



Lipocine KOL Event LPCN 2401 for Obesity Management

October 16, 2024

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Agenda

Introduction

Dr. Mahesh Patel
President and CEO
Lipocine

Obesity Treatment Landscape

Dr. Frank Greenway
Professor and Chief Medical Officer
Pennington Biomedical Research Center

LPCN 2401 P2 Results and Next Steps

Dr. Ben Bruno
VP of Clinical Development
Lipocine

Concluding Remarks

Dr. Mahesh Patel
President and CEO
Lipocine








Q and A

All

Forward-Looking Statements

This presentation contains "forward-looking statements" that are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and include statements that are not historical facts regarding our product development efforts, our strategic plans for developing product candidates, our ability to monetize product candidates, including through entering into partnering arrangements, the application of our proprietary platform in developing new treatments, our product candidates and related clinical trials, the achievement of milestones within and completion of clinical trials, the timing and completion of regulatory reviews, outcomes of clinical trials of our product candidates, and the potential uses and benefits of our product candidates. Investors are cautioned that all such forward-looking statements involve risks and uncertainties, including, without limitation, the risks that we may not be successful in developing product candidates, we may not have sufficient capital to complete the development processes for our product candidates, we may not be able to enter into partnerships or other strategic relationships to monetize our assets, the FDA will not approve any of our products, risks related to our products, expected product benefits not being realized, clinical and regulatory expectations and plans not being realized, new regulatory developments and requirements, risks related to the FDA approval process including the receipt of regulatory approvals and our ability to utilize a streamlined approval pathway for LPCN 1154, the results and timing of clinical trials, patient acceptance of Lipocine's products, the manufacturing and commercialization of Lipocine's products, and other risks detailed in Lipocine's filings with the SEC, including, without limitation, its Form 10-K and other reports on Forms 8-K and 10-Q, all of which can be obtained on the SEC website at www.sec.gov. Lipocine assumes no obligation to update or revise publicly any forward-looking statements contained in this presentation, except as required by law.

Lipocine Pipeline and Approved Product

Development Candidate (Indication)	Pre-Clinical	Phase 1	Phase 2	Pivotal	Status
LPCN 1154 <i>Postpartum Depression</i>					Anticipated NDA Filing Q4 2024
LPCN 2401 <i>Obesity Management</i>					Initial P2 study completed
LPCN 2203 <i>Essential Tremor</i>					P1 study completed
LPCN 2101 <i>Women With Epilepsy</i>					IND cleared for P2
LPCN 1107 <i>Prevention of Preterm Birth</i>					EOP2 meeting completed
LPCN 1148 <i>Decompensated Liver Cirrhosis</i>					P2 study completed
LPCN 1144 <i>Non-Cirrhotic NASH</i>					P2 study completed
TLANDO® commercialized in US through Verity Pharma <i>Testosterone Replacement Therapy</i>					

LPCN 2401 Novel Oral Treatment for Obesity and Weight Management

Proven potential to improve body composition - quality weight loss with quality fat loss

Product Candidate Attributes

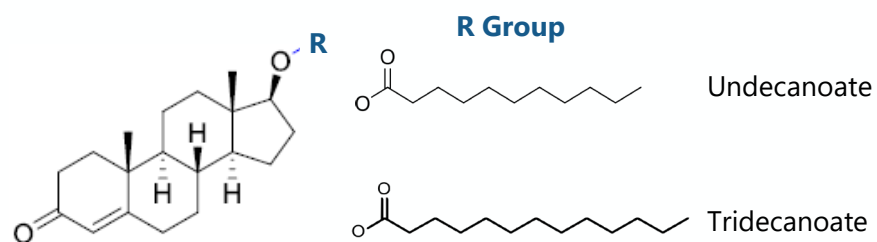
- Proprietary androgen receptor agonist, testosterone ester(s), targeted for once-a-day treatment - “LPCN 2401”
 - Androgen receptor agonist with α -tocopherol for once-a-day treatment – “LPCN 2401+E”

