

Palatin Technologies, Inc. NYSE American: PTN

CORPORATE PRESENTATION
February 2025

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CFO / COO

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The statements in this presentation that relate to future plans, events or performance are forward-looking statements, which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended. Such forward-looking statements involve significant risks and uncertainties, and actual results, events and performance may differ materially from those expressed or implied in this presentation. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements include, but are not limited to, statements concerning the following: (i) estimates of our expenses, future revenue and capital requirements; (ii) our ability to obtain additional funding on terms acceptable to us, or at all; (iii) our ability to advance product candidates into, and successfully complete, clinical trials; (iv) the initiation, timing, progress and results of future preclinical studies and clinical trials, and our research and development programs; (v) the timing or likelihood of regulatory filings and approvals; (vi) our expectation regarding timelines for development of our other product candidates; (vii) the potential for commercialization of our other product candidates, if approved for commercial use; (viii) our ability and the ability of our licensees to compete with other products and technologies similar to our product candidates; (ix) the ability of third party collaborators to timely carry out their duties under their agreements with us and our licensees; (x) the ability of contract manufactures to perform their manufacturing activities in compliance with applicable regulations; (xi) our ability to recognize the potential value of our licensing arrangements with third parties; (xii) the potential to achieve revenues from the sale of our product candidates; (xiii) our ability to maintain product liability insurance at a reasonable cost or in sufficient amounts, if at all; (xiv) the retention of key management, employees and third-party contractors; (xv) the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology; (xvi) our compliance with federal and state laws and regulations; (xvii) the timing and costs associated with obtaining regulatory approval for our product candidates; (xviii) the impact of legislative or regulatory healthcare reforms in the United States; and (xix) other risks disclosed in our SEC filings. The forward-looking statements in this presentation do not constitute guarantees of future performance. We undertake no obligation to publicly update these forwardlooking statements to reflect events or circumstances that occur after the date of this presentation.



### **Company Profile**

Technology platform – validated drug development based on the melanocortin system

### Therapeutics for Obesity, Inflammatory & Autoimmune Diseases, and Sexual Dysfunctions



Demonstrated expertise moving programs from discovery to FDA approval



Expertise in the biology and chemistry of melanocortin system (MCS)



1<sup>st</sup> company to gain FDA approval for a melanocortin agent (Vyleesi<sup>®</sup>)



MOA with potential to modify underlying disease pathologies – not just treat symptoms



Strategy leverages our expertise across multiple therapeutic opportunities



### Palatin Leadership – Strong Team with Broad / Extensive Biopharma Experience



Carl Spana, PhD President and Chief Executive Officer

Co-founder with 25-plus years in drug research, development, approval and board directorships



25-plus years in finance, operations, M&A, licensing, capital markets and board directorships



Senior Vice President Research / Development

> 40-plus years in drug discovery and development

Paul Kayne, PhD

Vice President **Biological Sciences** 

25-plus years in drug discovery and development J. Don Wang, PhD

Vice President Product Development

30-plus years in CMC and supply chain Stephen A. Slusher Chief Legal Officer

30-plus years of legal leadership with a focus on Intellectual property

#### **Robert Jordan**

Senior Vice President **Program Operations** 

20-plus years in drug development and clinical operations

#### **James Hattersley**

Senior Vice President **Business Development** 

> 25-plus years of identifying and executing deals





















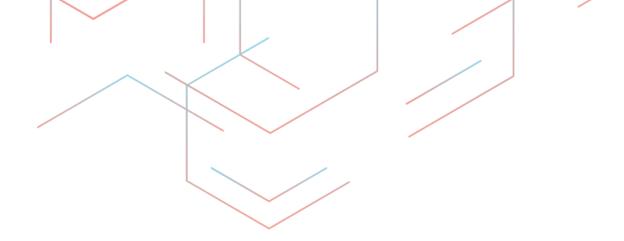




# Commercial Product and Development Programs

Commercial Product						
Vyleesi® (bremelanotide) Hypoactive Sexual Desire Disorder	Asset Sale for FSD Rights to Cosette December 2023					Up to \$159 million in potential sales milestones
Pipeline Development Programs	Preclinical	Phase 1	Phase 2	Phase 3	NDA	Status/Next Steps
Obesity Bremelanotide Obesity - GLP-1 adjunct therapy						Phase 2 MC4R agonist + GLP-1 in obese patients initiated Patient enrollment completed / Data 1Q 2025
<b>Novel Once-Weekly Peptide MC4R Agonist</b> Multiple obesity indications						IND enabling activities 1Q 2025 – 3Q 2025 IND filing / Phase 1 SAD/MAD 4Q 2025
PL7737 Oral Small Molecule MC4R Agonist Multiple obesity indications						IND enabling activities 1Q 2025 – 3Q 2025 IND filing / Phase 1 SAD/MAD 4Q 2025
Spin-Out / Out-License Product Candida	ates - Seeking De	evelopment & Co	mmercial Partne	rships (investmen	t bank engaged t	o support process)
Ocular PL9643 MCR Agonist Dry eye disease (DED)						Phase 3 MELODY-1 completed, positive data Phase 3 Melody-2 & -3 start targeted for 1Q 2025 FDA confirmation on protocols and endpoints
PL9588 MCR Agonist Glaucoma						IND-enabling tox program initiation 4Q 2024 Clinical program initiation 2H 2025
PL9654 MCR Agonist Retinal diseases						IVT delivery activities advancing / Topical delivery planned
Gastroenterology, Men's Health, Renal PL8177 Oral MC1R Agonist Ulcerative colitis (UC)						Phase 2 Proof-of-Concept / Patient enrollment completed <b>Topline data readout 1Q 2025</b>
Male Sexual Dysfunction Bremelanotide + PDE5i PDE5i non-responders						Clinical co-formulation program initiated PK Study data 2H 2025 Phase 2/3 initiation 2H 2025
MCR Agonist Diabetic nephropathy						Phase 2 Open Label Trial / Patient enrollment completed Positive topline data reported 4Q 2024





Melanocortin-4 Receptor Obesity Management

Co-administration of Bremelanotide & Tirzepatide (GLP-1/GIP)

- Bremelanotide (BMT) MC4R Agonist
  - ✓ FDA Approved (Vyleesi® for Female HSDD)
- Novel "Next Generation" MC4R Selective Agonists
  - MC4R Selective Peptides Once Weekly Dosing
  - Oral MC4R Selective Small Molecules





# **Emerging Obesity Treatment Landscape**

U.S. market value – obesity/metabolic over \$5 billion (2023) growing to \$44 Billion (2030)

#### Two treatment objectives will define the market

- Safe, tolerable weight loss for all patients
- Long-term maintenance of a healthy weight range

#### Incretin based therapeutics will be standard of care

- Can drive substantial rapid weight loss
- Issues are tolerability, safety and rebound
- New mechanisms are needed to meet long term treatment goals

#### The Opportunity

- 2<sup>nd</sup> line monotherapy
- Co-administration with incretin therapeutics
- Weight loss maintenance

- Central Leptin-Melanocortin pathway is a critical pathway that regulates feeding and body weight to maintain energy homoeostasis
- MC4R agonist is a validated drug target for treating obesity
- MC4R agonists are additive to incretin therapeutics
- MC4R agonists counter the negative pathology which drives weight regain

MC4R agonists will be a highly valuable addition to the emerging obesity treatment landscape.



### Review of Weight Loss Maintenance

Realizing the long-term benefits of obesity treatment



Excess body weight and fat is associated with negative health conditions

Including cardiovascular disease, diabetes, fatty liver disease, musculoskeletal disorders and some cancers



Current and next "generation" incretin based anti-obesity treatments result in significant weight loss and improved health outcomes but for most patients, weight loss stops after 1<sup>st</sup> year



Current research indicates that persistent long-term intervention will be required to maintain a "healthy" weight reduced state and realize the benefits of anti-obesity treatment

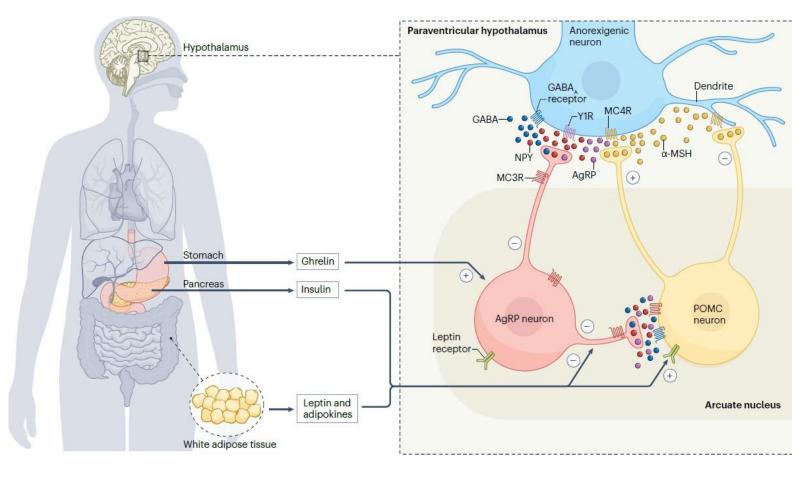


MC4R agonism counter acts many of the metabolic, autonomic, neuroendocrine and behavioral adaptations that strongly favor weight regain



