Beyond GLPs: The Multiple Roles for Novel Melanocortin Receptor 4 Agonists in Treating Obesity and Weight Loss Maintenance

May 8, 2024

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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 expectations on sales and market acceptance for bremelanotide (Vyleesi®) for hypoactive sexual desire disorder (HSDD), a type of female sexual dysfunction (FSD), including our licensees outside North America jurisdictions; (vii) our expectation regarding timelines for development of our other product candidates; (viii) the potential for commercialization of our other product candidates, if approved for commercial use; (ix) our ability and the ability of our licensees to compete with other products and technologies similar to our product candidates; (x) the ability of third party collaborators to timely carry out their duties under their agreements with us and our licensees; (xi) the ability of contract manufactures to perform their manufacturing activities in compliance with applicable regulations; (xii) our ability to recognize the potential value of our licensing arrangements with third parties; (xiii) the potential to achieve revenues from the sale of our product candidates; (xiv) our ability to maintain product liability insurance at a reasonable cost or in sufficient amounts, if at all; (xv) the retention of key management, employees and third-party contractors; (xvi) the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology; (xvii) our compliance with federal and state laws and regulations; (xviii) the timing and costs associated with obtaining regulatory approval for our product candidates; (xix) the impact of legislative or regulatory healthcare reforms in the United States; and (xx) 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 forward-looking statements to reflect events or circumstances that occur after the date of this presentation.

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Agenda

- Introduction
  - Meeting Objective
  - Introduction Dr. Richards
  - Opening remarks
- Dr. Richards Presentation
  - Current treatments
  - Need for new mechanism of action
  - Melanocortin’s in the treatment of obesity
  - Interaction of melanocortin and GLP1
- Palatin Melanocortin program
  - Phase 2 trial bremelanotide + tirzepatide
  - Melanocortin's in weight loss maintenance
- Question & Answer

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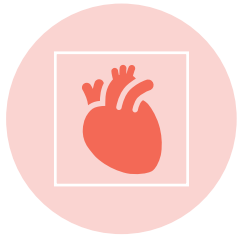
Evolving Obesity Treatment Landscape

~650M people are living with obesity, WHO estimates obesity is responsible for 5% of global deaths

INCRETIN THERAPEUTICS HAVE ESTABLISHED PHARMACOTHERAPY AS THE MAINSTAY FOR TREATING OBESITY

NOVO NORDISK'S LANDMARK SELECT STUDY HAS DEMONSTRATED TREATING OBESITY HAS PROVEN MORTALITY BENEFITS

THE OBESITY THERAPEUTICS MARKET IS ESTIMATED TO EXCEED $50B BY 2030



WEIGHT LOSS MAINTENANCE WILL BE REQUIRED TO REALIZE THE BENEFITS OF TREATING OBESITY

MELANOCORTIN AGONISTS CAN PLAY A N IMPORTANT ROLE IN WEIGHT LOSS AND WEIGHT LOSS MAINTENANCE

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Dr. Richards' Presentation

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Melanocortin Receptor 4 Agonists in Combination with GLP-1 Agonist in Treatment of Obesity