Targeted Mechanism of Actions

	Fat	Muscle	Bone
Androgen Receptor Agonist	<ul style="list-style-type: none">• Induces lipolysis¹• Lowers lipogenesis¹• Inhibits expression of adipocytokines (e.g., leptin, TNF-α, IL-6, IL-1)²	<ul style="list-style-type: none">• Stimulates muscle satellite activator, FGF2³• Modulates muscle growth suppressors MRF4 and myostatin (GDF8) expression in skeletal muscle³	<ul style="list-style-type: none">• Acts directly on osteoblasts and consequently promotes bone formation⁴• Increases AR expression level in osteoblasts^{4,5}

LPCN 2401: Enabling Effective Oral Delivery

Testosterone Esters

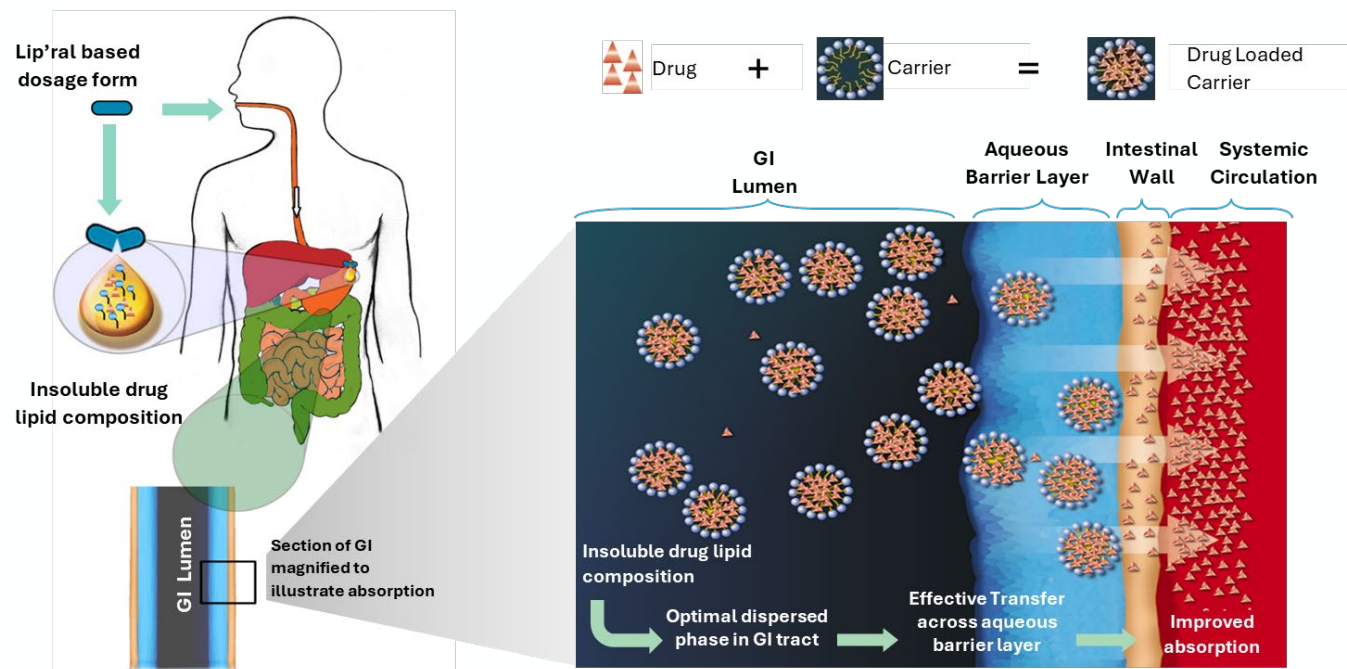


Testosterone Ester

Molecular Weight: 457-484 g/mol

Aqueous Solubility: ≤ 70 ng/ml (calculated)

clog P: ≥ 8.1



Giliyar et al. Drug Delivery Technology, Jan 2006, Vol 6 No.1



Speaker Introduction: Dr. Frank Greenway

- Professor and Chief Medical Officer at Pennington Biomedical Research Center, a globally recognized institution for metabolic health research
- Dr. Greenway's work encompasses a wide array of topics, including the development of pharmaceuticals for obesity
- Academic career spanning more than 30 years, with a focus on clinical trials aimed at developing treatments for obesity and metabolic disorders
- Published over 300 peer-reviewed articles in top-tiered journals; serves as a contributing member within many professional societies
- Actively involved in numerous clinical trials, many of which have led to advancements in obesity treatment
- Awarded the Distinguished Leader Award from the American Board of Obesity Medicine in 2018

