine that can block cell division in preclinical models
- Vinblastine can inhibit angiogenesis at very low doses which may not be toxic to other normal cells
  - *However, intravitreal vinblastine at doses >10µg in rabbits is toxic*
  - Intravitreal vinblastine has never been evaluated in ophthalmic diseases
- Suprachoroidal injection of CPD100 could become the first hypoxia-targeted therapy to distinctively block angiogenesis in wet AMD
  - CPD100 activation in hypoxic regions in the choroid space could block aberrant angiogenesis
  - Suprachoroidal injection with axitinib has been successfully used to inhibit angiogenesis in preclinical models

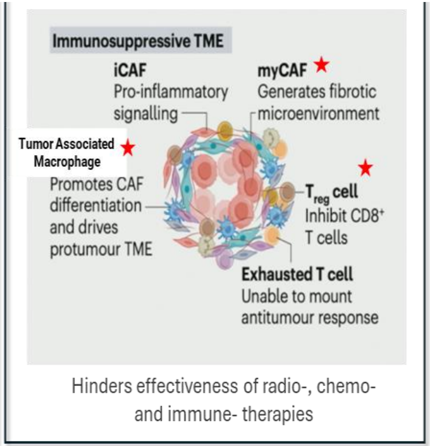
We See an Upside Parallel Pathway for CPD100 in Hypoxia-Prone Tumors

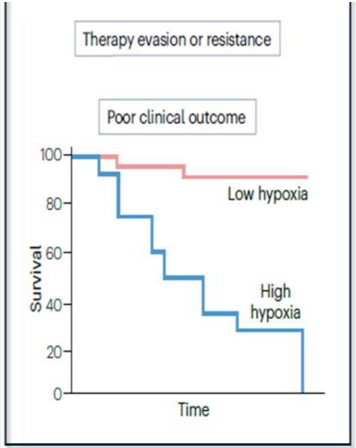
Cascade is developing a liposomal formulation of CPD100 – **CPD100Li** – for systemic administration to reverse the effects of a hypoxic microenvironment in cancer

HYPOXIA IN THE TUMOR MICROENVIRONMENT

Promotes Tumor Regression	Promotes Immuno-suppression	Worsens Prognosis	Common Feature of Solid Tumors







Tumor	Normal Tissue PO_2	Tumor Tissue PO_2
Pancreas	57	2 *(8 pts)*
Brain	26	13 *(104 pts)*
Lung	N/A	16 *(26 pts)*
Breast	52	10 *(212 pts)*
Cervix	42	9 *(730 pts)*

Adapted from Suvac A, 2025 and Dreyer SB, 2025

Compilation of studies: 2000+ cancer patients; reviewed in Vaupel, P. et al., 2007

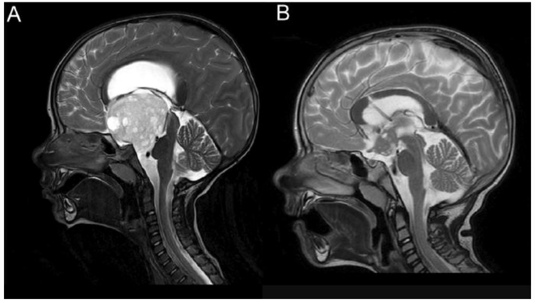
Our research supports the foundation of the development of CPD100Li in oncology

Shah VM, 2017 & 2022: Sick A, 2023

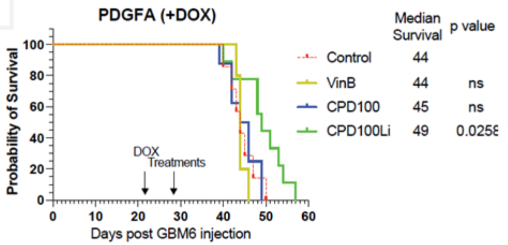
We Have Selected Pediatric Low-Grade Glioma (PLGG) as the Initial Indication for CPD100Li in a Hypoxia-Prone Tumor