Jesse Richards, DO, FACP, DABOM

Director of Obesity Medicine, University of Oklahoma SCM

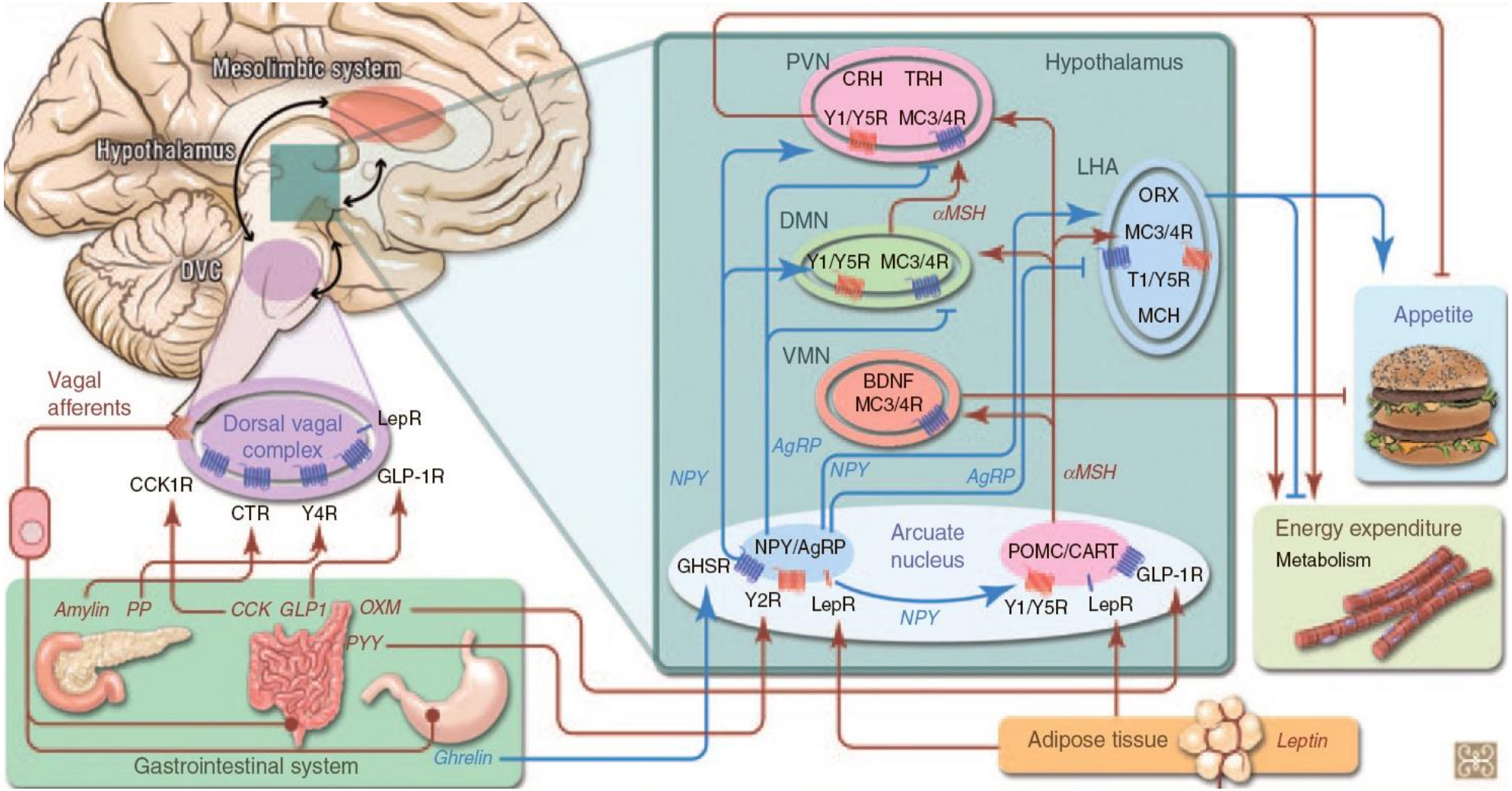
Clinical Background

- Director of Obesity Medicine at Tertiary multidisciplinary center
- Large population of patient with syndromic Bardet-Biedl Syndrome (BBS) and varieties of monogenic obesity, with ~100 patients prescribed imcivree over the past several years for various indications (mostly syndromic, not monogenic)
- Nearly 2-year duration of clinical experience with various combinations of MC4R agonists, GLP1 agonists, and Bariatric surgery for treatment of extreme obesity
- Routinely see patients lose 30-50% TBW on multi year combination therapy, truly life changing results

GLP-1 Agonists

- Powerful bodyweight reduction, limitations as monotherapy
- Dose dependent side effects and concerns for loss of lean mass (38% of weight with semaglutide in clinical trials)
- Main limitation of GI side effects

Gut Brain Pathways for Obesity Treatment



Clin Pharma and Therapeutics, Volume: 95, Issue: 1, Pages: 53-66, First published: 08 October 2013, DOI: (10.1038/clpt.2013.204)

Illustrated by Zina Deretsky

Melanocortin 4 Receptor Agonists

Bremelanotide shown to produce ~400 calorie daily reduction in caloric intake and drive short term weight loss

Setmelanotide: non-selective MC4R agonist

Healthy volunteers in safety trials lost approximately 3% TBW at 12 weeks. In BBS patients (not homozygous MC4R pathway loss of function) average change TBW in adults was 10% at 1 year.