Obesity Treatment Landscape

Dr. Frank Greenway, MD

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Obesity Is a Global Public Health Crisis

Obesity is a disease of excess and/or abnormal adipose tissue, not excess mass

- Cardiometabolic risk correlates with adiposity

By 2030, 1 billion people worldwide will be living with obesity, including 50% of American adults¹

- Obesity and its comorbidities including type 2 diabetes, CV disease, and cancer cost the US healthcare system \$175 billion annually²
- In the US, obesity accounts for nearly 20% of all deaths in adults ages 40–85³

Optimized treatment of obesity is a critical unmet medical need

1. www.worldobesity.org/resources/resource-library/world-obesity-atlas-2022; Accessed 17-NOV-2022. 2. CDC. Adult obesity facts. www.cdc.gov/media/releases/2023/p0922-adult-obesity.html#. Accessed May 2024. 3. Goldman D. 2020. <https://healthpolicy.usc.edu/article/obesity-second-to-smoking-as-the-most-preventable-cause-of-us-deaths-needs-new-approaches/#:~:text=Obesity%20is%20second%20only%20to,address%20this%20public%20health%20emergency>. Accessed 15-MAY-2024. 4. Primeau V et al, Int J Obes (Lond). 2011 Jul;35(7):971-81.

Complications of Obesity⁴

Endocrine

- Diabetes mellitus
- Cushing syndrome
- Hypothyroidism
- Subfertility

GI

- Hiatus hernia
- Gallbladder disease
- Inguinal hernia

Carcinoma

- Breast
- Colorectal
- Endometrial

Musculoskeletal

- Osteoarthritis
- Back pain

Cardiovascular

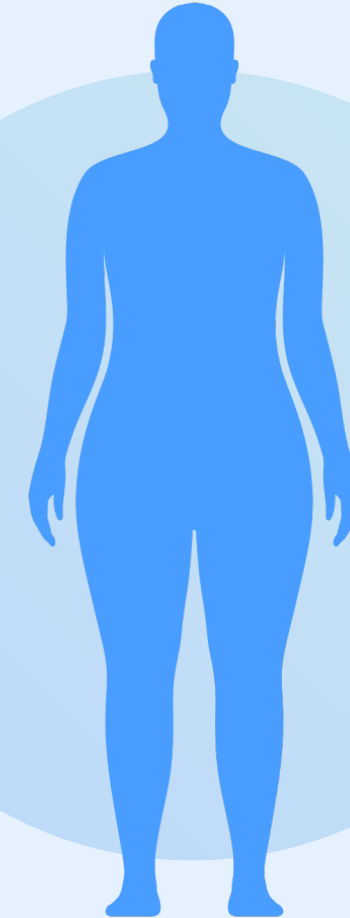
- Sudden death
- Cardiomyopathy
- Hypertension
- Ischemic heart disease
- Peripheral vascular disease
- Deep vein thrombosis
- Pulmonary embolism

Respiratory

- Restrictive lung disease
- Obstructive sleep apnea
- Obesity hypoventilation syndrome
- Difficult intubation