# The Melanocortin Receptor System

### Obesity and energy management



Central leptin-melanocortin pathway is a critical pathway that regulates feeding and body weight to maintain energy homoeostasis



# Value of Palatin's MC4R Agonist Portfolio

New mechanisms will be required for obesity therapy and weight loss maintenance

Clinically validated treatment for obesity

**Bremelanotide** 

Novel improved "Next Gen" Selective MC4R agonists

Obesity therapy will require combination therapy to achieve consistent, robust weight loss and for the long-term maintenance of healthy weight

There are multiple high value intervention points for an MC4R agonist

MC4R agonism is additive to GLP-1 treatments

Central mechanism of action

Low clinical risk

Defined development pathways

Potential for high returns

FDA approved

Extensive efficacy and safety data

Evaluated in obesity clinical studies

Can rapidly be expanded into additional indications

Long duration SC peptide agonists

Oral small molecule agonists PL7737 lead identified

Improved safety

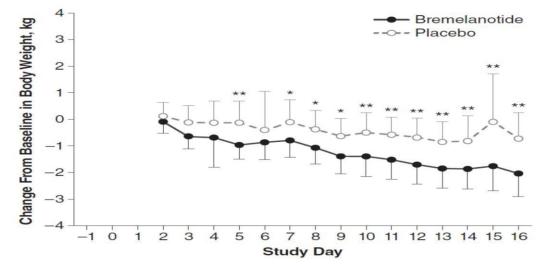
Address unmet need and chronic administration

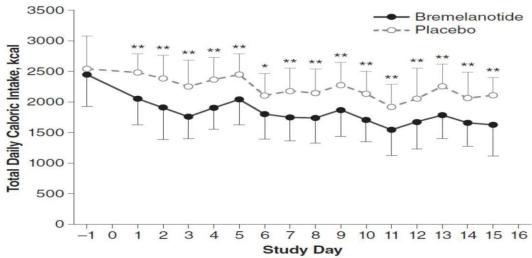
Could be additive to current treatments



# The Melanocortin Receptor System

Bremelanotide MC4R obesity management program and Phase 1b clinical weight loss study





### 2-Week Study

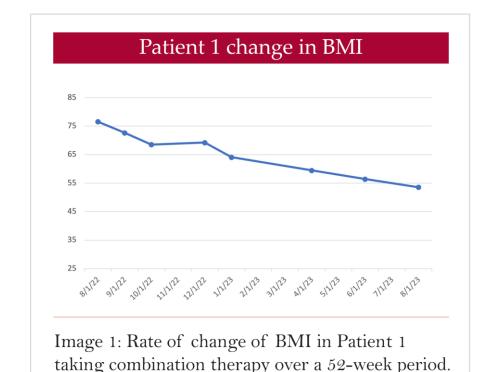
- Weight loss:
  - Placebo -0.7kg;
     Bremelanotide: -2.2kg p<0.001</li>
- Bremelanotide reduction daily caloric intake ~400kcal p<0.01</li>
- Steady weight loss over the duration of treatment

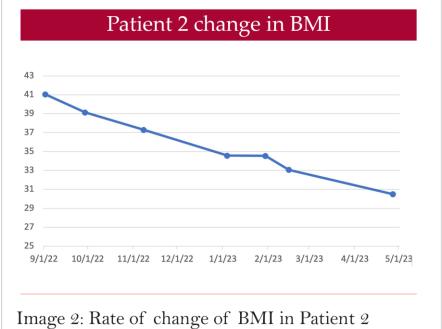
A second 1x & 2x day dosing study also demonstrated efficacy



# GLP-1/GIP Agonist + MC4R Agonist: Co-Administration Clinical data\*

- No prospective studies have been done with combination pharmacotherapy
- Previously published combination of setmelanotide plus 2.5mg of tirzepatide for obesity in BBS
- 2 patients lost 26% in 34 weeks and 30% TBW at 52 weeks never moving past 2.5mg dose





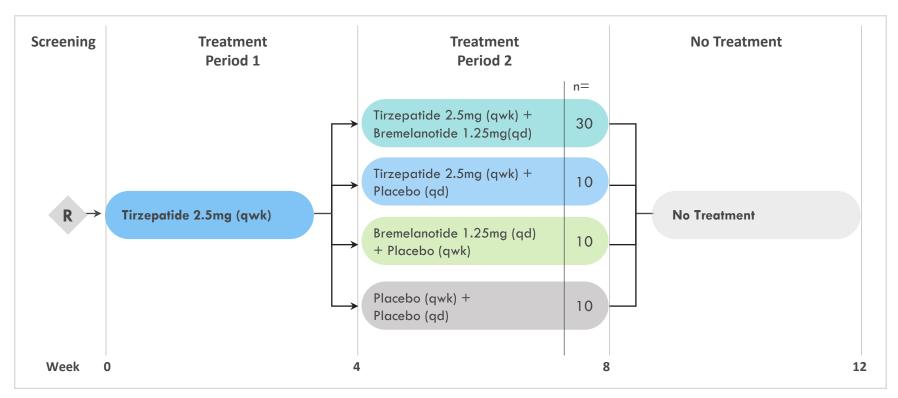
taking combination therapy over a 34-week period.

# GLP-1/GIP Agonist + MC4R Agonist: Co-Administration

Phase 2 co-administration of tirzepatide and bremelanotide (BMT-801)

#### **Study Design**

Randomized, double-blind, placebo-controlled trial evaluating the safety and efficacy of the addition of an MC4R agonist (BMT) to tirzepatide in obese subjects



#### **Enrollment Completed**

#### **Topline data 1Q 2025**

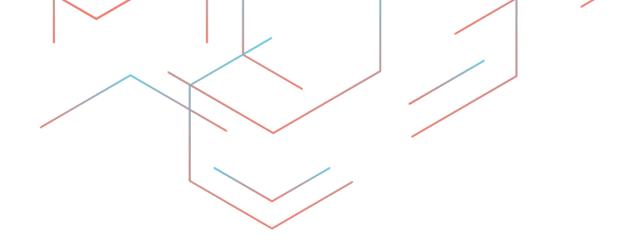
#### **Primary Endpoint**

Change in body weight: tirzepatide + bremelanotide vs. placebo at week 8

# Secondary Endpoints (evaluated at week 8)

- Weight loss maintenance
   bremelanotide + placebo compared
   to placebo
- Appetite suppression measured by visual analog scale (VAS)
- Lean muscle mass
- Cardiometabolic laboratory values
- Neck and waist measurements





Novel "Next Generation" MC4R Selective Agonists

- MC4R selective peptides once weekly dosing
- Oral MC4R selective small molecules



# The Melanocortin Receptor System

Legacy challenges of MC4R agonist have been solved

### **Current Therapy Challenges**

#### **Palatin Achieved Solutions**

Injection Frequency



Palatin's compounds with high potency coupled with structural elements, extend drug residency time ( $\geq 1$  week)

**Skin Pigmentation** 



Multiple structural elements have been identified by Palatin and demonstrate reduced MC1R agonism (a known contributor to hyperpigmentation)

Nausea / Vomiting



Palatin research has identified multiple approaches to reduce gastrointestinal AE's

Cardiovascular Effects



Palatin structure-function studies have identified achievable modifications which eliminate cardiovascular effects



# Novel "Next Generation" Selective MC4R Agonists

### First series of 'next generation' MC4R peptide agonists for obesity:

- Palatin studies in MC4R knock-out model confirm weight loss is dependent on a functional MC4R
- PL8905 lead development candidate
  - Selective MC4R agonist: Significant multiples of binding selectivity for MC4R over MC1R
  - Protein binding tail for extended duration
  - Efficacy in weight loss and food intake at doses that do not have blood pressure effects
  - Confirms validity of structure/function relationships, new compounds are extending the selectivity for MC4R over MC1R

### Second series of 'next generation' MC4R peptide agonists for obesity:

- Palatin has generated novel structures/compounds that bias for MC4R selectivity over MC1R
  - Extended in vivo stability allows for 1x weekly dosing



# MC4R Selective Oral Small Molecule Program

### Understanding what is required for success

Historically, MC4R small molecule programs have failed due to a lack of understanding the receptor biology and the structure/function relationship that determine weight loss versus side effects.