Combination Treatment with GLP1 & MC4R

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

Patient 1 change in BMI

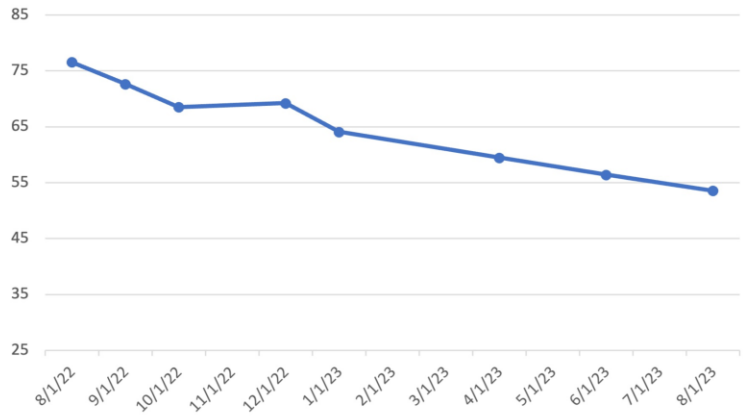


Image 1: Rate of change of BMI in Patient 1 taking combination therapy over a 52-week period.

Patient 2 change in BMI

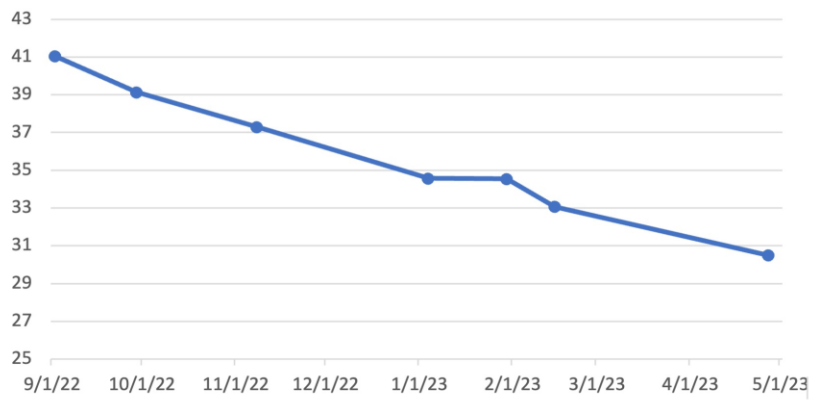


Image 2: Rate of change of BMI in Patient 2 taking combination therapy over a 34-week period.

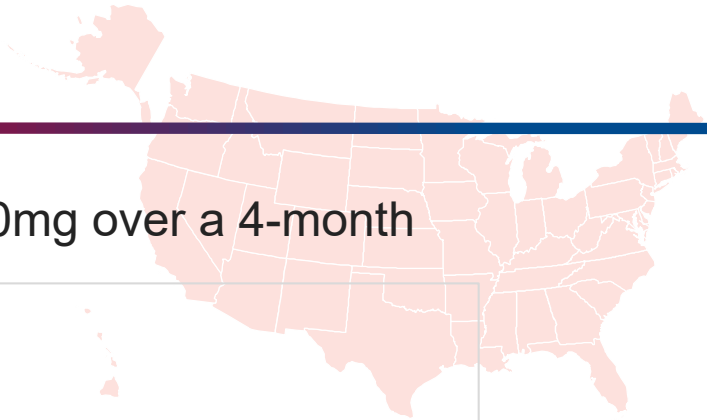
Surmounting GLP1 Rebound

- Follow up data, patient 1 from above stopped tirzepatide, continued setmelanotide without rebound weight gain and had an additional ~5% weight loss on monotherapy.
- This matches the known importance of leptin/MC4R signaling in weight reduced states as previously examined by the NIH*

Adaptations that Occur in the Weight Loss State	
Energy Expenditure	Resting & non-resting energy expenditure decrease Skeletal muscle becomes more efficient
Neuroendocrine	Thyroid hormone and leptin levels decrease
Autonomics	Parasympathetic nervous system signaling increases Sympathetic nervous system signaling decreases
Energy Intake	Food satiation decreases Hunger increases Decreased perception of caloric intake Decreased reward to caloric intake