Genitourinary

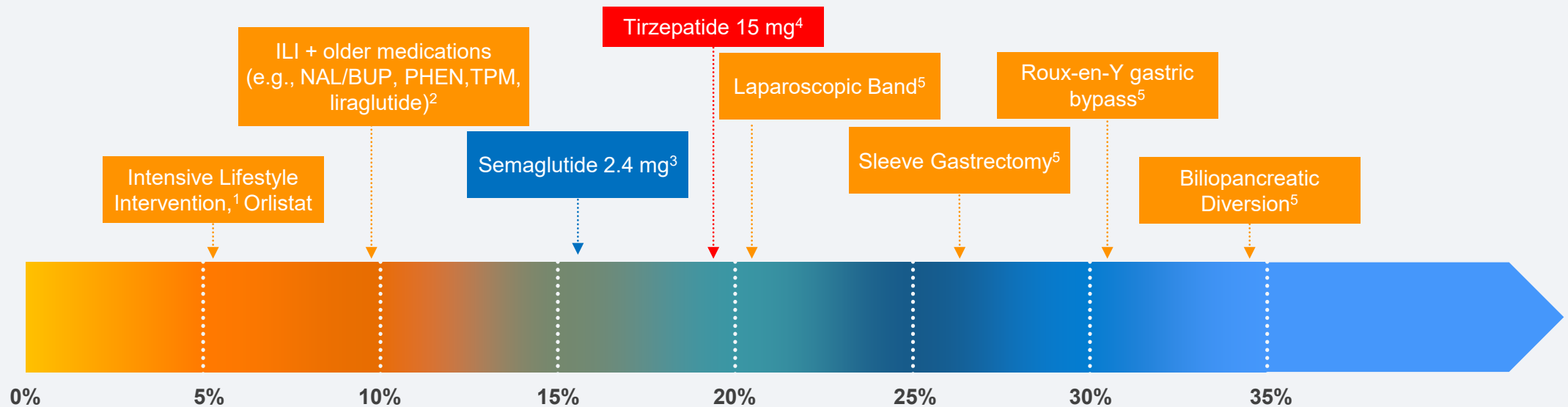
- Menstrual problems
- Female incontinence
- Renal calculi



New Medications Are Transforming the Treatment of Obesity

- Highly potent AOMs and combination therapies (based on gut hormones) are achieving reductions in total body weight previously only possible with bariatric surgery but are limited by heterogeneity, tolerability, and other factors
- Future treatment options with novel mechanisms, including those with synergistic or complimentary actions, will help clinicians optimize personalized regimens based on preference, comorbidities, and treatment response

