

Palatin Technologies, Inc. OTCQB: PTNT

CORPORATE PRESENTATION June 2025

Carl Spana, Ph.D.Stephen T. Wills, CPA/MSTPresident & CEOCFO / COO

Forward Looking Statements

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



Demonstrated expertise moving programs from discovery to FDA approval



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



1st company to gain FDA approval for a melanocortin agent - Vyleesi[®] for female sexual dysfunction



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 and extensive biopharma experience



Development Programs

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 Positive topline data reported 1Q25
Novel Once-Weekly Peptide MC4R Agonist Multiple obesity indications						IND enabling – CMC activities 1Q25 – 4Q25 IND filing 1Q26 Phase 1 SAD/MAD data 1H26
PL7737 Oral Small Molecule MC4R Agonist Multiple obesity indications						IND enabling – CMC activities 1Q25 – 4Q25 IND filing 1Q26 Phase 1 SAD/MAD data 1H26
Spin-Out / Out-License Product Candid	ates - Seeking De	evelopment & Co	mmercial Partner	rships (investment	t bank engaged to	o support process)
Ocular PL9643 MCR Agonist Dry eye disease (DED)						Phase 3 MELODY-1 completed, positive data FDA confirmation on protocols and endpoints Phase 3 Melody-2 & -3 start targeted for 1H26
PL9588 MCR Agonist Glaucoma						IND filing 1H26 Clinical program initiation / data 1H26
PL9654 MCR Agonist Retinal diseases						IVT delivery activities advancing / Topical delivery planned
Gastroenterology, Renal PL8177 Oral MC1R Agonist Ulcerative colitis (UC)						Phase 2 Proof-of-Concept Positive topline data reported 1Q25
MCR Agonist Diabetic nephropathy						Phase 2 Open Label Trial Positive topline data reported 4Q24





- 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



Melanocortin-4 Receptor Obesity Management Emerging obesity treatment landscape

U.S. market value – metabolic/obesity 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

- 2nd 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.

Melanocortin-4 Receptor Obesity Management

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 1st 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



Melanocortin-4 Receptor Obesity Management

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



Melanocortin-4 Receptor Obesity Management 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



Melanocortin-4 Receptor Obesity Management

Bremelanotide MC4R agonist obesity Phase 1b clinical weight loss study in general obese subjects



2-Week Study

- General obese subjects: BMI ~35
 - Bremelanotide: n=27
 - Vehicle: n=26
- Weight loss:
 - Placebo -0.7kg;
 Bremelanotide: -2.2kg p<0.001
- Bremelanotide reduction daily caloric intake ~400kcal p<0.01
- Steady weight loss over the duration of treatment



Melanocortin-4 Receptor Obesity Management 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





Melanocortin-4 Receptor Obesity Management BMT-801 Phase 2 signal detection study objectives

Co-Administration GLP1/GIP Agonist Tirzepatide (2.5mg Weekly) + MC4R Agonist Bremelanotide (1.25mg Daily)

Main Research Questions

- Does co-administration result in increased weight loss?
- Does MC4R agonism blunt the weight regain seen post-incretin treatment?
- Evaluate the safety and tolerability of co-administration

<u>Pro's</u>

- Appropriate control arms included
- Co-administration arm powered to see a statistically significant weight loss effect
- Evaluating a comprehensive set of secondary end points

Limitations

- MC4R agonist given at a low dose 1x day in the morning
- Not powered for between arm comparisons
- Short duration of treatment

Combination therapy will be an important approach in helping many subjects reach their weight loss goals.



