Cascade PRODRUG™

CPD100

First-in-Class Prodrug Therapy Targeting the Primary Drivers of Age-Related Macular Degeneration (AMD)

October 7, 2026

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Cascade's CPD100 Investment Thesis

(in Wet Age-Related Macular Degeneration)

Large market	• Total addressable market > $10 billion • Aging population contributing to sustained growth
Unmet medical need	• Clinical and commercial market heavily driven by anti-VEGF therapies • Opportunity for novel MOA with more direct & sustained effect
Novel technical approach	• Dual mechanism of action (anti-neovasculature/inflammatory) • Suprachoroidal injection (limits exposure vs intravitreal) • 1st in class opportunity – no other agent with similar mechanism/profile
Robust IP	• Composition of matter and method of use patents for wet AMD filed in 2026 • Issued patents for prodrug, polymorph vinblastine, checkpoint inhibitors
Clear path to execution	Highly efficient pathway to IND, with two staged FDA meetings to validate plan
Experienced management	Senior level development expertise (Preclinical, Manufacturing, Regulatory) balanced with Ophthalmology & Transactional experience
$12M investment to get to IND approval (key value inflection point)	

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Wet AMD & CPD100 Summary

- Wet AMD results from an increase in vascular endothelial growth factor ***(VEGF)*** production in the back of the aging eye driven by (1) locally low levels of oxygen ***(hypoxia)*** & (2) chronic inflammation

Abnormal blood vessel growth ***(neovascularization)***

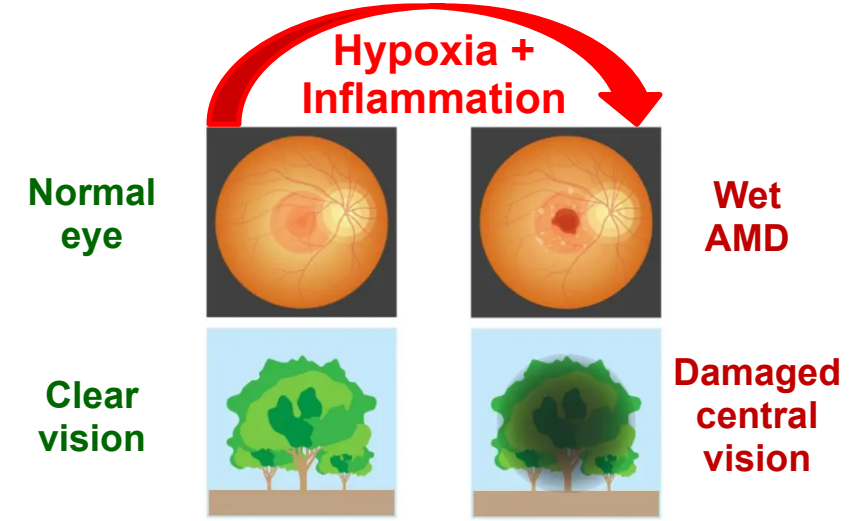
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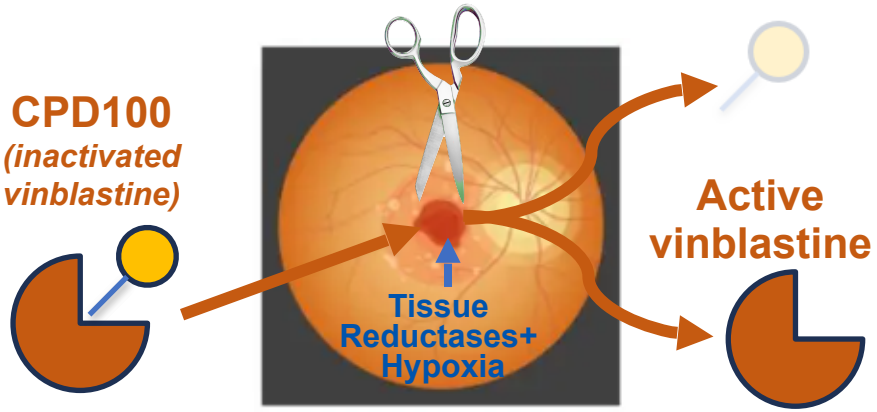
Leakage under the retina