Total body weight reduction by most common intervention

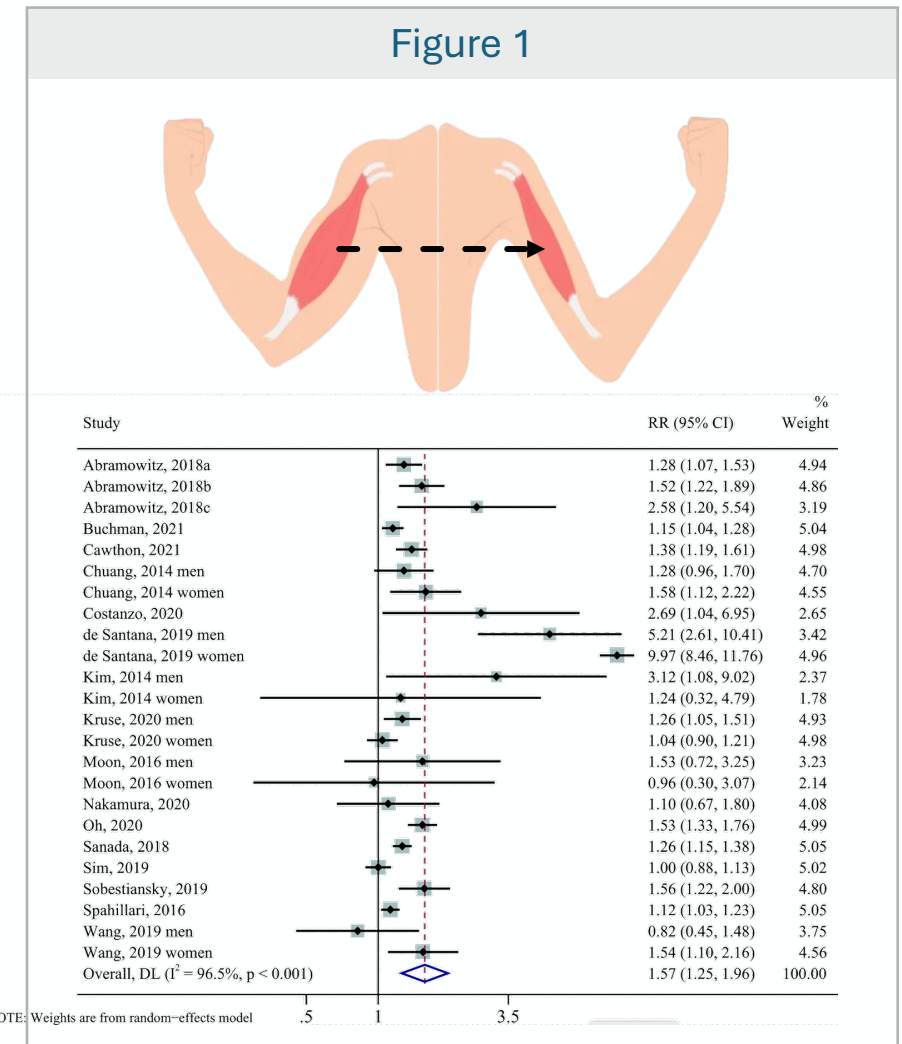


AOM, anti-obesity medications; NAL, Naltrexone; BUP, Bupropione; PHEN, Phentermine; TPM, Topiramate.

1. Look AHEAD Research Group. Obesity. 2014;22(1):5-13. 2. Yanovski SZ., et al., JAMA. 2014;311(1):74-86. 3. Wilding JPH., et al., N Engl J Med. 2021;384(11): 989-1002. 4. Jastreboff AM., et al., N Engl J Med. 2022;387(3):205-16. 5. Sylivris A., et al., Obes Rev. 2022;23(7):e13442. 6. Jastreboff AM., et al., N Engl J Med. 2023;389(6):514-26.

GLP-1 Agonists Have Been Associated With Excess Lean Mass Loss

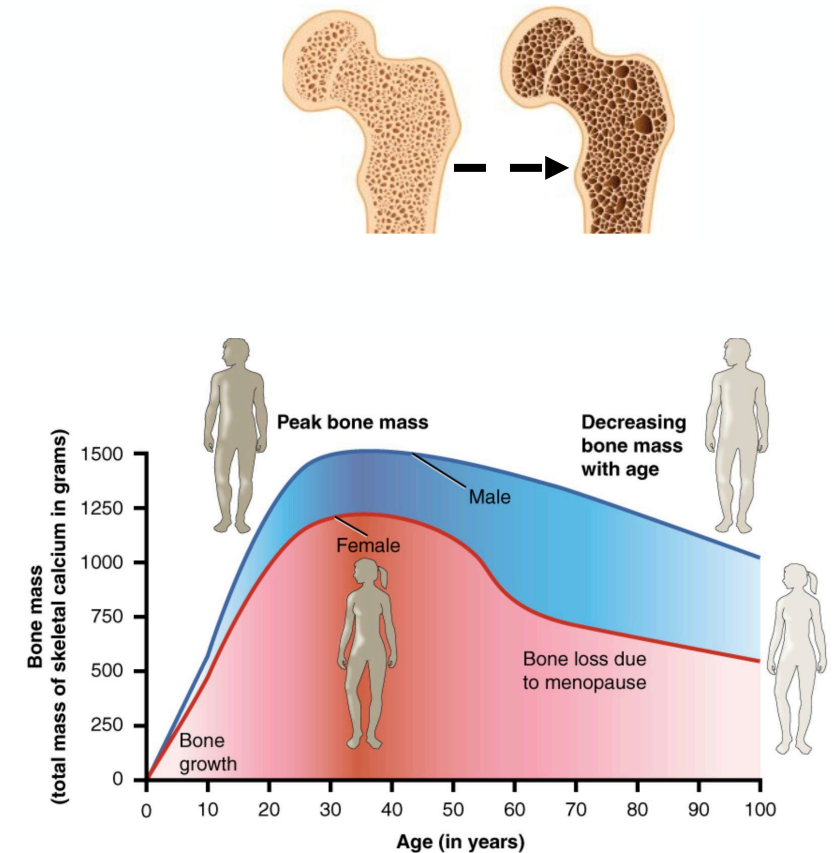
- Up to 40% of total body weight loss realized with GLP-1 agonists is due to lean mass loss^{1,2} Dietary weight loss gives less than 25%.
- With aging, there is an involuntary loss of muscle mass (~3–8% per decade) after age 30^{3,4}
- There are important benefits of retained muscle mass beyond power including improved glucose tolerance, increased bone density, and cognitive function⁵
- In a meta-analysis of 16 studies, low muscle mass index is a major risk factor for all-cause mortality (RR 1.57; 95% CI 1.25–1.96; $p < 0.001$) (Figure 1)⁶
 - In people living with obesity, low muscle volume and low muscle quality (e.g., intramuscular fat) is associated with increased risk for early all-cause mortality, even when controlling for strength and comorbid disease⁷



RR, risk ratio/relative risk; CI, confidence interval.