Melanocortin-4 Receptor Obesity Management BMT-801 Phase 2 signal detection study

Co-Administration GLP1/GIP Agonist Tirzepatide & MC4R Agonist Bremelanotide

Study Design: Randomized, double-blind, placebo-controlled trial evaluating the safety and efficacy of the addition of an MC4R agonist (BMT) to tirzepatide in n=96 obese subjects



 Additive effect of BMT:
 % of subjects with ≥5% weight loss at week 8 tirzepatide/bremelanotide compared to tirzepatide/pbo

 % subjects greater weight loss in Treatment Period 2 vs Treatment Period 1, tirzepatide/bremelanotide compared to tirzepatide/pbo

 % change in weight loss tirzepatide/bremelanotide compared to tirzepatide/pbo

 % change in weight loss tirzepatide/bremelanotide compared to tirzepatide/pbo

 % change in weight loss tirzepatide/bremelanotide compared to tirzepatide/pbo

 % change in weight loss tirzepatide/bremelanotide compared to tirzepatide/pbo

Weight loss maintenance: % change weight loss bremelanotide/pbo vs pbo/pbo (week 4-week 8)



Melanocortin-4 Receptor Obesity Management BMT-801 patient weight loss from baseline to end of study

Primary Endpoint – Co-Administration Group Greatest Weight Loss

Patient Weight Change (%) from Baseline to End of Study Compared to PBO

Group	РВО/РВО	Visit	LS Mean Difference	Prob. Value
1 (n=49)	4 (n=16)	Baseline end of study	-2.7523	0.0001
2 (n=15)	4 (n=16)	Baseline end of study	-1.9220	0.0257
3 (n=16)	4 (n=16)	Baseline end of study	0.2212	0.7913

Patient Weight Change (%) from Baseline to End of Study

Group	LS Mean	Visit	Prob. Value
1 (n=49)	-4.4087	Baseline end of study	<0.001
2 (n=15)	-3.5896	Baseline end of study	<0.001
3 (n=16)	-1.4269	Baseline end of study	0.0174
4 (n=16)	-1.6472	Baseline end of study	0.0062

Group 1: Tirzepatide (2.5 mg SC) weekly/BMT (1.25 mg SC) daily; Group 2: Tirzepatide (2.5 mg SC) weekly/placebo SC daily Group 3: Placebo SC weekly/BMT (1.25 mg SC) daily; Group 4: Placebo SC weekly/placebo SC daily



Patient Weight Change (%) from Baseline to End of Study Compared to PBO

Patient Weight Change (%) from Baseline to End of Study



GROUP ■1 ■2 ■3 ■4



Melanocortin-4 Receptor Obesity Management Co-administration additive effect – primary analysis

Analysis for Additive Effect Percent of Subjects with ≥5% Reduction in Percent Weight Loss at End of Study



PALATIN

Melanocortin-4 Receptor Obesity Management Effect of co-administration on increased weight loss



Weekly Change in Percent Body Weight (%) by Group

- Comparison of Group 4 to Group 3 during Treatment Period 2 demonstrates a weight loss maintenance effect
- Comparison Group 1 to Group 2 at week-8 demonstrates additive effect of co-administration
- Rapid weight regain seen posttreatment



Melanocortin-4 Receptor Obesity Management BMT-801 Phase 2 signal detection study questions / outcomes

Co-Administration GLP1/GIP Agonist Tirzepatide (2.5mg Weekly) + MC4R Agonist Bremelanotide (1.25mg Daily)

Main Research Questions

 Does co-administration result in increased weight loss?

2. Any increased safety and tolerability issues with co-administration?

Main Study Outcomes

1. YES

- Primary endpoint met (statistically significant)
- Co-administration resulted in increased weight loss
- 2. NO
 - No increase of safety and expected tolerability observed across all treatment arms

- 3. Does MC4R agonism blunt the weight regain seen post-incretin treatment?
- **3**. YES
 - MC4R agonism blunts the weight regain seen post-incretin treatment

Combination therapy could be an important approach in helping many subjects reach their weight loss goals.