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Damage to central vision

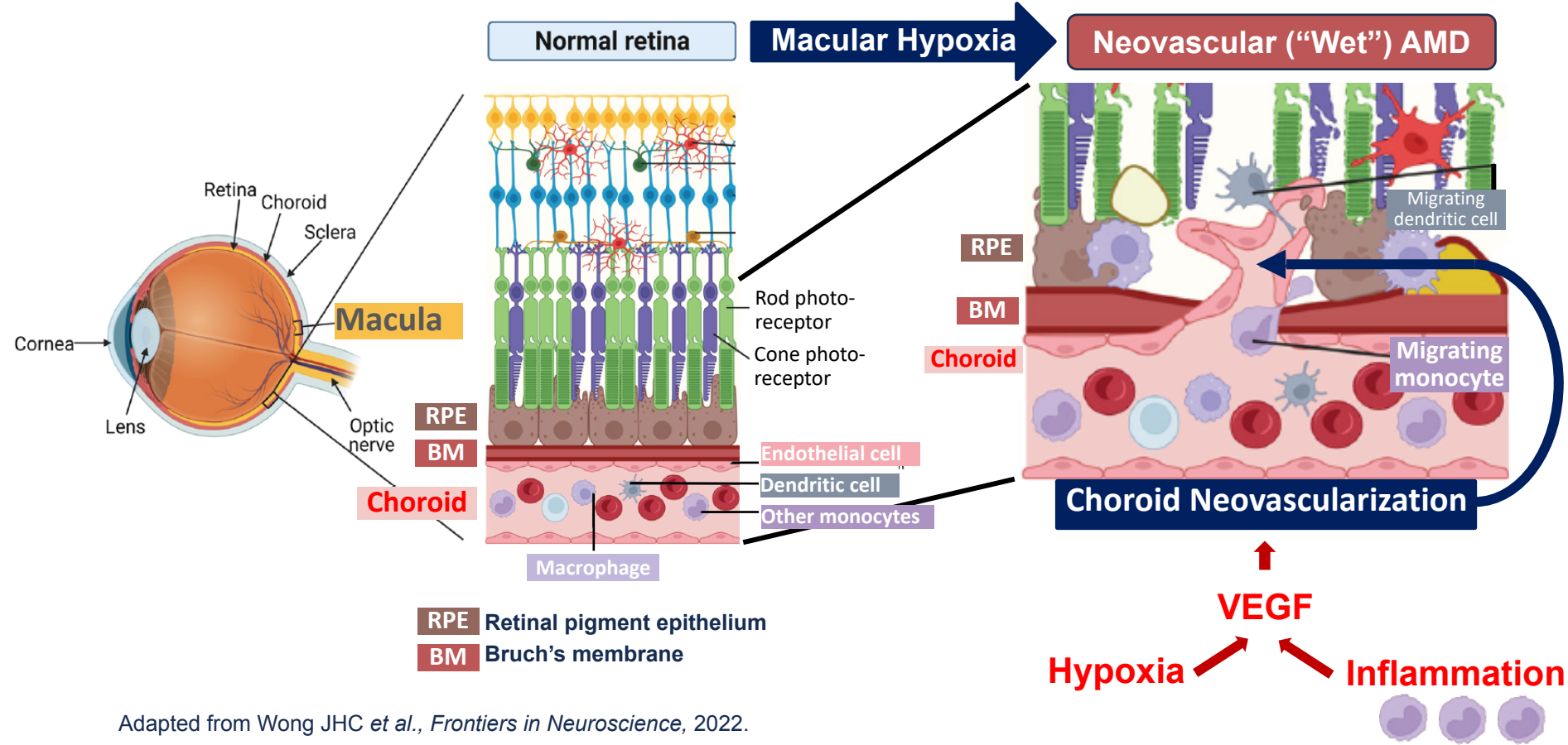
- Current effective treatment is based on chronic VEGF suppression
- Cascade's CPD100 prodrug has a differentiated mechanism of action => dual impact on neovascularization:
  i. ***Direct*** suppression of abnormal blood vessel growth[1]
  ii. Reduction of cells that produce VEGF &inflammation – in particular monocytes[2,3]
- CPD100 has the potential to become the first targeted therapy to selectively inhibit neovascularization in wet AMD through a dual mechanism of action *that is enhanced by hypoxia*





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Wet AMD: Evolution in the Aging Eye[4-6]



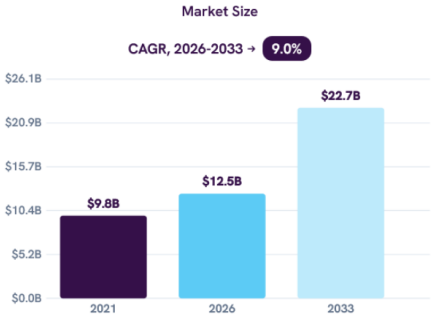
RPE Retinal pigment epithelium

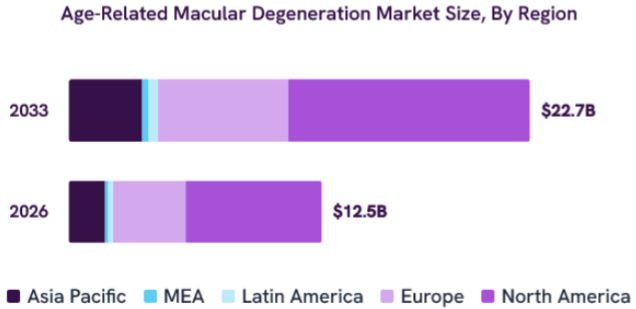
BM Bruch's membrane

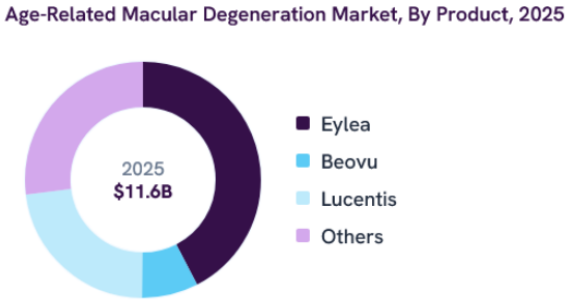
Adapted from Wong JHC *et al., Frontiers in Neuroscience,* 2022.