GLP-1 Agonists Have Been Associated With Accelerated Bone Loss

- Chronic use of GLP-1 agonists has been associated with reduced bone mass in the spine and hips, and decreased tibial cortical thickness relative to placebo². May also increase reoperation for lumbar fusion ¹¹.
- Muscle loss and bone loss often occur together³
 - Stress exerted by skeletal muscle can promote growth and development of bone
 - Bone loss and muscle loss occur naturally with aging
 - Bone loss is accelerated in individuals who develop sarcopenia
- In a CV outcomes trial, fractures of the hip and pelvis were 4–5x more common on Wegovy vs. PBO in females and participants ≥75 years old.⁴
- Complications of low bone density (osteoporosis) is expensive and a major cause of morbidity and mortality⁵
- Myostatin is a known promoter of osteoclast differentiation and inhibitor of osteoblast differentiation contributing to bone loss^{6,7}
 - Inhibition of myostatin can accelerate bone regeneration⁸
 - Activin A signaling can adversely affect osteoblast gene expression and reduce bone mineralization^{9,10}

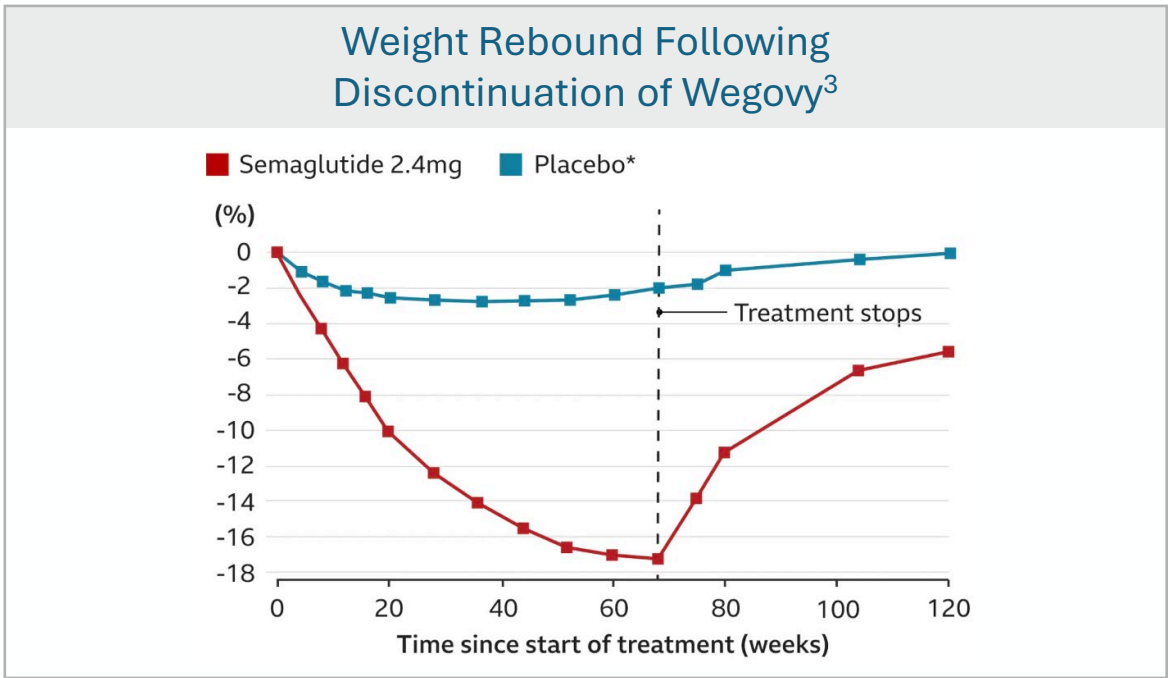


Discontinuation of GLP-1 Agonists Is Associated With Rapid Weight Regain, Often in the Form of Visceral Fat