*_Obesity_ 2021 April; 29(Suppl 1): S9-S24

Case Report GLP1 Nonresponder



- Obese patient (BMI>35) initial treatment lifestyle and Ozempic titrated to 1.0mg over a 4-month period with weight gain of 12 lbs
- Genetics suspicious for BBS and clinical workup diagnosed with BBS
- Treatment was was initiated with setmelanotide and lifestyle counseling, patient lost 102 lbs over next 14 months
- Patient has been able to maintain a stable BMI <30 without significant issues on setmelanotide monotherapy

Current projections are that 8-20 million people in the United States will potentially fail to tolerate or respond to glp1 monotherapy: Alternative mechanisms are highly needed

MCR4 Agonism for Treating Obesity

Significant Expertise in the Design and Development of MCR4 Agonists.

Demonstrated expertise moving programs from discovery to FDA approval

Expertise in the biology and chemistry of melanocortin system (MCS) & natriuretic peptides (NPR)

1st company to gain FDA approval for a melanocortin agent (Vyleesi®)

Strategy leverages our expertise across multiple therapeutic opportunities

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

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The Value of Palatin's MCR4 Assets

Clinically validated treatment for obesity	Differentiated product profile Low clinical risk Defined development pathways Potential for high returns
Bremelanotide	FDA approved product Has extensive efficacy and safety data Evaluated in obesity clinical studies Can rapidly be expanded into additional indications
New mechanisms will be needed for obesity therapy and weight loss maintenance	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 MCR4 agonist MCR4 agonism is additive to GLP1 treatments
Novel improved "Next Gen" MCR4 agonists	MCR4 selective extended duration peptides and orally active small molecule MCR4 agonists Extend IP Improved PK and delivery Address unmet need and chronic administration

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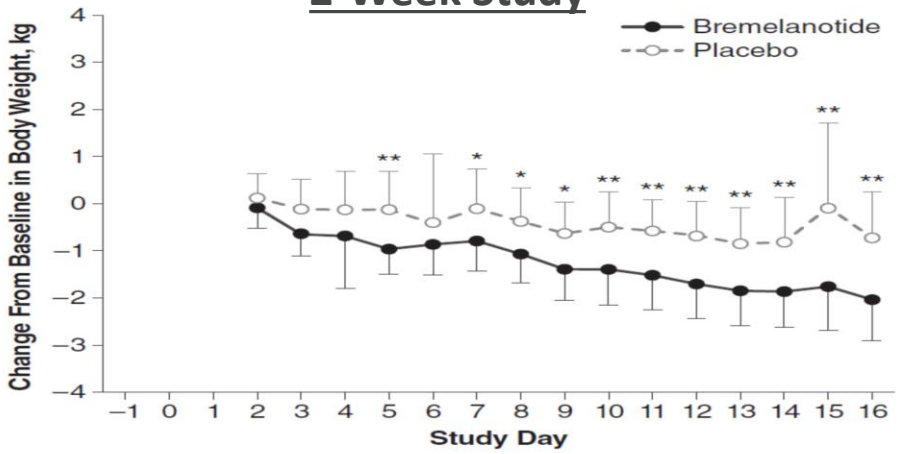
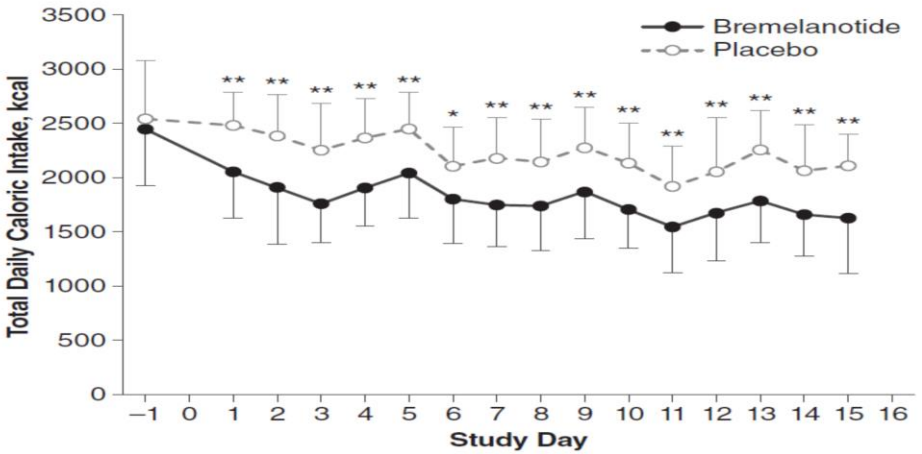
MCR4 Weight Loss Clinical Studies