- ~1,700 new cases annually in the U.S. and 4,000–5,000 across major global markets
- Current standard of care: Surgery, radiotherapy, chemotherapy (carboplatin + vincristine or vinblastine monotherapy)[1] and/or mutation-targeted therapy (tovorafenib)[2]
- **Unmet Need**: Many patients relapse or suffer long-term toxicity from chemotherapy; mutation-targeted therapies benefit only subsets
    - CPD100Li could improve therapeutic index & decrease frequency of administration
- Opportunity for **Orphan Drug Designation** & **accelerated approval** with single-arm trial
- **Rare disease economics** support premium pricing
    - Orphan Drug Designation => extended market exclusivity
    - Comparable therapies priced at ≥ $200K/year
- **Preliminary preclinical data with CPD100Li in glioma cancer model[3] warrant continued investment in this indication**

Example of response to vincristine + carboplatin [1]



PDGFA expressing-GBM PDX mice



[1] *Lassaletta A, et al., 2024;* [2] *Kilburn LB et al., 2023;* [3] *Charest A et al., 2019*

CPD100Li Oncology Indication Rationale

Rationale	Comment
Cascade current resources	• Non-dilutive funding opportunities through CPRIT and NCI SBIR/NeXT
Lead candidate	• CDP100Li for systemic delivery in oncology with optimal therapeutic index
Target patient population selected	• Pediatric low-grade glioma (pLGG)
Hypoxia-targeting MOA	• Direct, measured presence of hypoxia in patient tumors
Preclinical *in vivo* POC	• CPD100Li has significant monotherapy activity & combination synergy with gemcitabine and anti-CTLA4 therapies *(e.g., ipilimumab, marketed as Yervoy®)* • Efficacy in glioma model
Timeline to clinic	• Phase 1 opportunity in 2028
Vinblastine clinical validation	• Vinblastine is a standard of care in pLGG
Attractive regulatory pathway	• Precedence for Phase 2 single arm accelerated approval in pLGG
Pediatric populations underserved by new drug development	• Orphan Drug Designation opportunity; potential for Orphan Drug grant for clinical trial • High opportunity for patient advocacy engagement

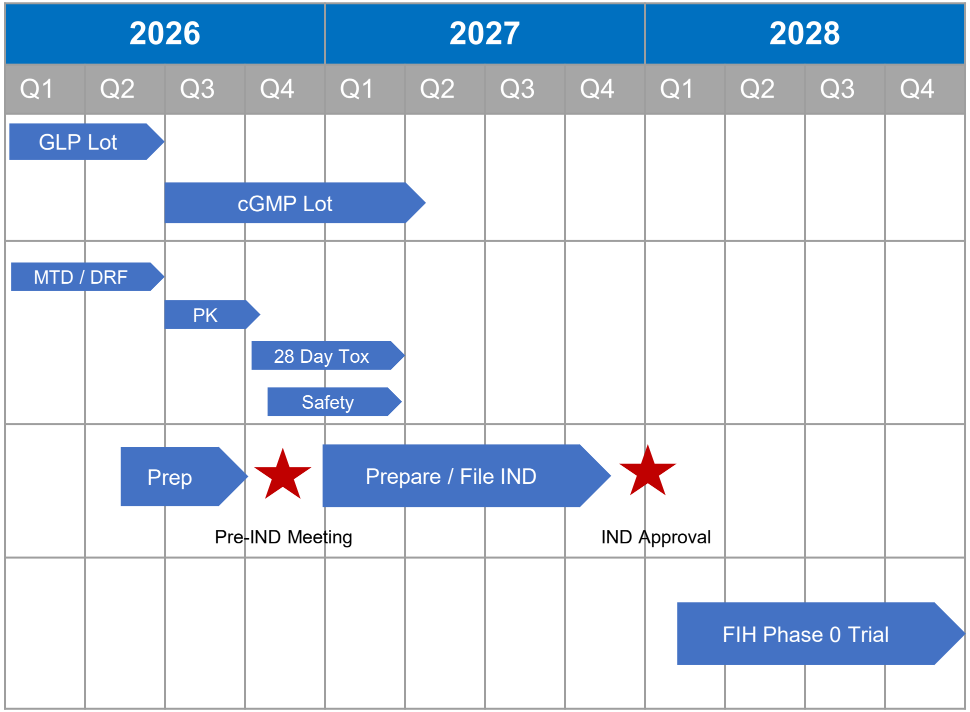
CPRIT – Cancer Prevention & Research Institute of Texas