CPD100 Market Opportunity in Wet AMD

- Estimated prevalence of wet AMD in US ~ 2M patients
- Total addressable market > $10 billion and (wet AMD 90+% of AMD market)
- US represents > 50% of global market
- Medicare spends >$4B/year on anti-VEGF drugs
- Multiple blockbusters supported (Eylea®, Lucentis®, Beovu®, Vabysmo®)
- Strong investor and pharma activity (e.g., EyeBio/Merck $1.3B upfront at Phase 1b/2a stage)





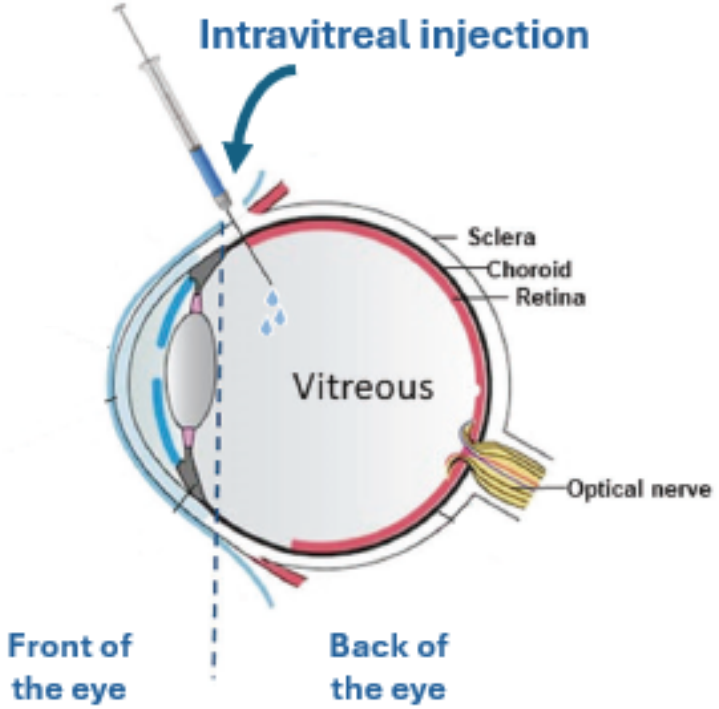


https://www.grandviewresearch.com/industry-analysis/age-related-macular-degeneration-market-report

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Limitations of Anti-VEGF Therapies

- Require **intravitreal injections** *(painful)*
- Monthly loading + maintenance every 2-4 months
- Do not address **direct action on**
  - —growth of endothelial cells
  - —VEGF-producing cells
  - —inflammation
- **Risks**: retinal tear, hemorrhage, cataract, uveitis, intra-ocular pressure elevation

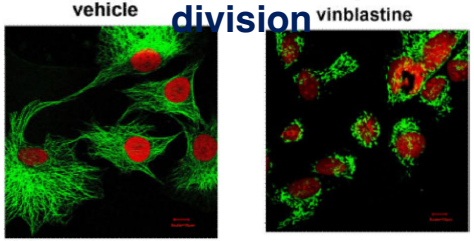


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CPD100 (Vinblastine-N-Oxide): First-in-Class Hypoxia-Enhanced Therapy for Wet AMD

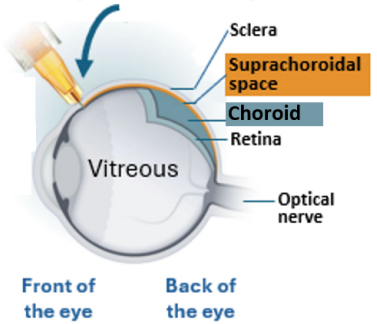
- **CPD100 prodrug activation:** Releases vinblastine (VBL), particularly amplified in hypoxic microenvironments[7-9]
- Vinblastine targets proliferating cells directly through microtubule destabilization, mitotic arrest & cell death

Vinblastine destabilizes microtubules & stops cell division



- Suprachoroidal injection delivers CPD100 directly to the target tissue:
  1. **Endothelial cells** involved in formation of abnormal blood vessels
  2. **Inflammatory cells** (monocytes) that produce VEGF

Suprachoroidal injection



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Preclinical Studies Validate the Mechanism of CPD100 & Support IND-Enabling Studies Starting in 2027