Bremelanotide Clinical Weight Loss Studies

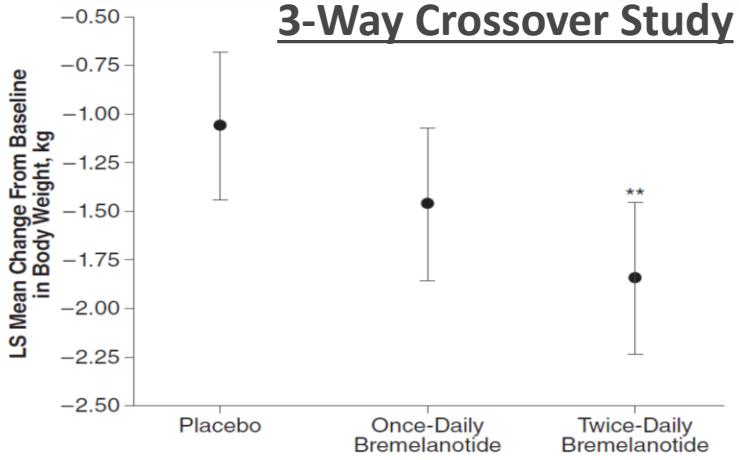
2-Week Study

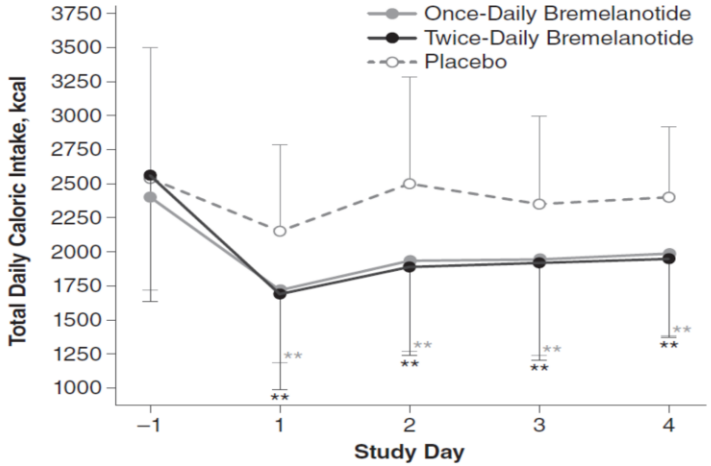




- Weight loss placebo -0.7kg; bremelanotide -2.2kg p<0.001
- Bremelanotide reduction daily caloric intake ~400kcal p<0.01

3-Way Crossover Study





- Weight loss placebo -0.9kg, bremelanotide -1.7kg p<0.001
- Reduction daily caloric intake p<0.001