Melanocortin-4 Receptor Obesity Management BMT-801 MC4R/GLP-1-GIP co-administration detection study

Appetite Suppression (Patient-Reported Outcomes)

- Patients receiving co-administered bremelanotide + tirzepatide, tirzepatide alone, and bremelanotide alone, experienced significant improvements in appetite suppression, fullness, and satiety
- Patients who transitioned to placebo after initial weight loss on tirzepatide showed no improvement for appetite suppression
 - Overall appetite suppression
 - Bremelanotide + tirzepatide: 71% increase
 - Tirzepatide only: 73% increase
 - Bremelanotide only: 71% increase
 - "How full do you feel (fullness)?"
 - Bremelanotide + tirzepatide: 65% increase
 - > Tirzepatide only: 62% increase
 - Bremelanotide only: 79% increase
 - "How satisfied do you feel (satiety)?"
 - Bremelanotide + tirzepatide: 56% increase
 - Tirzepatide only: 56% increase
 - Bremelanotide only: 68% increase



Melanocortin-4 Receptor Obesity Management BMT-801 MC4R/GLP-1-GIP co-administration detection study

Value of the study results and next steps







Novel "Next Generation" MC4R Selective Agonists

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



Novel "Next Generation" Selective MC4R Agonists The melanocortin receptor system

Legacy Challenges of MC4R Agonism Have Been Solved!

Current Therapy Challenges

Palatin Achieved Solutions



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



Nausea / Vomiting

Cardiovascular Effects

Injection Frequency



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



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



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



Novel "Next Generation" Selective MC4R Agonists 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.



Novel "Next Generation" Selective MC4R Agonists Obesity focused development programs

Multiple clinical trials targeted in 1H26 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 Positive Topline data reported 1Q25
Novel Once-Weekly Peptide MC4R Agonist Multiple obesity indications						Identify optimal compound 1H25 Daily and extended dosing formats IND enabling – CMC activities 1Q25-4Q25 IND filing 1Q26 Phase 1 SAD/MAD data 1H26
PL7737 Oral Small Molecule MC4R Agonist Multiple obesity indications						Daily dosing format IND enabling – CMC activities 1Q25-4Q25 IND filing 1Q26 Phase 1 SAD/MAD data 1H26

PL7737 granted FDA orphan drug designation for obesity due to leptin receptor (LEPR) deficiency.

Hypothalamic Obesity (HO) patients to be included in Phase 1 SAD/MAD studies.



Novel "Next Generation" Selective MC4R Agonists 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 development and clinical milestones
 - IND enabling / CMC activities 1Q25-4Q25
 - IND filings target 1Q26
 - SAD/MAD Phase 1 data readout target 1H26 (includes HO patients)





Spin-Out / Out-License Programs





Spin-Out / Out-License Programs

Product/Indication	R&D	Phase 1	Phase 2	Phase 3	NDA	Status/Next Steps
Ocular PL9643 MCR Agonist Dry eye disease (DED)						Phase 3 MELODY-1 completed - positive data FDA confirmation on protocols and endpoints Phase 3 Melody-2 & -3 target start 1H26 Phase 3 Melody-2 & -3 target data 1H27
PL9588 MCR Agonist Glaucoma						IND filing 1H26 Clinical program initiation / data 1H26
PL9654 MCR Agonist Retinal diseases						IVT delivery activities advancing Topical delivery planned
Gastroenterology, Renal PL8177 Oral MC1R Agonist Ulcerative colitis (UC)						Phase 2 Proof-of-Concept Positive topline data reported 1Q25
MCR Agonist Diabetic nephropathy						Phase 2 Open Label Trial Positive topline data reported 4Q24





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

 Global Market (2032 Est.)
 \$12

\$7.0 Billion \$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.) Global Mkt (2027 Est.) DR/DME (2023 Act.) DR/DME (2034 Est.) \$20 Billion \$27 Billion \$10 Billion \$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

Global Market (2022 Act.) Global Market (2030 Est.)

Ophthalmic

Disease

Glaucoma

\$8.03 Billion \$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



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 billion²⁰²⁴ projected to reach ~\$7.46 billion²⁰²⁹

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

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







PL9643 for Dry Eye Disease U.S. market value \$1.65 billion¹

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

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



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.