I. *In vitro* testing in retinal and endothelial cells cultured under hypoxia & normoxia and exposed to CPD100 or Vinblastine

II. CPD002: Ocular distribution and tolerability study in Dutch belted rabbits (DBRs)

III. CPD001: Proof of concept study – DL-AAA-Induced Capillary Leakage Model[11]

DL-AAA: DL-α-aminoadipic acid, a relatively selective toxin for retinal Müller glial cells

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Commercial Opportunity for CPD100 in Wet AMD

- Wet AMD prevalence: **~2M US patients**
- **CPD100 advantages**:
  - **Differentiated dual MOA**: anti-neovascularization + anti-inflammatory
  - **Potential to improve vision** & decrease frequency of administration
  - **Suprachoroidal administration** avoids intravitreal morbidity
  - **Significant market opportunity** by mid-2030s

- **Pipeline optionality — not resourced in this round:**

  Predominant Antiangiogenic Effect
  - Diabetic macular edema (DME)
  - Macular edema following retinal vein occlusion (MEfRVO)

  Predominant Anti-Inflammatory Effect
  - Dry AMD – Geographic atrophy
  - Prior retinal transplantation in retinitis pigmentosa, AMD, etc.

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Uses of Proceeds: $12M Preclinical Budget to IND Filing

27-Month Key Project Milestones

Months 1 – 4 *(through end of 2026)*

1. Derisking biology (17% | $2.0M)

- *In vivo* proof-of-concept
- INTERACT meeting with the FDA *(4Q 2026)*

Months 5 – 15 *(through Nov 2027)*

2. *In vivo* studies, mfg (46% | $5.5M)

- PK: single suprachoroidal dose tolerability in NZW rabbit
- Dose-range finding in pigs
- GMP manufacturing
- Pre-IND meeting with the FDA *(4Q 2027)*

Months 16 – 27 *(through Nov 2028)*

3. Safety, team, IND (37% | $4.50M)

- GLP toxicity study in pigs
- Build clinical team
- Prepare & submit IND application

INTERACT: INitial Targeted Engagement for Regulatory Advice on CBER/CDER ProducTs

PK: Pharmacokinetics
GMP: Good Manufacturing Practice

GLP: Good Laboratory Practice
IND: Investigational New Drug

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Board of Directors



Allan Cochrane

- Former President Epoch Pharma
- Former COO Pacific Biometrics
- CEO Saigene Corp
- Adjunct Professor, Entrepreneur in Residence University of Oregon



Eric Malek

- Former SVP Corp Dev Threshold Pharma
- Previously, BiPar, Allos, Gilead, JNJ
- Consulting BD advisor for multiple companies



Ken Mandell, MD, PhD

- Founder & former CEO, LayerBio, Inc.
- Former CMO, Aramis Biosciences, Intergalactic Therapeutics, & Neurotech Pharmaceuticals
- Former Independent Safety Monitor, National Eye Institute
- Co-inventor TYRVAYA® (Viatris), FDA-approved for dry eye disease



Manny Litchman, MD

Chair

- CEO Mustang Bio
- Former CEO Arvinas
- Multiple senior roles at Novartis



Andres Gutierrez, MD, PhD

- Former CMO at Ayala, Advaxis, Oncolytics Bio & Sellas Life Sciences.
- Previously, BMS, Sunesis, BioMarin, Proteolix, Oculus



Thomas K. Wuest, MD, MMM

Board Observer

- CEO Ulcer Solutions
- Orthopedic trauma surgeon 25 years
- Past President, Slocum Orthopedics



John Nepute

Fractional CFO

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

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Harvard, MIT, Brandeis
AsclepiX, J&J

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MIT/ UC Berkeley,
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ARDENA

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Uneedle

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MERIT
Your Clinical Endpoint Expert

BioAgilytix

NANOLIVE
Looking inside life

CMC: Chemistry, Manufacturing, and Controls

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Anticipated Transition to Full Management Team

Current board members will fulfill the majority of senior positions listed, with candidates identified to fill gaps post-acquisition or funding

Board

Manny Litchman, MD
Chair

Allan Cochrane

Eric Malek

Andres Gutierrez, MD, PhD

Ken Mandell, MD, PhD

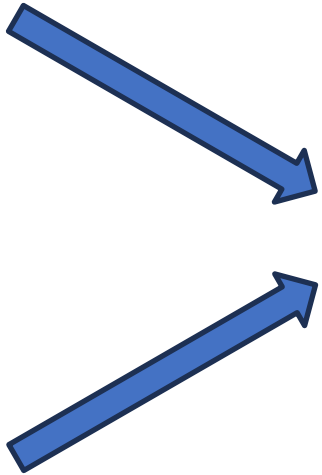
Thomas K. Wuest, MD, MMM
Board Observer

Advisors

Niranjan Pandey, PhD

Daniel Levy, PhD

Gina Capiaux, PhD



Management Team

CEO

Head, Program Management

Head, Quality Assurance

Chief Scientific Officer
Head, CMC
Head, Preclinical Development

Chief Medical Officer
Head, Regulatory Affairs
Head, Clinical Operations

Chief Financial Officer

Chief Business Officer

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12. https://www.grandviewresearch.com/industry-analysis/age-related-macular-degeneration-market-report