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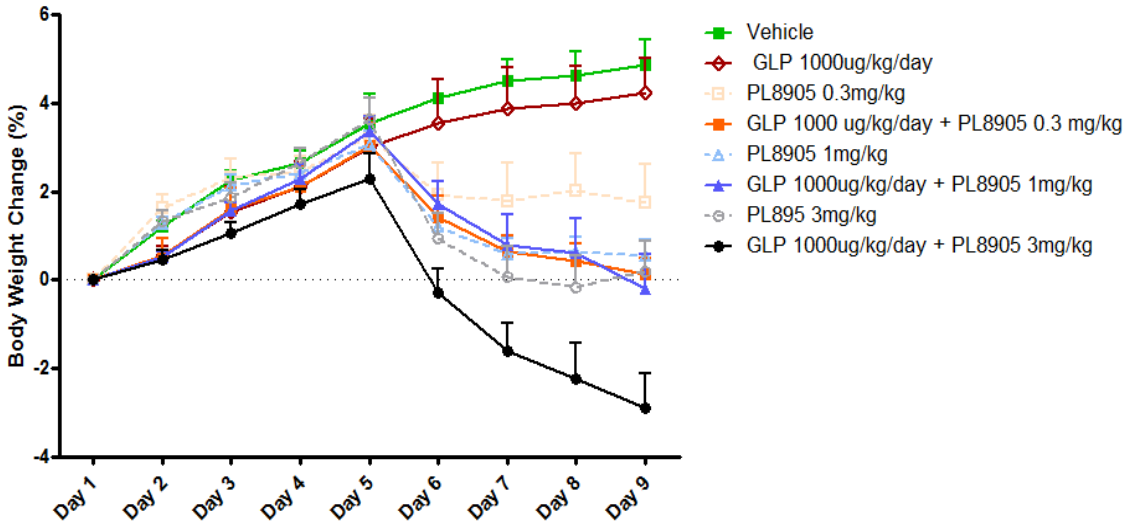
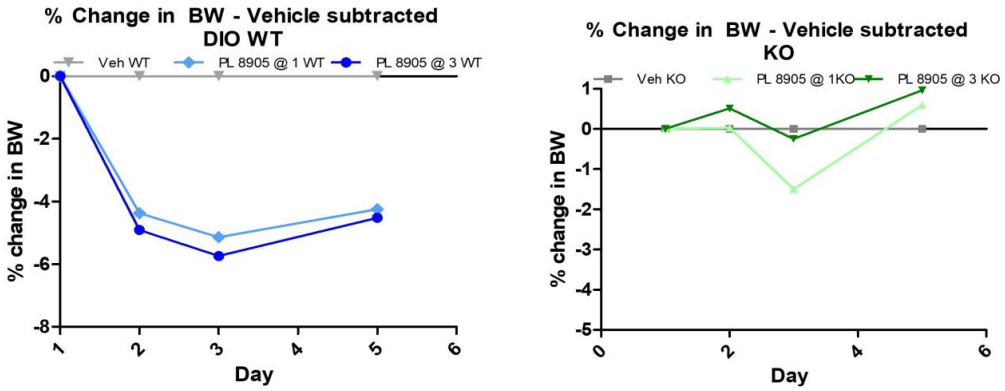
GLP-1 and PL8905: Combination Therapy in DIO Rats

Body Weight Changes



Body weight normalized to baseline (day 1)

Body Weight in Wild Type DIO Mice and MCR4-Knockout Mice



- PL8905 is selective MCR4 peptide agonist
- Body weight and food intake in diet induced obese (DIO) rat model
- GLP-1 dosed by continuous infusion pump and PL8905 by SC injection
- Pump installed at Day 1; Days 1-4 sham dosing; Days 5-9 active dosing

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BMT-801 Phase 2 Co-administration of Bremelanotide & Tirzepatide

Study Objective

- Randomized, double-blind, placebo-controlled trial evaluating the safety and efficacy of the addition of the MCR4 agonist bremelanotide to tirzepatide in obese subjects

Study Week	0	Treatment Period 1	4	Treatment Period 2	8	No Treatment	12
Screening		Tirzepatide 2.5mg (qwk)	n=60	Tirzepatide 2.5mg (qwk)+ Bremelanotide 1.25mg(qd)	n=30		
				Tirzepatide 2.5mg (qwk) +Placebo (qd)	n=10		
				Bremelanotide 1.25mg (qd)+ Placebo (qwk)	n=10		
				Placebo (qwk)+ Placebo (qd)	n=10		

Primary Endpoint

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

Secondary Endpoints (evaluated at week 8)

- Appetite suppression measured by visual analog scale (VAS)
- Appetite suppression subscales (hunger, fullness, satiety, prospective food consumption)
- Lean muscle mass
- Cardiometabolic laboratory values
- Neck and waist measurements

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Review of Weight Loss Maintenance