Target profile for orally active selective MC4R agonist:

- Properties required for a successful oral small molecule
  - ✓ Molecular weight
  - ✓ Polar surface area
  - ✓ hERG activity
  - ✓ Human plasma protein binding
  - CYP activity
- MC4R mechanism-based weight loss
- No MC1R activity
- No sexual or blood pressure effects
- 30-day non-GLP toxicity completed



Palatin's PL7737 has the TARGET PROFILE for a successful MC4R selective, oral small molecule entity.



# **Obesity Focused Development Programs**

Multiple clinical trials targeted in 2025 with novel, long-acting MC4R peptide and PL7737 small molecule compound for treating general obesity, weight loss management, and rare MC4R pathway diseases such as hypothalamic obesity.

Product/Indication	R&D	Phase 1	Phase 2	Phase 3	NDA	Status/Next Steps
Bremelanotide (PoC Study) Obesity GLP-1 adjunct therapy						Phase 2 - tirzepatide patients Patient enrollment completed Data 1Q 2025
Novel Once-Weekly Peptide MC4R Agonist Multiple obesity indications						Identify optimal compound 1H 2025 Daily and extended dosing formats IND enabling activities 1Q 2025 - 3Q 2025 IND filing 4Q 2025 Phase 1 SAD/MAD start 4Q 2025 Data 1Q 2026
PL7737 Oral Small Molecule MC4R Agonist Multiple obesity indications						Daily dosing format IND enabling activities 1Q 2025 - 3Q 2025 IND filing 4Q 2025 Phase 1 SAD/MAD start 4Q 2025 Data 1Q 2026

Hypothalamic Obesity (HO) treatment being assessed



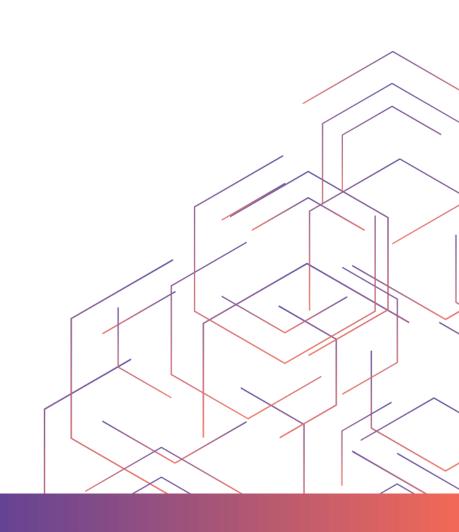
# Summary – Palatin's MC4R Obesity Program

### Experts in the design and development of MC4R agonists

- Clinically validated mechanism for safe, effective treatment of obesity
- Mechanism addresses the negative physiology that drives weight regain
- IP, know-how and assets for the successful development of an MC4R obesity treatment
- First company to get FDA approval for an MC4R agonist (Vyleesi® approved 2019)
- 1x weekly & oral small molecule MC4R selective agonists ready to advance into development
- Multiple near term clinical and development milestones to increase value
  - IND enabling activities target start 1Q 2025
  - IND filings target 4Q 2025
  - SAD/MAD Phase 1 target 4Q 2025 Topline data readout 1Q 2026





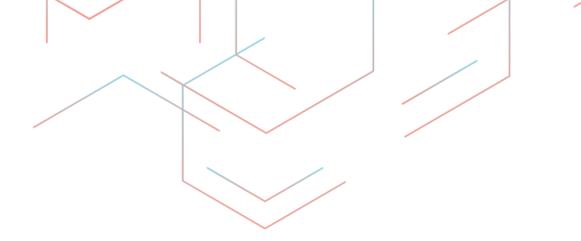




# Spin-Out / Out-License Programs

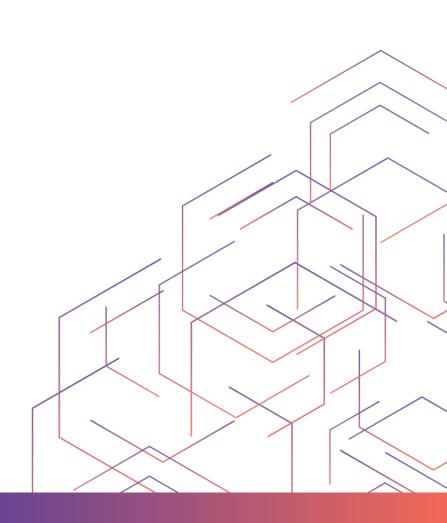
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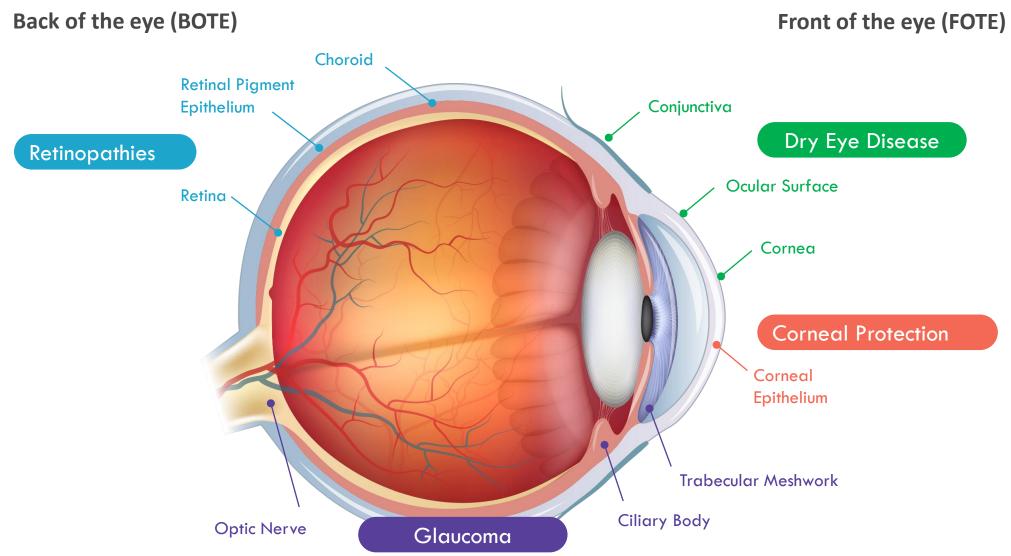
# **Ophthalmology MCR Programs**

- Dry Eye Disease PL9643
- Glaucoma PL9588
- Retinal Diseases PL9654





# Melanocortin Agonists for Ophthalmic Disease





# Melanocortin Agonists for Ophthalmic Disease

### Target markets and opportunities

#### **Dry Eye Disease**

Global Market (2024 Est.) \$7.0 Billion
Global Market (2032 Est.) \$12.3 Billion

- Unsatisfied need for better tolerability, and more rapid relief of symptoms
- Current market leaders have high discontinuation rates after initial Rx's

#### Retinopathies

Global Mkt (2021 Act.) **\$20 Billion**Global Mkt (2027 Est.) **\$27 Billion**DR/DME (2023 Act.) **\$10 Billion**DR/DME (2034 Est.) **\$17.5 Billion** 

- Novel MOA expands treatment, addresses non-responders in addition to neovascularization, and treats fibrosis
- Potential for topical formulation to treat patients with early-stage disease before onset of substantial retinal damage

### Glaucoma

Global Market (2022 Act.) \$8.03 Billion
Global Market (2030 Est.) \$11.52 Billion

- Important dual effects; lowers IOP <u>and</u> protects the optic nerve (neuroprotection)
- No current therapy provides direct protection of the optic nerve!

#### **Cornea Protection**

Significant Unmet Medical Need
Novel Indication

Protection against serious ocular adverse events

**Ophthalmic** 

Disease



### Dry Eye Overview

Dry eye disease (DED) or **keratoconjunctivitis** is a multifactorial disorder of the tears and ocular surface

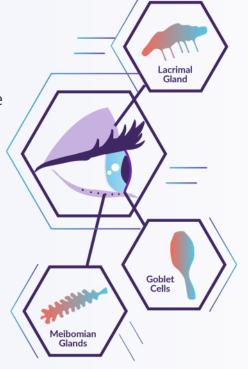
Symptoms include dryness, irritation, redness, discharge and blurred vision

**Inflammation** plays a prominent role in the development and amplification of the signs and symptoms of DED

A few of the approved **Treatments** within the current global dry eye products market ~\$6.1 billion<sup>2024</sup> projected to reach ~\$7.46 billion<sup>2029</sup>

- Restasis® / Cequa® topical cyclosporine
- Xiidra® topical integrin inhibitor
- Tyrvaya<sup>®</sup> nasal varenicline
- Eyesuvis® topical steroid(s)
- Miebo perfluorohexyloctane
- Artificial tears

Current treatments have **efficacy and tolerability issues - PL9643** addresses a high medical need for innovative treatments that treat underlying disease processes with better ocular tolerability.