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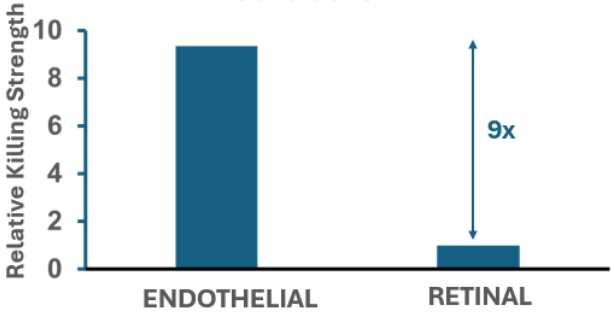
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Back-Up Slides

CPD100 Dual Mechanism of Action

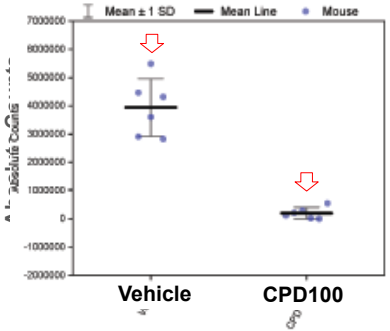
- **Vinblastine N-oxide** is a **prodrug** converted to vinblastine by tissue-reductases, with enhanced antiangiogenic activity in hypoxic environments
- **Endothelial cells** – but not retinal cells – are highly sensitive to **low doses of CPD100** under hypoxic conditions[1] → potential rapid shutdown of abnormal vessel growth while sparing toxicity to retinal pigmented epithelial (RPE) cells *(Figure 1)*

Figure 1. CPD100 Induces Endothelial Cell Death at a 9-Fold Lower Dose vs. Retinal Cells under



Relative killing strength is shown at 24 hours after switching to low-oxygen condition

Figure 2 Reduction of monocytes in an *in vivo* model treated with CPD100

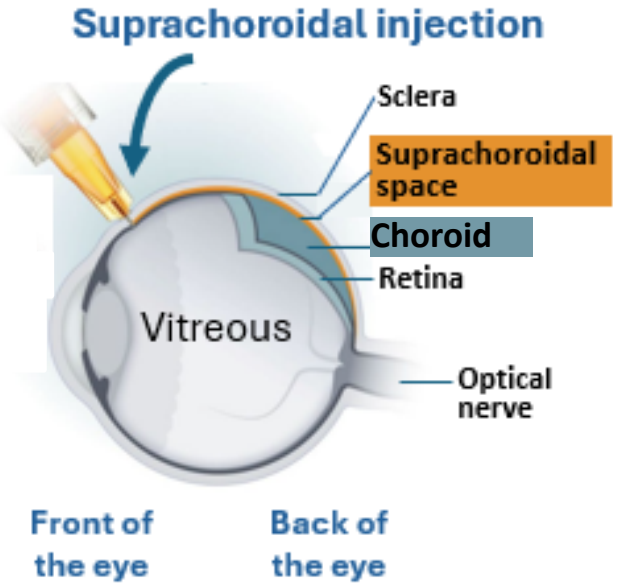


- VEGF producing-monocytes reduced[2-3] → upstream VEGF suppression *(Figure 2)*
- Potential for **more durable** and **more complete** disease control

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Suprachoroidal Space (SCS) Delivery Advantage

- Direct access to **choroid**, the site of pathology
- Enables potentially **safer** and **more targeted** therapy to the choroid
  - Minimizes vitreous exposure & systemic toxicity
  - Potentially less pain & less risk of retinal tear, hemorrhage, uveitis, intra-ocular pressure elevation
- FDA-cleared **micro-injection technology** (e.g., Bella-Vue / Uneedle) validated in AMD trials
- Growing clinical adoption of suprachoroidal injection, with multiple indications under clinical investigation



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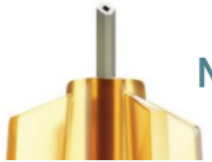
CPD100 to Be Administered Suprachoroidally Using Bella-Vue (Uneedle) Microneedles

- Chosen for CPD100 — proven safety and precision in Phase 1/2a wet AMD trials (AXT107, N=15)[10]
- **Excellent safety & tolerability** — no adverse events, leakage, reflux, hemorrhage, or perforation[10]
- **Precision delivery** — Optical coherence tomography 1 hour post-injection confirmed full drug distribution[10]
- Easy and reliable to use — 100% user satisfaction; single microneedle length[10]
- The favorable safety profile & tissue distribution data in the first *in vivo* study with CPD100 support continued development in the planned proof-of-concept (POC) studies