The other side of obesity treatment

- Excess body weight and fat is associated with negative health conditions including cardiovascular disease, diabetes, fatty liver disease, musculo-skeletal disorders and some cancers
- Current and next “generation” incretin based anti-obesity treatments result in significant weight loss and significantly improved health outcomes
  - Maintenance of the weight loss state is difficult for almost all individuals with most failing to maintain a weight reduced state
- To experience the many health benefits of anti-obesity treatment will require the long-term maintenance of the reduced weight state
- Current research indicates that persistent long-term intervention will be required to maintain a “healthy” weight reduced state

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Concluding Remarks

- Melanocortin agonism is a well validated mechanism and there are multiple roles for a “next generation” melanocortin agonist in treating obesity
- Weight loss maintenance will be key to the long-term success of obesity treatment and melanocortin agonists may be an ideal treatment option
- Palatin is well positioned to advance a melanocortin agonist for weight loss management
  - FDA approved Bremelanotide
  - MCR4 selective extended duration peptide agonists
  - Orally active small molecule MCR4 agonists
- Thank you Dr. Richards

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Question & Answer

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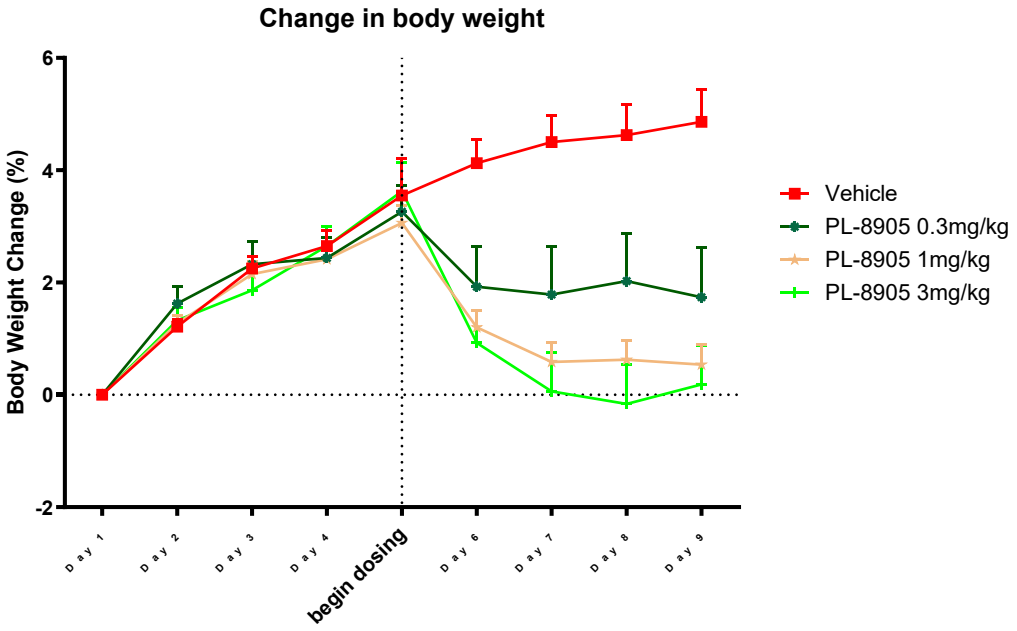
PL8905 *In Vivo* Studies

Weight loss studies: diet induced obese (DIO) & MCR4 KO mice



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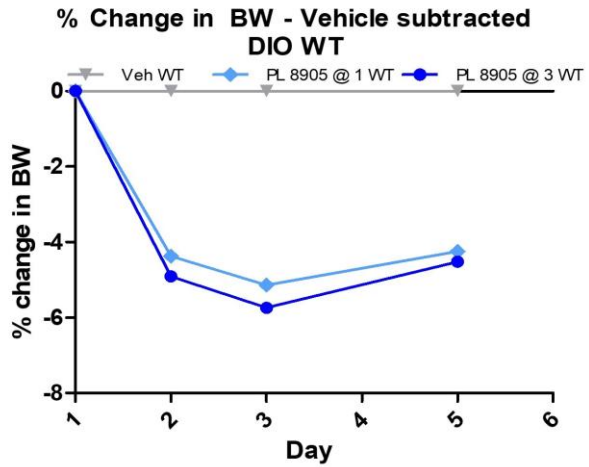