U.S. market value \$1.65 billion<sup>1</sup>

#### **The Problem**

• No effective chronic treatment that can provide rapid relief of dry eye disease symptoms without tolerability issues

#### **The Opportunity**

- 30MM patients (18MM diagnosed)
- <10% treated by Rx</p>

#### **Current Treatment**

- OTC artificial tears, Rx anti-inflammatories and nasal tear stimulants
- Current Rx products are not effective in many patients
- Approved products have significant tolerability issues

#### Melanocortin agonism

Resolves
inflammation of
corneal surface

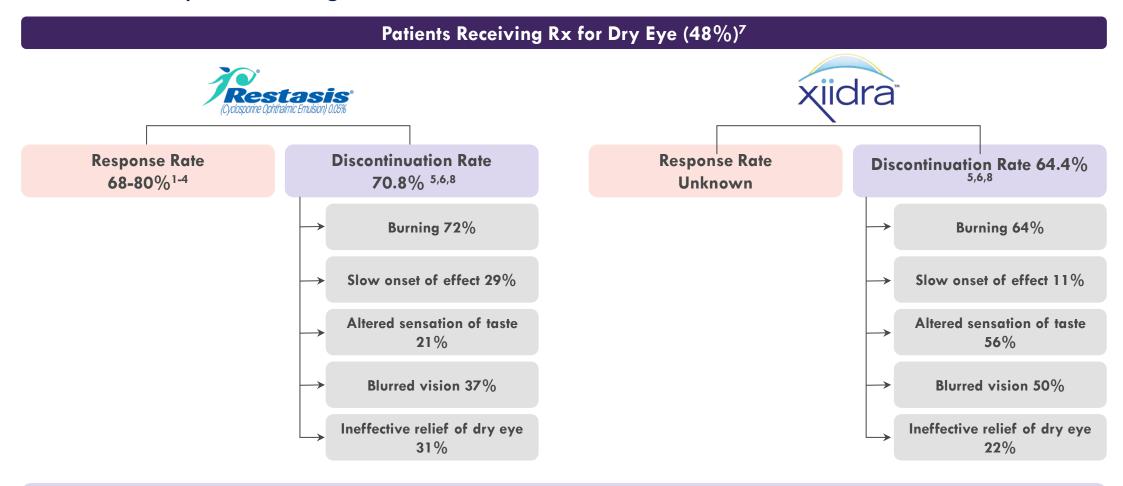
Melanocortin
Receptors present on
multiple cell types of
the ocular surface

Melanocortin agonism leads to resolution of inflammation and promotes tissue repair, resulting in rapid relief of dry eye symptoms.

PL9643 solves 3 recognized problems with current treatments: Efficacy, Onset Time to Effect, and Tolerability.



# Patient Satisfaction is an Issue with Current Therapies Poor tolerability leads to high discontinuation rates



Side effects such as burning, blurry vision, and bad taste are main reasons for poor compliance, while lack of efficacy is also a main driver for discontinuation of Restasis

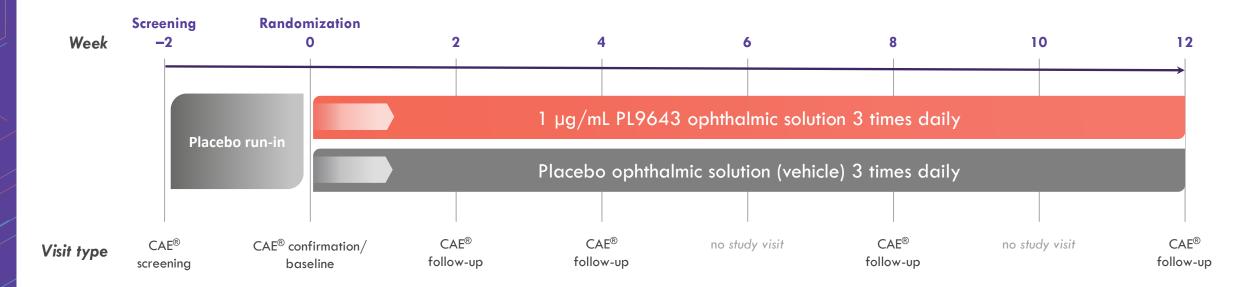


# PL9643 Melody-1 Phase 3 Study Design

12-week, multicenter, 1:1 randomized, double-masked, vehicle-controlled adaptive design study

Evaluate the efficacy and safety of PL9643 (575 patients enrolled) with moderate or severe dry eye disease defined as:

Disease duration  $\geq 5$  years; Inferior Corneal Staining score  $\geq 1$ ; Eye Discomfort score  $\geq 25$  as measured by the Visual Analog Scale (VAS)



**Co-Primary Sign Endpoint (Week 12)**Conjunctival Sum Lissamine Green Staining

Co-Primary Symptom Endpoint (Week 12)
Ocular Pain



### Melody-1 Phase 3 clinical trial

Solves 3 recognized problems with current treatments: Efficacy, Onset Time to Effect, and Tolerability

#### Broad Efficacy Across Multiple Signs and Symptoms

- Co-Primary symptom endpoint of pain met statistical significance (P<0.025)</li>
- 7 of 11 Secondary symptom endpoints met statistical significance (P<0.05)</li>

#### Rapid Onset of Efficacy in 2-weeks

- Statistically significant efficacy for multiple signs and symptoms at 2-Weeks
- Continual improvement in symptom endpoints over the 12-week treatment period
- Fluorescein sign 2-Week evaluation all 4 fluorescein staining endpoints met statistical significance (P<0.05)</li>

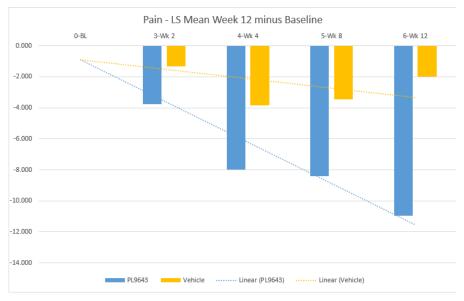
#### **Excellent Ocular Tolerability & Safety**

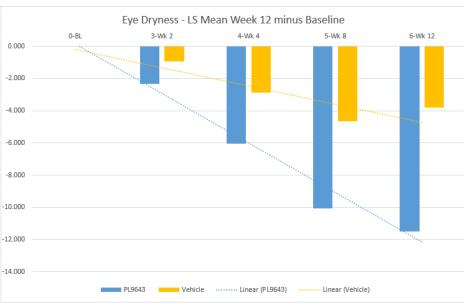
- PL9643 had numerically fewer ocular AEs than artificial tears
- No discontinuations due to ocular AE's

Symptom relief and tolerability will drive market uptake. PL9643 is differentiating on both symptom relief and tolerability.



### Pain & Eye Dryness symptoms: best-in-class symptom relief





- Multiple symptom endpoints statistically significant including co-primary Pain endpoint
- Rapid onset of efficacy at 2-weeks (earliest time point measured)
- Continuous improvement over the 12 weeks of treatment
- DED studies enroll mainly older women (65%-80%, mean age ≥60) and response can vary by age and gender

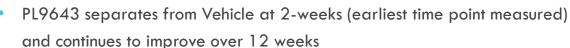
DED Symptom	ITT Population P-value	All Subjects Age >60 P-value
Burning	0.0370	0.0111
Burning/Stinging	0.1792	0.0026
Dryness	0.0417	0.0136
Eye Dryness	0.0043	0.0119
Grittiness	0.2357	0.0255
Ocular Discomfort	0.0091	0.0077
Pain	0.0217	<mark>0.0017</mark>
Photophobia	0.0078	0.0032

Change from baseline at 12-weeks pre-CAE PL9643 v. Vehicle

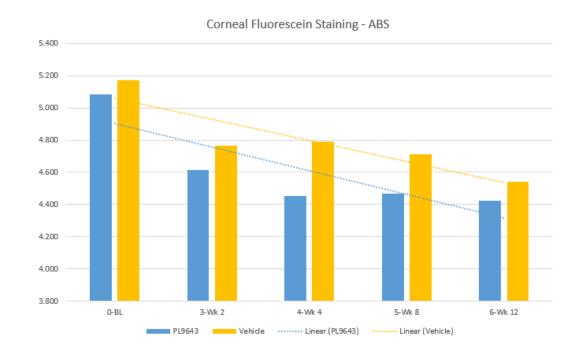


### MELODY-1 sign endpoint





- Primary sign endpoint did not reach statistical significance
- Fluorescein staining endpoints statistically significant ITT population at 2-weeks post-CAE
- IFCS 2-weeks post-CAE primary sign endpoint for MELODY 2 & 3