- Approximately two-thirds of Americans stop GLP-1 therapy within 1 year of initiation¹
 - GI-related side effects are the most common reasons for discontinuation²
- Approximately two-thirds of lost body weight returns within one year of stopping GLP-1 therapy³
 - After stopping GLP-1 therapy, weight returns in the form of central obesity and visceral adiposity¹

Most common GI-related Reasons for Discontinuation of GLP-1 Therapy ²	
Reason	Rate
Made me feel sick	64.4%
Made me throw up	45.4%
Caused diarrhea/gas/bloating	26.3%

GLP-1 agonists slow GI tract motility, double the risk of GI tract rupture and can cause gastroparesis but rare



1. Scientific American. What happens when you quit Ozempic. APR 2024. <https://www.scientificamerican.com/article/you-quit-ozempic-or-wegovy-what-happens-next/#:~:text=About%20two%2Dthirds%20of%20those,according%20to%20an%20industry%20analysis>. Accessed 15-MAY-2024. 2. Sikirica MV. Et al., Diabetes Metab Syndr Obes. 2017;10:403-12. 3. Wilding, et. al., Diabetes Obes Metab. 2022; 24(8):1553-64. doi: 10.1111/dom.14725.

BMI and Total Body Weight Are Insufficient for Determining Obesity-Related Health Risk or Treatment Response

- Obesity is a disease of excess and abnormal adipose tissue, not excess mass
- In 2023, the AMA adopted a policy discouraging the use of BMI alone in the diagnosis of obesity¹
 - Body Mass Index (BMI) is not a measure of body fat. Body Roundness Index (BRI) may be better.
- Incorporating more sensitive measures of body composition including anthropometric measures of central obesity, imaging, and bioimpedance can provide important information about an individual's risk for cardiometabolic disease^{2,3}
 - DEXA measures fat free mass which is only ~50% muscle. Imaging is needed to measure skeletal muscle mass.

Limitations of Current Monitoring Techniques for Obesity⁴



Current practices to measure weight loss outcomes focus on weight/BMI which has limited value



BMI is a poor surrogate for body fat, body composition, fat distribution (visceral fat), and risk stratification as it cannot distinguish lean muscle mass from adipose tissue

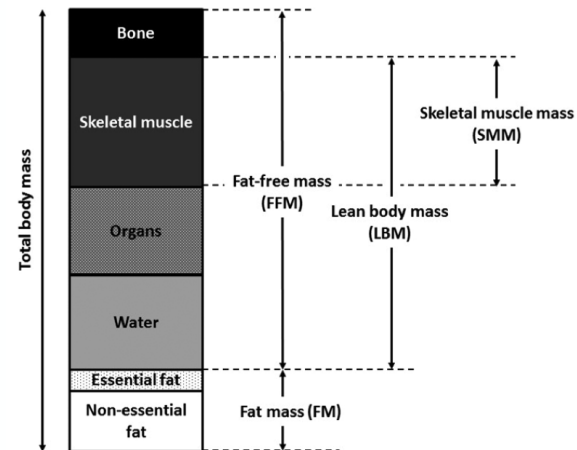


It is more important than ever to know where weight loss is coming from so you don't leave someone worse off than when they started!



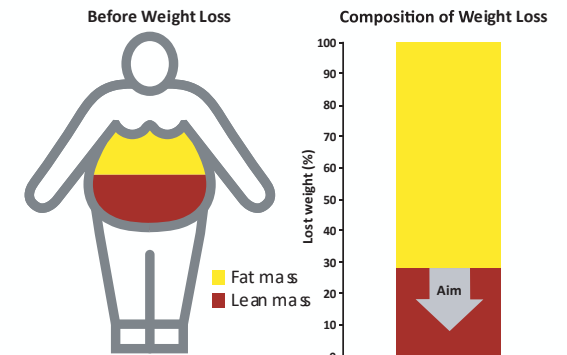
Losing too much lean mass has serious health consequences (sarcopenia, frailty, psychological/emotional and neurological effects, and weight gain)

Limitations of DEXA Scans in Determining Body Composition Changes



Change in TBW is a Combination of FM + LM

GOAL: Loss of excess abnormal fat mass and preservation of lean mass



Christoffersen BØ, et al. Obesity (Silver Spring). 2022 Apr;30(4):841-857.