Sources: 1. Sall K et al., (2000); 2. Schultz et al., (2014); 3. Torricelli et al., (2014); 4. Williamson et al., (2015); 5. Mah et al., Clin Ophthalmol (2012); 6. White et al. Clin Ophthamol (2019); 7. Lum et al. Amer. Academy of Optometry (2018), 8. White et al. Clin Ophthalmol (2020)



34

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 ≥ 5 years; Inferior Corneal Staining score ≥ 1 ; Eye Discomfort score ≥ 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



PL9643 for Dry Eye Disease 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)
- 7 of 11 Secondary symptom endpoints met statistical significance (P<0.05)

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)

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.



PL9643 for Dry Eye Disease

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	<mark>0.0043</mark>	<mark>0.0119</mark>
Grittiness	0.2357	0.0255
Ocular Discomfort	0.0091	0.0077
Pain	<mark>0.0217</mark>	<mark>0.0017</mark>
Photophobia	0.0078	0.0032

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



PL9643 for Dry Eye Disease MELODY-1 sign endpoint



- PL9643 separates from Vehicle at 2-weeks (earliest time point measured) and continues to improve over 12 weeks
- 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



Corneal Fluorescein Staining - ABS

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



PL9643 for Dry Eye Disease MELODY-1 symptom responder analysis

The First DED Therapy to Demonstrate Significant Clearing of Multiple Symptoms!



- For ALL symptoms PL9643 had a higher percentage of patients clearing symptoms
- 6 of 13 symptom endpoints were significant (p<0.05) in favor of PL9643</p>
- 2 of the 13 symptom endpoints were highly suggestive (p<0.1) in favor of a PL9643</p>
- Clearing is defined as the patients score going to 0
- FDA guidance supports complete clearing of a symptom an approvable endpoint

Updated Phase 3 analyses position PL9643 as a potential first-in-class therapy achieving full symptom resolution in dry eye disease.



PL9643 for Dry Eye Disease Safety and ocular tolerability

PL9643 [°]	Phase 2 Study		Phase 3	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	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



PL9643 for Dry Eye Disease

Program summary / next steps

Robust Phase 3 Program

- 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: Efficacy, Safety and CMC data
- NDA File Date (Est.): 2H 2027
- FDA Approval/Launch (Est.): 2H 2028



Expected Phase 3 Data Read Out

- Remaining Phase 3 pivotal trials
 - Melody-2 & -3 initiation target 1H 2026
 - ✓ Topline data readout 1H 2027
- MELODY-2 & MELODY-3 safety extension:
 - \circ 6-month data in 1H 2027 /12-month data in 2H 2027

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
- Breakthrough symptom resolution
- Excellent ocular safety and tolerability

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



PL9588 for 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), 2nd leading cause of blindness
- In U.S. \sim 3.4M people have open angle glaucoma*
 - $\circ~~\sim 50\%$ diagnosed and on treatment
- Goal of drug therapy is reduction & maintenance of lower IOP
 - Prostaglandins, 1st line therapy
 - \circ β -agonists and α -agonists, main adjunct treatments
 - $\circ~~\sim\!62\%$ of patients discontinue therapy within 18 months**
- PL9588 novel mechanism addressing unmet needs in treating glaucoma
 - Provides neuroprotection
 - Lowers IOP with improved ocular safety and tolerability
 - Treating disease progression
 - Prepared to initiate clinical development

*IQVIA 2019 (TD Cowen , March 2023, Thera DED and Glaucoma, p. 35) **Spooner, JJ et. al. Am J Manag Care Aug:8(10suppl):S262-70 Ocular safety & tolerability issues





PL9588 for Treating Glaucoma Mechanism of action lowering IOP



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.