2-weeks post-CAE	P-Value
Inferior Fluorescein Staining	0.0082
Corneal Fluorescein Staining	0.0065
Central Fluorescein Staining	0.0080
Total Eye Fluorescein Staining	0.0551



### Safety and ocular tolerability

PL9643`	Phase 2 Study		Phase 3 Study		
Ocular Adverse Events	PL9643 (N=80)	Vehicle (N=80)	PL9643 (N=287)	Vehicle (N=288)	
Instillation Site Pain	0%	9%	3.1%	4.5%	
Blurred Vision	0%	1%	0.3%	0.3%	
Reduced Visual Acuity	0%	1%	0.3%	0.3%	
Eye Redness	0%	0%	0%	0.3%	
Conjunctival hyperemia	0%	0%	0%	0.3%	
Instillation Site Irritation	0%	0%	0%	0%	
Dysgeusia	0%	0%	0%	0%	
Ocular Burning	0%	0%	0%	0%	
Sneezing	0%	0%	0%	0%	
Cough	0%	0%	0%	0%	
Throat Irritation	0%	0%	0%	0%	

PL9643`	Phase 2 Study		Phase 3 Study	
Discontinuations	PL9643 (N=80)	Vehicle (N=80)	PL9643 (N=287)	Vehicle (N=288)
Adverse Event	0%	1%	1%	2%
Ocular Adverse Event	0%	0%	0%	0%
Lost to Follow-up	0%	0%	0.7%	2%
All other reasons	1%	2.5%	5.6%	7.3%

#### Phase 3 Melody-1 Study (n=575)

- PL9643 eye drop formulation was well-tolerated, similar to artificial tears
- No treatment related serious adverse events
- Ocular adverse events were mild
- Fewer ocular treatment related adverse events and discontinuations in the PL9643 arm compared to vehicle

#### Phase 2 (n=160)

 No treatment-related serious AE's or ocular adverse events were observed with PL9643 treatment



### Program summary / next steps

#### **Robust Phase 3 Program**

F

- Three Efficacy/Long Term Safety Studies:
  - MELODY-1 (completed)
  - MELODY-2 & -3
    - FDA confirmation of protocols & endpoints
  - Long term safety study

#### **NDA Package & Target Filing**



- NDA File Date (Est.): 2026
- FDA Approval/Launch (Est.): 2027



#### **Expected Phase 3 Data Read Out**

- Remaining Phase 3 pivotal trials
  - Melody-2 & -3 initiation target 1Q 2025
    - Topline data readout 4Q 2025
- MELODY-2 & MELODY-3 safety extension:
  - 6-month data in 1H 2026 /12-month data in 2H 2026

#### **Best Overall Product Profile**



- Broad efficacy across multiple signs and symptoms
- Rapid onset of efficacy in as little as 2-weeks
  - Teats multiple symptoms and signs
- Excellent ocular safety and tolerability

Solves 3 main problems with current treatments: Efficacy, Onset Time, and Tolerability



# PL9588 Treating Glaucoma

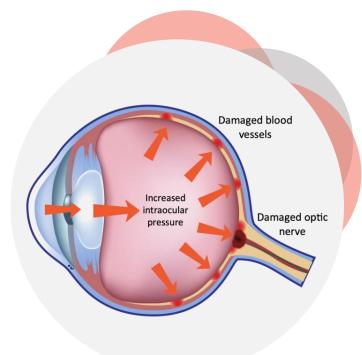
### Lowers IOP and direct neuroprotection

- Progressive eye diseases characterized by elevated intraocular pressure (IOP) resulting in loss of retinal ganglion cells and progressive loss of vision (open angle glaucoma), 2<sup>nd</sup> leading cause of blindness
- In U.S. ~3.4M people have open angle glaucoma\*
  - ~50% diagnosed and on treatment
- Goal of drug therapy is reduction & maintenance of lower IOP
  - Prostaglandins, 1<sup>st</sup> line therapy
  - $\beta$ -agonists and  $\alpha$ -agonists, main adjunct treatments
  - ~62% of patients discontinue therapy within 18 months\*\*

Ocular safety & tolerability issues



- Provides neuroprotection
- Lowers IOP with improved ocular safety and tolerability
- Treating disease progression
- Prepared to initiate clinical development

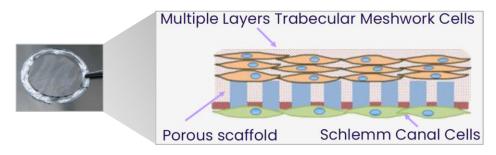




# PL9588 Treating Glaucoma

### Mechanism of action lowering IOP

#### **Humonix' Model**



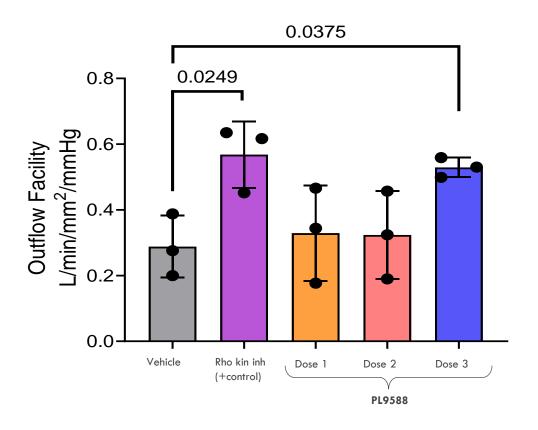
PL9588 tested in a fluid outflow model

 Human donor trabecular meshwork and Schlemm's canal cells reconstituted

PL9588 as effective as rho kinase inhibitor

- Most potent IOP lowering glaucoma treatment
- ROCKi\* has poor tolerability and safety

PL9588 mechanism of action supports monotherapy or combination therapy





### PL9588 for Glaucoma

### Program summary / next steps

#### **PL9588-Lead Development Compound**



- Topical eyedrops
- Ocular tox programs are short
- $\sim$ 3 quarters &  $\sim$ \$5 million to Phase 1 safety/IOP data

#### NDA Package & Target Filing



- NDA File: Efficacy, Safety and CMC data
- NDA File Date (Est.): 2028
- FDA Approval/Launch (Est.): 2029

#### **Efficient Development Program**

- IND 1H 2025
- Phase 1 study data 2H 2025
- Phase 2 study data 2H 2026
- Phase 3 study data 2H 2027

#### **Overall Product Profile**



- Differentiated profile that addresses unmet needs
- Lowers IOP
- Improved ocular safety and tolerability

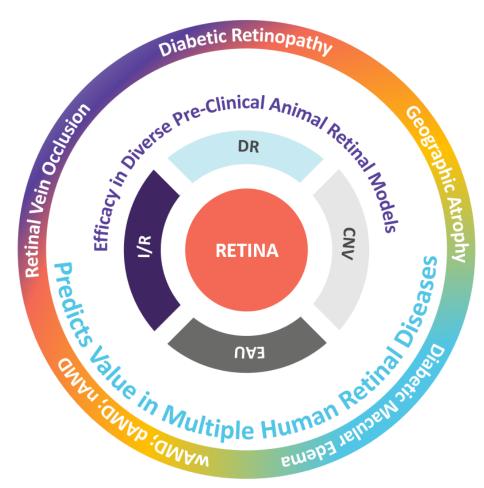
Treatment differentiation: provides neuroprotection, lowers IOP with improved ocular safety and tolerability



## PL9654 For Retinal Diseases

## **Executive Summary**

- Retinal disorders current drug market was USD \$12.57B (2022) and is projected to be \$25.6B by 2030
  - DR/DME estimated was  $\sim$ \$10B (2023)
- IVT anti-VEGF and steroids 1<sup>st</sup> line treatments
- New treatments with novel MOA needed to expand treatment and address non-responders
- Palatin melanocortin agonists active in 4 pre-clinical retinal disease models\*
  - Predictive of potential efficacy in multiple retinal diseases
- PL9654 lead candidate is prepared for clinical development





## PL9654 For Retinal Diseases

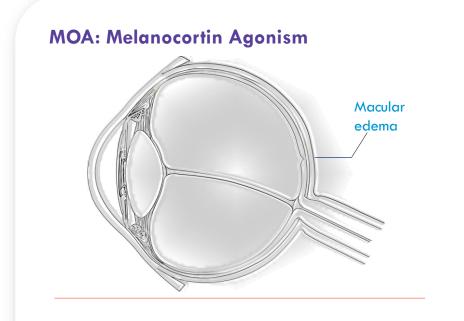
## U.S. diabetic retinopathy market value \$2.4 billion

### The Problem

 Retinal diseases are associated with neurodegeneration processes and fibrosis that have a long-term impact on vision

### **Current Treatment**

- IVT angiogenesis inhibitors do not treat the neurodegeneration and fibrosis associated with retinal diseases
- IVT steroids have long term safety issues



PL9654 protects against neurodegeneration, resolves inflammation, reduces fibrosis, maintains retinal-blood barrier and enhances retinal cell response to stress.