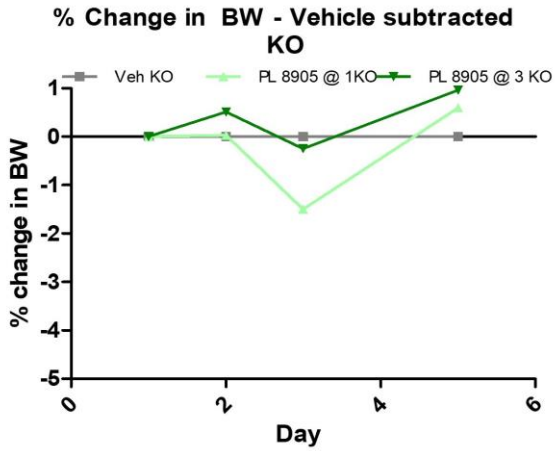

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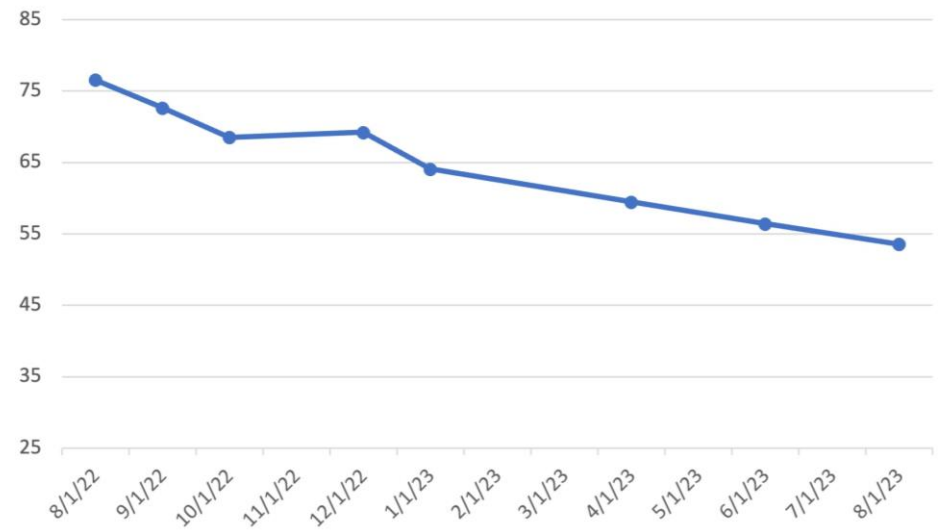
Results

Patient 1 change in BMI



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Patient 2 change in BMI

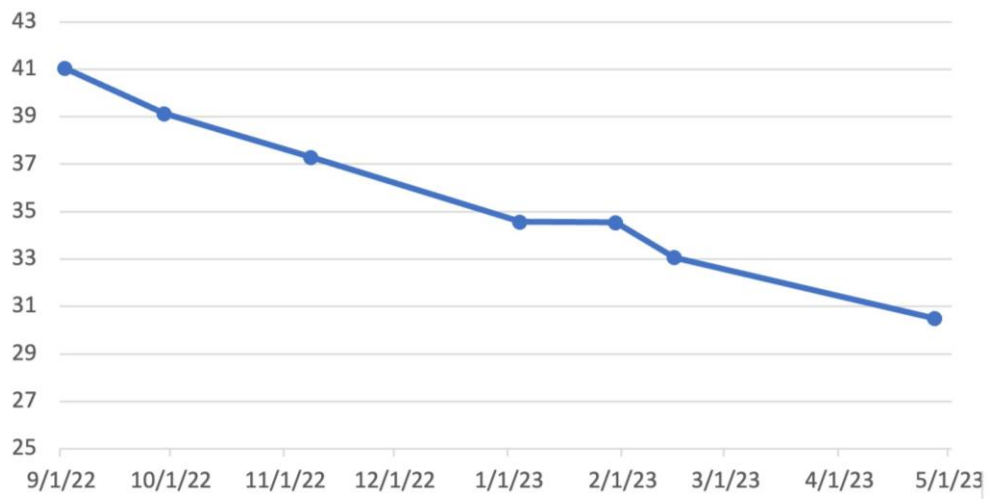

Image 2: Rate of change of BMI in Patient 2 taking combination therapy over a 34-week period.