43

PL9588 for Treating 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.): 2029
- FDA Approval/Launch (Est.): 2030



Efficient Development Program

- IND 1H 2026
- Phase 1 study data 1H 2026
- Phase 2 study data 2H 2027
- Phase 3 study data 2H 2028

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 Treating 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 1st 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 Treating 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 Treating Retinal Diseases

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 Diseases 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 Formulation 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



PL8177 Oral Formulation for Ulcerative Colitis UC patient treatment paradigm

Opportunity for PL8177 in Treating UC Indication Throughout the Treatment Paradigm



PL8177 Oral Formulation for Ulcerative Colitis 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 Oral Formulation for Ulcerative Colitis PL8177-205 Phase 2 study design & timelines

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





PL8177 Oral Formulation for Ulcerative Colitis Topline data PL8177-205 Phase 2 UC study

- Clinical Remission
 - Achieved in 33% of PL8177 treated subjects versus 0% on placebo after 8-weeks of treatment
- Clinical Response
 - Achieved in 78% of PL8177 treated subjects versus 33% on placebo (p<0.005) after 8-weeks of treatment
- Symptomatic Remission
 - Achieved in 56% of PL8177 treated patients versus 33% of on placebo
- Safety and tolerability was excellent no adverse events
- For the subset of patients with moderate disease (segment endoscopic score of greater than or equal to 1 in the rectum, descending colon, and sigmoid colon segments) at baseline were
 - Three of five (60%) PL8177-treated patients showed improvement in all three segments
 - Four of five (80%) PL8177-treated patients showed improvement in two of the three segments
 - Zero of one (0%) placebo patients showed improvement in two or more segments

PL8177 Oral Formulation for 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
- Positive Phase 2 study in UC patients: PL8177 treated patients had improvement in clinical remission and response

PL8177 Oral Formulation – Novel, Non-Immunosuppressive Mechanism of Action







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



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
- 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 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

- 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 / Cap Table Snapshot Milestones Recap





Financial Snapshot / Cap Table

Financial Highlights as of March 31, 2025

Cash and Cash Equivalents

\$2.5 million*

No debt

*Cash above does not include net proceeds from the ATM facility & equity offering of \$3.5 million in April and May

Summary Capitalization as of May 31, 2025				
	Common Shares and Equivalent			
Common Stock	46.5 million shares			
Warrants	25.6 million shares			
Options	2.3 million shares			
RSUs	1.1 million shares			
Fully Diluted Shares	75.5 million shares			
Total Shares Authorized	300.0 million shares			



Milestones Recap

Melanocortin System Development Programs	Date
Obesity - MC4R Agonists – Weight Loss (Maintenance)	
Phase 2 BMT-801 Clinical Study Bremelanotide + GLP-1 – Positive Topline Data Reported Novel MC4R Selective Long-Lasting Agonist – IND Filing / SAD/MAD Data (to include HO patients) PL7737 MC4R Oral Small Molecule Agonist – IND Filing / SAD/MAD Data (to include HO patients)	Completed 1Q26 / 1H26 1Q26 / 1H26
Spin-Out / Out-License Product Candidates: Seeking Development & Commercial Partnerships (investment bank enga	aged to support process)
PL9643 – Dry Eye Disease (DED)	
Phase 3 Melody-1 Clinical Trial - Positive Results Reported Melody-2 and -3 Phase 3 Pivotal Clinical Trials Initiation Target (FDA Confirmation on Protocols and Endpoints)	Completed 1H26
PL9588 MCR Agonist – Glaucoma	
IND Filing Clinical Program Initiation / Data	1H26 1H26
PL9654 MCR Agonist – Retinal Diseases	
IVT Delivery Activities Advancing	Topical delivery planned
PL8177 Oral – Ulcerative Colitis	
Phase 2 Proof-of-Concept – Positive Topline Data Reported	Completed
MC4R Agonist – Diabetic Nephropathy	
Phase 2 Open Label Trial – Positive Topline Data Reported	Completed





Thank You.