PL9654 demonstrated robust efficacy in multiple retinal disease models with the potential for topical administration



## PL9654 for Retinal Disease

## Summary

Novel mechanism to advance the treatment of retinal diseases:

### PL9654 lead compound ready to advance to clinical development

- Efficacy established in 4 models of retinal disease
- Genomic and proteomic data advances understanding of MoA
- Sustained release IVT formulation with potential for topical administration

### Key efficacy effects

- Preserves vision in diabetic retinopathy model
- Neuroprotective
- Anti-angiogenesis through novel mechanism
- Resolves pathological inflammation & reduces fibrosis
- Maintains Blood-Retinal-Barrier



# Palatin Melanocortin Agonists for Ophthalmic Disease *Summary*



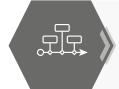
Novel differentiated products for ophthalmic indications



Melanocortin MoA delivers efficacy with excellent safety & tolerability



Proprietary compounds with long term IP estate



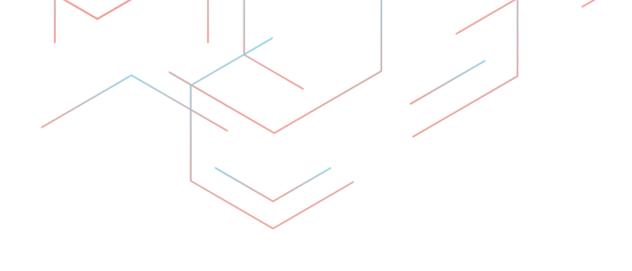
Short, well defined, clinical pathways for regulatory approval



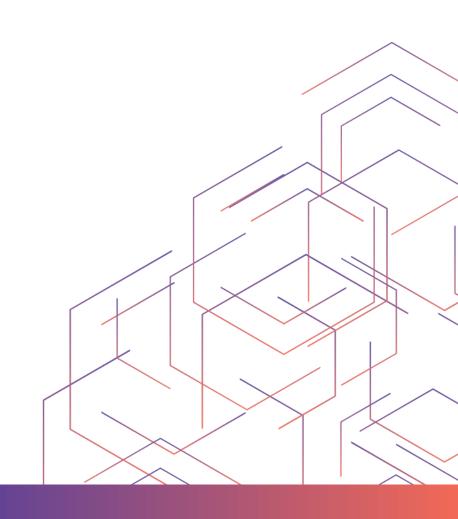
Potential high return on investment

Multi-billion USD portfolio with low upfront investment





PL8177 Oral for Ulcerative Colitis





## PL8177 Oral Formulation for Ulcerative Colitis

Global ulcerative colitis (UC) market USD **\$5.5 billion** 2021, projected to be **\$8 billion** by 2026

Most treatments for UC are systemic and have tolerability and safety limitations

PL8177 is a *highly potent selective* agonist at melanocortin receptor 1

Why a
Melanocortin
Peptide for
Ulcerative Colitis?

Phase 2 study evaluating safety and efficacy of PL8177-Oral in UC patients ongoing; enrollment completed; topline data1Q 2025

MC1R on colon epithelial cells is accessible from the lumen of the colon. PL8177-Oral demonstrated robust efficacy in UC animal models

### PL8177 is not systemically absorbed

- Potential for excellent efficacy without safety concerns
- Phase 1 SC SAD/MAD study no significant findings
- Oral Phase 1 study confirms colon delivery

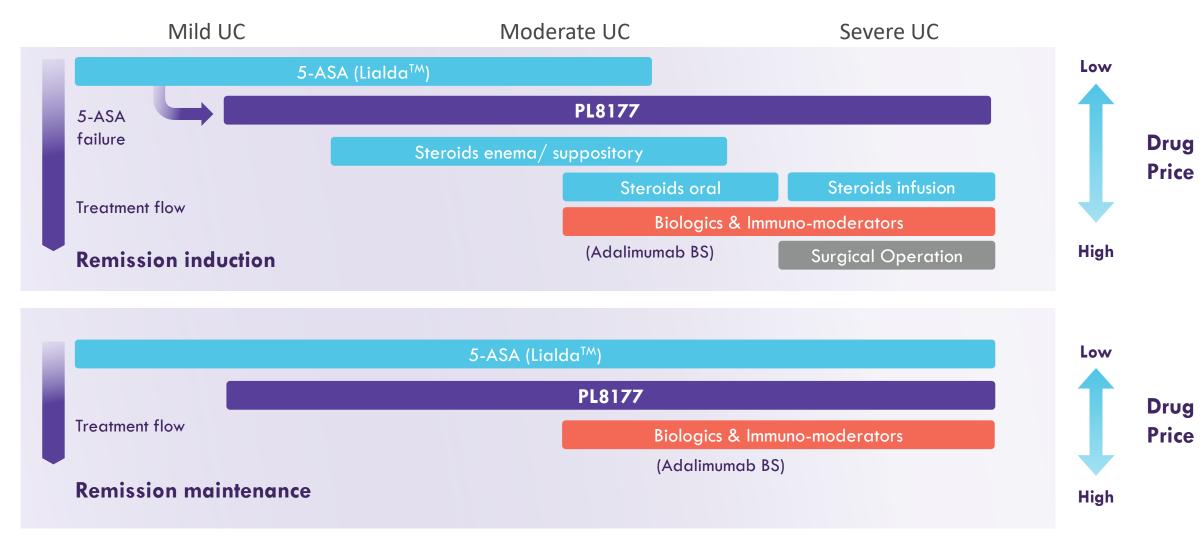
"Currently available therapies cannot cure IBD, but many of them target various inflammatory pathways, resulting in more or less durable remission. However, these therapies come at a high price economically and physically, with potentially life-threatening side effects."

N. ENGL J MED 385:14 September 30, 2021



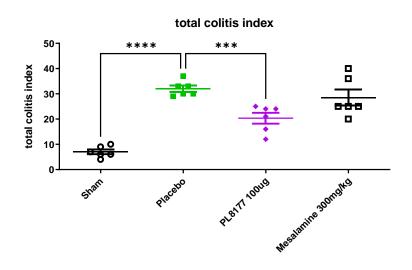
## **UC Patient Treatment Paradigm**

Opportunity for PL8177 in UC Treatment throughout the treatment paradigm



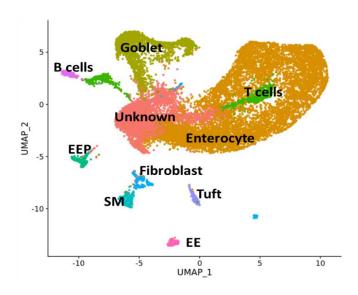


## PL8177-Oral Preclinical Data Rat DSS Model



### Total colitis index

- Abnormalities of mucosal architecture
- Extent of inflammation
- Erosion & ulceration
- Epithelial regeneration
- Percentage involvement by the disease process



### Single nuclei RNAseq of DSS rat colon

- Preserves enterocyte cell population
- Prevents increase of inflammatory T cell population
- Down regulation of multiple inflammatory pathways



## PL8177-205 Phase 2 Study Design & Timelines

Phase 2 RCT Parallel Group Study Using an Adaptive Design to Evaluate Safety, Tolerability and Efficacy

2022 2023 2024 2025 **Patient Population** Licensing **PL8177 Oral UC Study**  Adult patients with active UC Study Part A (n=12-16) • Modified Mayo endoscopic subscore  $\geq 2$ **Primary Safety Endpoint Full Data** N=14 • The overall incidence of treatment-emergent adverse events (TEAEs) Corporate decision made to end enrollment and pursue **Primary Efficacy Endpoint** licensing with current patient numbers (N=14) Proportion of patients that have MES of 0 or 1 (endoscopic improvement)



## Ulcerative Colitis – Target Product Profile for Commercial Success

#### **PL8177 Preclinical Profile**

- High potency at melanocortin receptors 1
- Efficacy in multiple animal models including gold standard disease model
- Efficacy as good/better than 5-ASA and glucocorticoids in animal model data
- No toxicological findings in pre-clinical studies doses >100-fold above planned clinical doses

#### **PL8177 Oral Formulation PK**

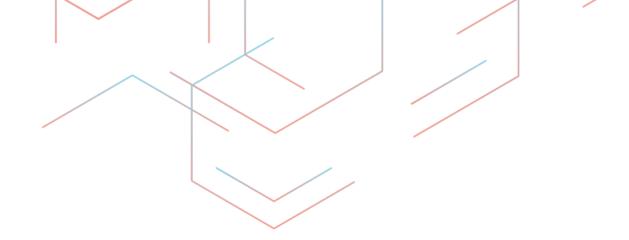
- Phase 1 radiolabeled micro-dose study with the oral formulation, confirmed colonic delivery of PL8177
- Orally dosed PL8177 remains in the colon there is no systemic exposure

#### **PL8177 Clinical**

- Phase 1 clinical SAD/MAD study with the systemic formulation (SC) completed, no adverse events or safety signals
- Phase 2 study UC patients
  - Enrollment completed
  - Data 1Q 2025

PL8177 Oral Formulation – novel, non-immunosuppressive mechanism of action.