100% User satisfaction on

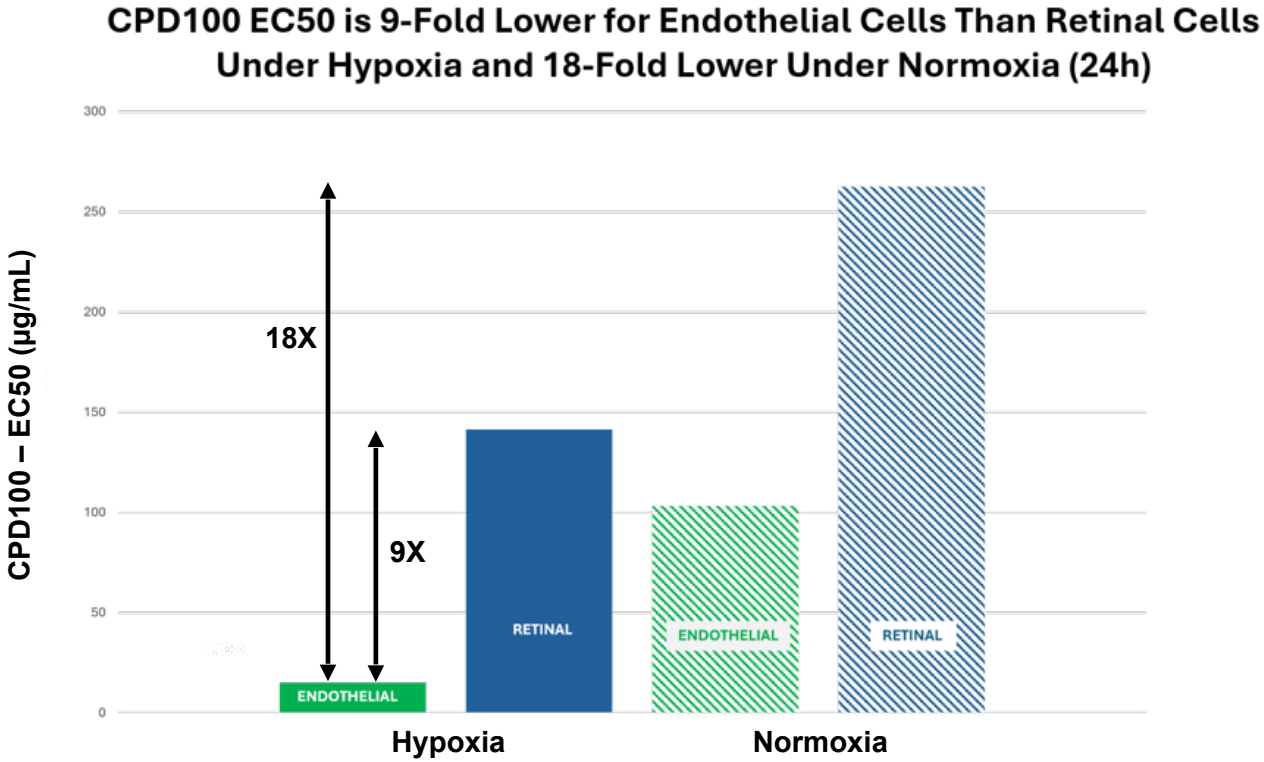
- Product Integrity
- Risk
- Ease of injection
- Reflux



Single Microneedle Length !

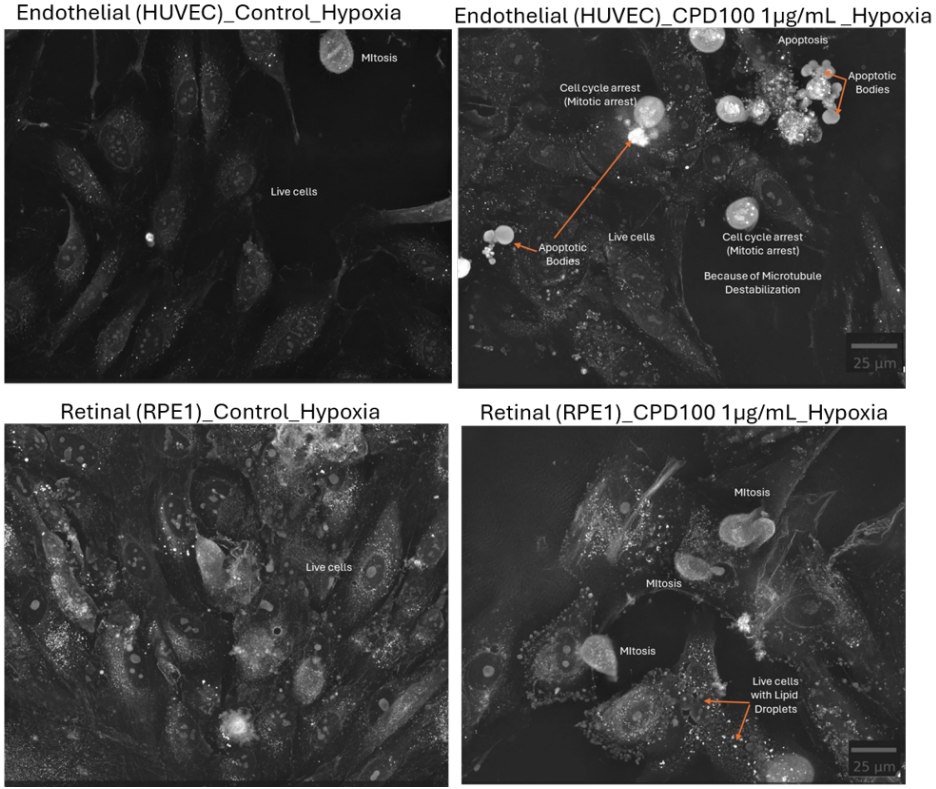
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In Vitro: CPD100 Demonstrates Hypoxia-Dependent Enhancement of Cytotoxic Potency in Endothelial & Retinal Cells