NCI SBIR – National Cancer Institute Small Business Innovation Research

NeXT – NCI Experimental Therapeutics Program

CPD100Li Program Goals, Objectives, Budget, Timeline

Goal	Objectives (sub-goals)
Manufacturing (CMC)	• Drug product formulation & scale up – Good Laboratory Practice (GLP) lot • cGMP production for IND toxicity & clinical site distribution
Tox/Pharm/PK	• Maximum tolerated dose (MTD) / Dose range finding (DRF) in rats/dogs • Pharmacokinetics (PK) (rats/dogs) • 28 day GLP toxicity (rats/dogs) • Safety pharmacology battery
Regulatory	• Pre-IND Meeting • Prepare IND Package • IND Submission
Phase 0 first-in-human (FIH) trial	• Finalize clinical protocol • Principal investigator / Site selection • Site feasibility assessment • Dose escalation



Investment Need and Rationale

Seeking ~$5M to advance CPD100 through Phase 1

- Complete IND-enabling GLP-studies and Phase 1 trial
- Support business development and partnering outreach
- Position for strategic exit or asset sale pre-efficacy readout

References

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- Lassaletta A et al., *Child's Nervous System* 2024, 40:3229
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- Vaupel P et al., *Antioxidants & Redox Signaling* 2007, 9: 1221

Q&A

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CPD100

Opportunity to Invest in a Novel Hypoxia-Activated Therapy

CPD100Li Defensibility

FDA granted Orphan Drug Designation for the treatment of pancreatic cancer in Oct. 2022
- Eligibility for market exclusivity for 7 years AFTER pre-market approval
- Waiver of new drug application (NDA) Fee (Approximately $2 million benefit)
- Tax Credits up to 50% for research and clinical drug testing expenses

Treatment of Hyperproliferative Diseases with Vinca Alkaloid N-Oxide Analogs
- PCT/US2007/04252/US 8,048,872 and US 8,883,775
- Expires February 20, 2027 (with extensions up to 2028/2029 for US patents)
- Geographies covered: US, Canada, China, France, Germany, UK, Japan, Hong Kong, Israel

Mannich Base N-Oxide Drugs
- PCT/US2008/03550
- Expires March 19, 2028
- Geographies Issued: US, Canada, China, France, Germany, UK, Japan, Hong Kong, Israel

Combination Therapy with a Vinca Alkaloid N-Oxide and an Immune Checkpoint Inhibitor
- PCT/US2021/06505
- Filed December 23, 2021 (active patent prosecution)

Additional Orphan Drug Applications (US/EU) in other target tumor types where future preclinical POC support.

CPD100Li
ORPHAN DRUG
DESIGNATION

CPD100Li
US PATENTS
APPROVED

***Combination patent and Orphan Drug Designations will drive market exclusivity**

Partnering Outreach

Eric Malek
Chief Business Officer

Current Financing Strategy Supports Partnering Process

Goal is to either license or sell asset within a deal structure that:

- Funds CPD100Li development through clinical POC and commercialization
- Provides a return to investors via upfront, development and downstream contingent regulatory and commercial milestone payments
- Maximizes asset value through multiple development pathways

Targeting pharma, public and private biotech (US/ex-US) with following profile:

- Seeking and/or developing preclinical/clinical oncology assets
- Sufficient capitalization to support clinical development through at least POC
- Interest in pancreatic cancer (or other pathways relevant to vinblastine warhead – i.e. GBM)
- Pipeline that could synergize with CDP100Li
- Opportunistic oncology companies seeking to augment pipeline

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 / www.cascadeprodrug.com

Use of Investor Funds

1. Pathway to and thru Pre-IND Meeting with FDA: $2.5 Million

2. Business Development $200k

3. Admin Expenses $300k

Funding & Exit Strategy

- Execute [$3M Investment] the development plan to advance CPD100Li toward the clinic (later stage=higher interest by partners).

- In parallel pursue:
  - non-dilutive sources of funding (*RO1, STTR, CPRIT, **NCI Pivot Program)
  - publication of additional value enhancing translational data
  - continued partnering effort with target pharma/biotech companies

- Goal is to partner or sell company at or prior to clinical proof of efficacy.