Melanocortin-4 Receptor Erectile Dysfunction (ED)

- Bremelanotide (BMT) MC4R Agonist
  - FDA Approved Vyleesi® for Female HSDD
- Co-administration (co-formulation) of BMT & Tadalafil
  - PDE5i Non-Responders





## Value of MC4R Agonists for Sexual Dysfunction

Low clinical risk, defined development pathways with potential for high returns

### Bremelanotide has extensive efficacy and safety data and can be rapidly expanded to ED indication

Evaluated in over 45 clinical studies and 10,000 patients

### Novel co-formulation of bremelanotide with a PDE5i

- Extend IP
- 505(b)(2) regulatory pathway
- Potential to effectively and safely treat PDE5i failures

### PDE5i failures large underserved market

- >30 million men in US have ED
- ~35% of ED patients are inadequately treated by PDE5i therapy with limited treatment options
  - Vacuum devices
  - Direct penile injection of vasodilators
  - Surgery for installation of penile implants
- A safe and effective non-invasive treatment is needed



## Bremelanotide Sexual Dysfunction Clinical Experience

The MC4R agonist bremelanotide has been evaluated in multiple sexual dysfunction trials

## Female sexual dysfunction studies

- Clinical studies in pre and post menopausal patients with HSDD and/or FSAD
- Statistically significant and clinically meaningful effects on improving desire, arousal and distress
- Vyleesi<sup>®</sup> FDA approved for treating premenopausal women with HSDD

### Male sexual dysfunction studies

- Multiple clinical studies in men with erectile dysfunction (ED)
- Monotherapy in ED patients and ED patients with diabetes
- Co-administration with PDE5 inhibitor in ED patients that failed PDE5i therapy
- Statistically significant and clinically meaningful effects on improving erectile activity

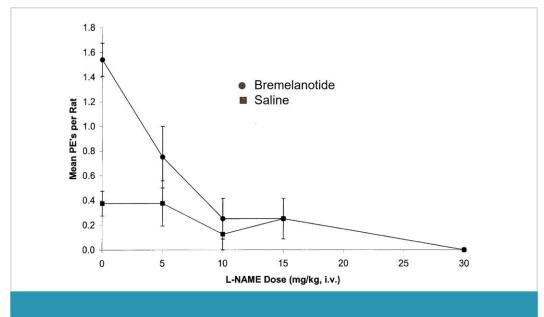
## Post-approval experience in men with sexual dysfunction

- Bremelanotide is being prescribed off-label to men with ED and low sexual desire
- Re-fill rates ~70%

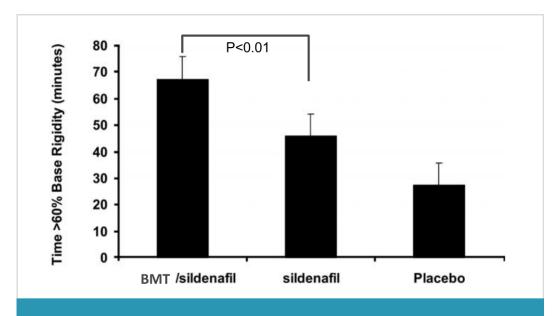


## Bremelanotide for Treating ED

30%-40% of ED patients have an inadequate response to PDE5i therapy, there remains an unmet need for drugs to treat men in whom PDE5i treatment fails\*



BMT drives erectile activity through production of NO and cGMP



IN ED patients BMT co-administered with sildenafil significantly improves rigidity of penile erections

In multiple Phase 2b clinical studies bremelanotide has demonstrated statistical and clinically significant effects on improving erectile function in a broad range of ED patients including moderate/severe and patients inadequately treated by a PDE5i



## BMT/Tadalafil Co-Formulation Development Program



Pre-IND FDA meeting 2Q 2025



IND filing 1H 2025



Phase 1 PK clinical study initiation/data 2H 2025



Phase 2/3 safety and efficacy studies initiation target 2H 2025

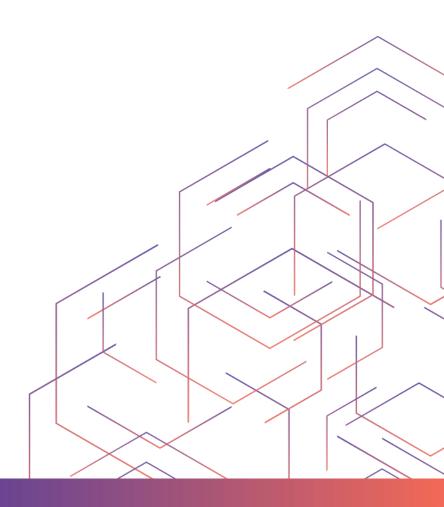


NDA potential target submission 2027



## Vyleesi® - FDA Approved for Female HSDD

- Developed by Palatin
- Acquired by Cosette (December 2023)





## FDA Approved Vyleesi® for Female HSDD

Helping Premenopausal Women with Hypoactive Sexual Desire Disorder (HSDD)



# Hey, you. Meet Vyleesi. ...it's Now Approved

Vyleesi is the first and only as-needed\* treatment for premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD).







Visit: <a href="https://www.vyleesipro.com">www.vyleesipro.com</a>



## Sale of Vyleesi <sup>®</sup> to Cosette Pharmaceuticals – December 2023



Cosette acquired Vyleesi asset and rights for FSD (HSDD)



\$12 million upfront



Potential sales-based milestones of up to \$159 million
Based on annual net sales ranging from \$15 million to \$200 million

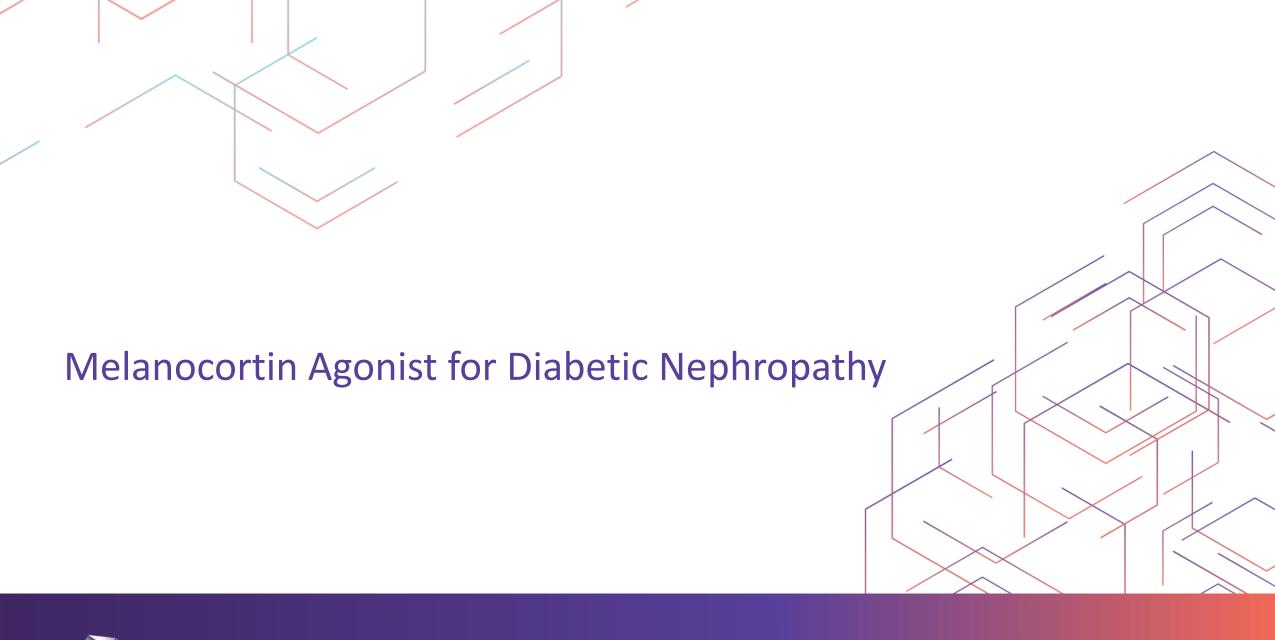


Palatin retained rights and use of bremelanotide (Vyleesi) for obesity and male ED treatment indications