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In Vitro: CPD100 is Cytotoxic to Endothelial Cells but Spares Retinal Cells from Damage



Endothelial cells (HUVEC)

- Mitotic arrest
- Apoptosis

Retinal pigment epithelial (RPE) cells

- Lipid-laden stress, but cells remain viable

HUVEC: Human umbilical vein endothelial cells

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Study CPD002: Suprachoroidal CPD100 is Well Tolerated and Is Delivered to the Choroid

1. Injection was well tolerated with mild inflammation observed on Days 2-4, improving on Day 8.
2. Intraocular pressure (IOP) was normal on Day 2
3. CPD100 was converted efficiently to vinblastine (VBL) in retinal pigment epithelium (RPE) /choroid
4. VBL concentration in RPE/choroid at Day 2 (and half as much at Day 8) was ***sufficient for endothelial cell killing activity****
5. Less than 10% of vinblastine's concentration in the RPE/ choroid was detected in the retina at Days 2 and 8

Only small amounts of CPD100 and VBL are present in whole blood & disappear by 4 hours

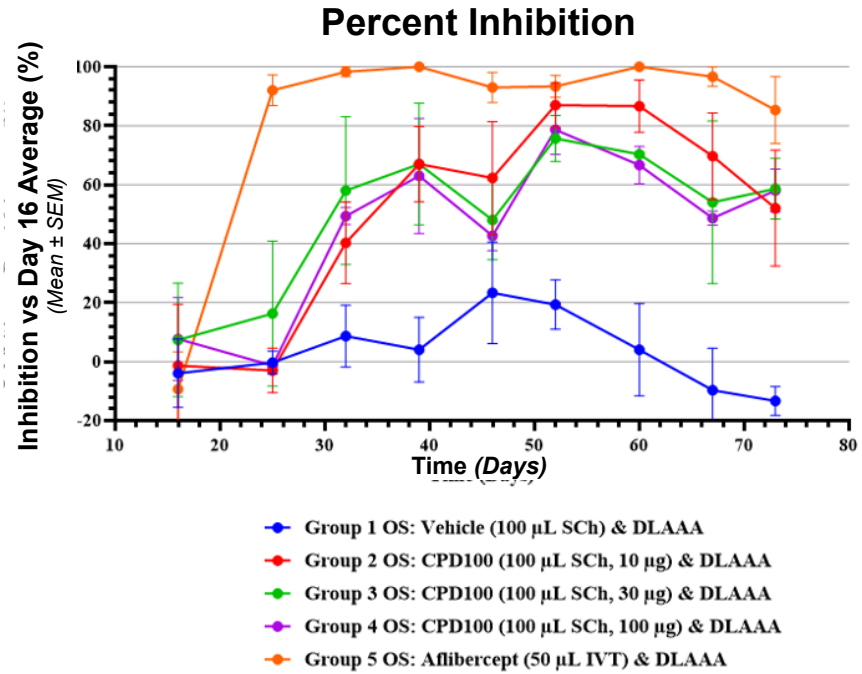
Time point	CPD100 ng/ml	Vinblastine ng/ml
0.5 h	20.4	2.0
1 h	14.1	1.1
2 h	2.8	0.6
4 h	BQL	BQL

*Targeted choroid exposure while retina is spared

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Study CPD001: CPD100 is Well Tolerated at Various Doses and Inhibits Retinal Capillary Leakage Caused by DL-AAA

- Injection of CPD100 10 -100μg was well tolerated with mild inflammation observed on Day 2, improving on Day 4
- Intraocular Pressure (IOP) was normal
- There was no evidence of intraocular inflammation or posterior segment toxicity
- CPD100 inhibits retinal vascular leakage at all doses tested, despite <10% of vinblastine in RPE/choroid reaches the retina



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CPD100 Development Summary

- CPD100 is enzymatically reduced to vinblastine in normoxic tissues, but its cytotoxic potency increases under hypoxic conditions.
- Under hypoxia, low CPD100 concentrations kill endothelial cells more effectively than retinal pigment epithelial (RPE) cells and more than vinblastine at equivalent doses.
- Suprachoroidal administration delivers CPD100 directly to the choroid/RPE, with <10% of the dose reaching the retina — exclusively as vinblastine — and with minimal systemic exposure.
- Suprachoroidal CPD100 is well tolerated up to the highest dose tested (100 μg/eye).
- Across tested doses (10, 30, and 100 μg/eye), suprachoroidal CPD100 produces sustained anti-angiogenic activity for ≥5 weeks in the AAA rabbit model.
  - Retinal capillary leakage inhibition begins by Day 14 and reaches ~80% by Day 30, despite extremely low vinblastine levels in the retina (~0.8 and 0.04 μg/mL).
- Preferential endothelial sensitivity to CPD100 — especially under hypoxia — combined with targeted choroidal delivery is expected to limit retinal toxicity.
- Robust and defensible patent estate.
- Next steps: INTERACT meeting, GLP toxicology, systemic exposure characterization by literature review, bioanalytical method validation, API/GMP manufacturing activities.

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Recent Ophthalmology Deal Activity

Data show that meaningful upfront value is paid well before Phase 3 — even at Phase 1/2, novel-MOA assets have commanded nine- and ten-figure upfronts

Asset	Acquirer / Partner	Mechanism	Stage at Deal	Deal Structure	Upfront	Total Deal Value
Restoret (MK-3000)	Merck / EyeBio	Tri-specific Wnt-pathway antibody (DME, wet AMD)	Phase 1/2	Acquisition	$1.3B	Up to $3.0B
Avacincaptad pegol	Astellas / Iveric Bio	Complement C5 inhibitor (geographic atrophy)	NDA filed, PDUFA-pending	Acquisition	—	$5.9B equity value
PER-001	Bayer / Perfuse Therapeutics	Endothelin receptor antagonist (glaucoma, diabetic retinopathy)	Phase 2	License/acquisition	$300M	+ milestones
RGX-314 (Japan rights)	Nippon Shinyaku / REGENXBIO	AAV8 gene therapy, anti-VEGF transgene	Phase 3	Territory license	$110M	+ milestones/royalties
4D-150	Otsuka / 4D Molecular Tx	AAV gene therapy (aflibercept + anti-PDGF)	Phase 2/3	Collaboration/license	$85M	+ milestones
Ixo-vec (ADVM-022)	Eli Lilly / Adverum	AAV.7m8 gene therapy, aflibercept transgene	Phase 2	Proposed license → acquisition	$25M license / $91M acquisition	+ $470M milestones / $25M CVR

Investigational Competitive Landscape in Wet AMD

Multiple next-gen approaches aim to reduce anti-VEGF treatment burden — none combine hypoxia-selective dual MOA with suprachoroidal delivery

Program	Company	Mechanism	Delivery	Stage (Sep 2026)	vs. CPD100
RGX-314	REGENXBIO / AbbVie	AAV8 gene therapy, anti-VEGF transgene	Subretinal or suprachoroidal	Phase 3 (ATMOSPHERE/ ASCENT, data expected 2026)	Same delivery route category, but single-MOA (anti-VEGF only) & one-time irreversible gene therapy vs. CPD100's redosable small-molecule prodrug
Ixo-vec (ADVM-022)	Adverum (proposed Lilly deal)	AAV gene therapy, aflibercept transgene	Intravitreal	Phase 2	Retains intravitreal morbidity; single-MOA anti-VEGF
AXPAXLI (OTX-TKI)	Ocular Therapeutix	Axitinib (pan-VEGF TKI) hydrogel implant	Intravitreal	Phase 3 (SOL-1)	Reduces injection frequency but still intravitreal, still VEGF-pathway only
4D-150	4D Molecular Tx / Otsuka	AAV gene therapy (aflibercept + anti-PDGF)	Intravitreal	Phase 2/3	Adds anti-PDGF but no anti-inflammatory/monocyte arm; intravitreal
Restoret (MK-3000)	EyeBio / Merck	Tri-specific Wnt-pathway antibody	Intravitreal	Phase 2	Novel MOA (vascular stabilization) but intravitreal, no hypoxia-selectivity
Sozinibercept (OPT-302)	Opthea	Anti-VEGF-C/D, add-on to anti-VEGF-A	Intravitreal	Discontinued — missed primary endpoint in both Phase 3 trials (ShORe, COAST), March 2025	**Cautionary precedent:** Additive VEGF-pathway blockade alone did not improve outcomes — supports case for a genuinely orthogonal MOA rather than more VEGF-pathway stacking
CPD100	**Cascade Prodrug**	**Hypoxia-activated dual MOA: direct antiangiogenic (endothelial) + anti-inflammatory (monocyte/VEGF-producing cell)**	**Suprachoroidal**	**Preclinical**	—

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