Palatin provided, and was reimbursed for, certain transitional services to Cosette over a defined period of time







# Melanocortin Agonist for Diabetic Nephropathy Diabetic nephropathy

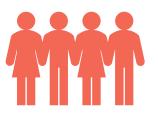


## Diabetic nephropathy (DN) is a severe microvascular complication of diabetes mellitus (DM)

It is the most common form of chronic kidney disease (CKD)

A leading cause of renal failure in end-stage renal disease

No currently available treatment can achieve complete cure



### **Diabetes and DN prevalence**

~ 30 million US patients have CKD secondary to the combination of hypertension and Type 2 diabetes mellitus

>590 million people are predicted to have diabetes worldwide by the year 2035

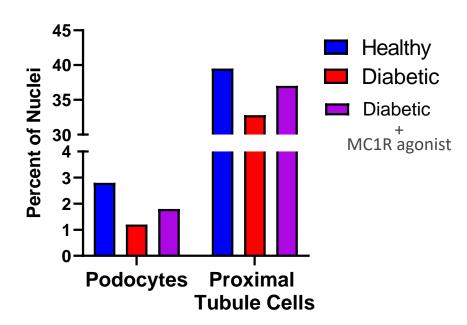
~50% of patients with diabetes will develop DN



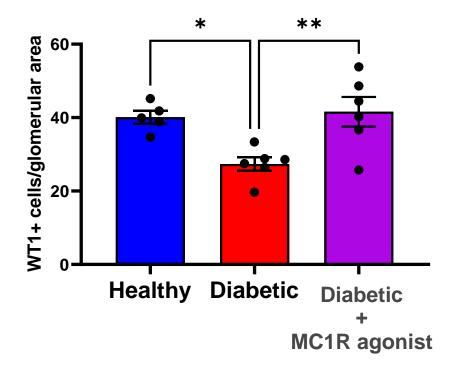
## Melanocortin Agonist for Diabetic Nephropathy

Melanocortin agonists increase key kidney cell types in diabetic rats

Cell Populations by snRNAseq\*



Melanocortin agonist increases relative podocyte and proximal tubule cell populations in diabetic rat, essential for healthy kidney function Podocyte Density by Histopathology

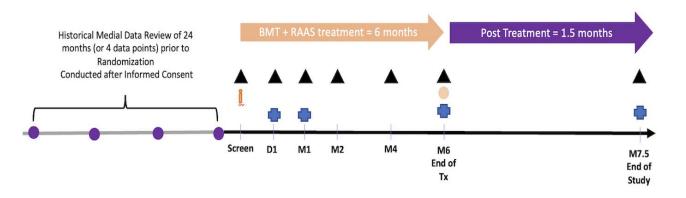


Podocyte density increases in diabetic rats when treated with a melanocortin agonist



# Melanocortin Agonist for Diabetic Nephropathy BREAKOUT study in diabetic nephropathy

## BREAKOUT Study Schema





### **Study Drug Administration:**

In-clinic administration every study visit day Drug administration at home all other days

### **Timelines:**

Treatment Duration = 6 months

Post Treatment Duration = 1.5 months

Total Study Duration = 7.5 months

### **Primary Research Question**

Proportion of subjects with a ≥50% reduction in UP/Cr

### **Secondary Research Questions**

- Proportion of subjects that achieve a reduction in UP/Cr ratios of ≥ 30% from baseline
- Proportion of subjects that achieve a <5.0 ml/min/year drop in eGFR</li>
- Proportion of subjects with a ≥ 50% increase in urinary VEGF levels

All evaluated at six months in subjects on maximum tolerated RAAS inhibition therapy plus BMT

- Patients with biopsy-proven type II diabetic kidney disease and <a>1000</a> mg/gm UP/Cr ratio
- Enrollment concluded with N=16 (N=8 evaluable patients)
- BMT 0.5 mg SC (BID) plus maximum tolerated RAAS inhibition



# Melanocortin Agonist for Diabetic Nephropathy Topline results — BREAKOUT Study in Diabetic Nephropathy

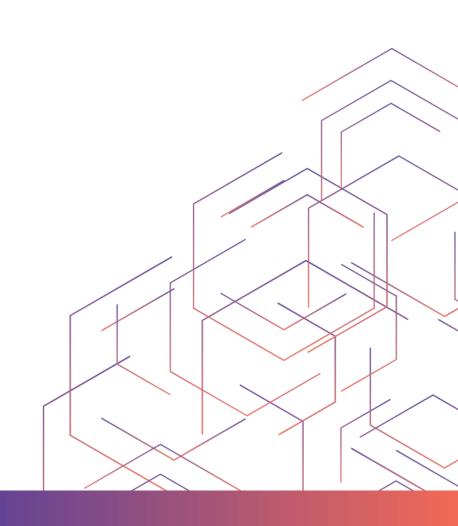
- Addition of Bremelanotide to maximum tolerated RAAS inhibition therapy
  - Resulted in positive and clinically beneficial improvements in kidney function and delaying disease progression
- The data from this trial is encouraging
  - Validates modulation of the melanocortin system as a potentially new therapeutic strategy
  - Potential disease-modifying treatment option for people living with this progressive kidney disease

### **Results Include**

- 57% of patients achieved a clinical response >30% reduction from baseline in UP/Cr
- 14% of patients achieved partial remission >50% reduction from baseline in UP/Cr
- 71% of patients achieved improved or stabilized estimated glomerular filtration rate (eGFR)
- 37.5% of patients had a > 50% increase in urinary vascular endothelial growth factor (VEGF) levels
- 50% of evaluable patients had a >30% reduction in urinary synaptopodin









## Financial Snapshot / Cap Table

### Financial Highlights as of September 30, 2024

Cash and Cash Equivalents

\$2.4 million

No debt

Note: \$2.5 million received November 2024 (deferred payment from Cosette for sale of Vyleesi)

\$3.4 million gross proceeds received December 2024 (exercise of warrants)

### Summary Capitalization as of December 31, 2024

### **Common Shares and Equivalent**

Common Stock 23.4 million shares

Warrants\* 9.9 million shares

Options 2.3 million shares

RSUs 1.1 million shares

Fully Diluted Shares 36.7 million shares

Total Shares Authorized 300.0 million shares

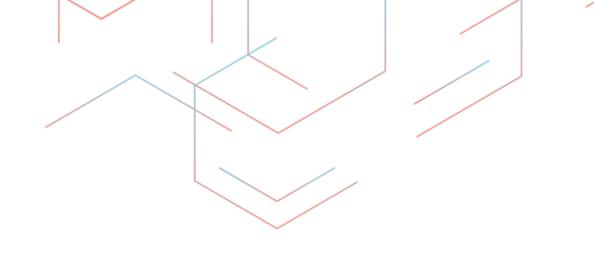


<sup>\*</sup>Exercise prices: 2.0M at \$5.46, 2.0M at \$1.88, 5.9M at \$0.875

## Milestones

Melanocortin System Development Programs	Date
Obesity - MC4R Agonists – Weight Loss (Maintenance)	
Phase 2 BMT-801 Clinical Study Bremelanotide + GLP-1 - Patient Enrollment Completed - <b>Data Readout</b> Novel MC4R Selective Long-Lasting Agonist – <b>IND Filing / SAD/MAD Start</b> PL7737 MC4R Oral Small Molecule Agonist – <b>IND Filing / SAD/MAD Start</b>	1Q 2025 4Q 2025 4Q 2025
Spin-Out / Out-License Product Candidates Seeking Development & Commercial Partnerships (investment bank engaged to support process)	
PL9643 – Dry Eye Disease (DED)	
Phase 3 Melody-1 Clinical Trial - Positive Results  Melody-2 and -3 Phase 3 Pivotal Clinical Trials Initiation Target  FDA Confirmation on Protocols and Endpoints	Completed 1Q 2025
PL8177 Oral – Ulcerative Colitis	
Phase 2 Proof-of-Concept – Patient Enrollment Completed – <b>Topline Data Readout</b>	1Q 2025
Bremelanotide/MC4R + PDE5i (Co-Formulation Single Injection) – Erectile Dysfunction (ED)	
Development and Clinical Study Program in PDE5i Non-Responder ED Patients Initiated  Pharmacokinetics (PK) Study  Phase 2/3 Clinical Study Initiation	2Q 2025 2H 2025
MC4R Agonist – Diabetic Nephropathy	
Phase 2 Open Label Trial – Positive Topline Data Reported	4Q 2024
Vyleesi (bremelanotide) for Hypoactive Sexual Desire Disorder (HSDD)	
Asset Sale for FSD Rights to Cosette Pharmaceuticals December 2023	Completed
Up to \$159 Million in Potential Sales Milestones	Ongoing





Thank You.