BMI, body mass index.

1. AMA. AMA adopts new policy clarifying role of BMI as a measure in medicine. 14-JUN-2023. <https://www.ama-assn.org/press-center/press-releases/ama-adopts-new-policy-clarifying-role-bmi-measure-medicine#:~:text=Under%20the%20newly%20adopted%20policy,circumference%20and%20genetic/metabolic%20factors>. Accessed 16-MAY-2024. 2. Browning LM et al, Nutr Res Rev 2010;23(2):247-69. 3. Roriz AP et al, Nutr clin diet hosp 2016;36(2):168-79. 4. Willoughby D. et. al., Nutrients. 2018;10(12):1876.

Obesity Is Overfat – Just Weight is Inaccurate

BMI

Body Mass Index

Correlation
Coefficient
0.60 to 0.70

Simple Measure

BRI

Body Roundness Index

Correlation
Coefficient
0.80

App-derived

BIA

Bioelectrical Impedance Analysis

Correlation
Coefficient
0.78 to 0.93

Office suited

DXA

Dual X-ray Absorptiometry

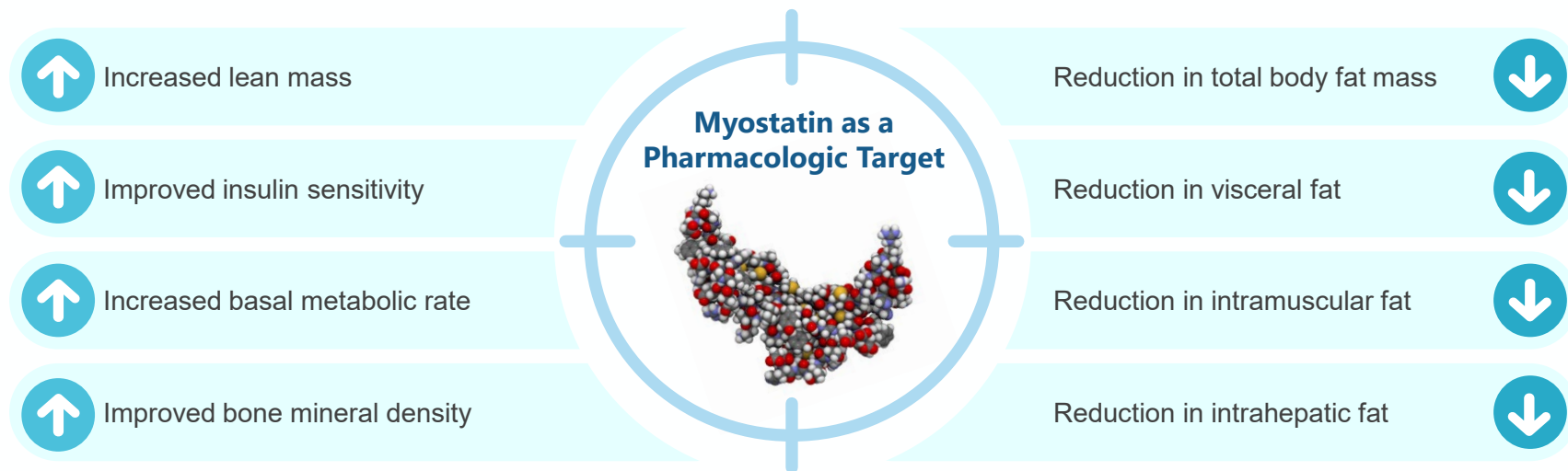
Gold
Standard

Too expensive For
routine Clinical use

There Is Still More that can be Done to Improve the Quality of Care for People Living with Obesity

- Blocking myostatin and other key TGF-beta ligands, including activin A, can produce metabolic and body composition changes relevant to people with obesity^{1,2,3}
- Myostatin inhibition increases muscle size but does not increase muscle strength. Frailty and sarcopenic obesity need muscle strength.
- May potentially be used alone or in combination with gut hormone-based treatments in the future

Anti-myostatin-Induced Physical and Metabolic Changes Important to People living with Obesity



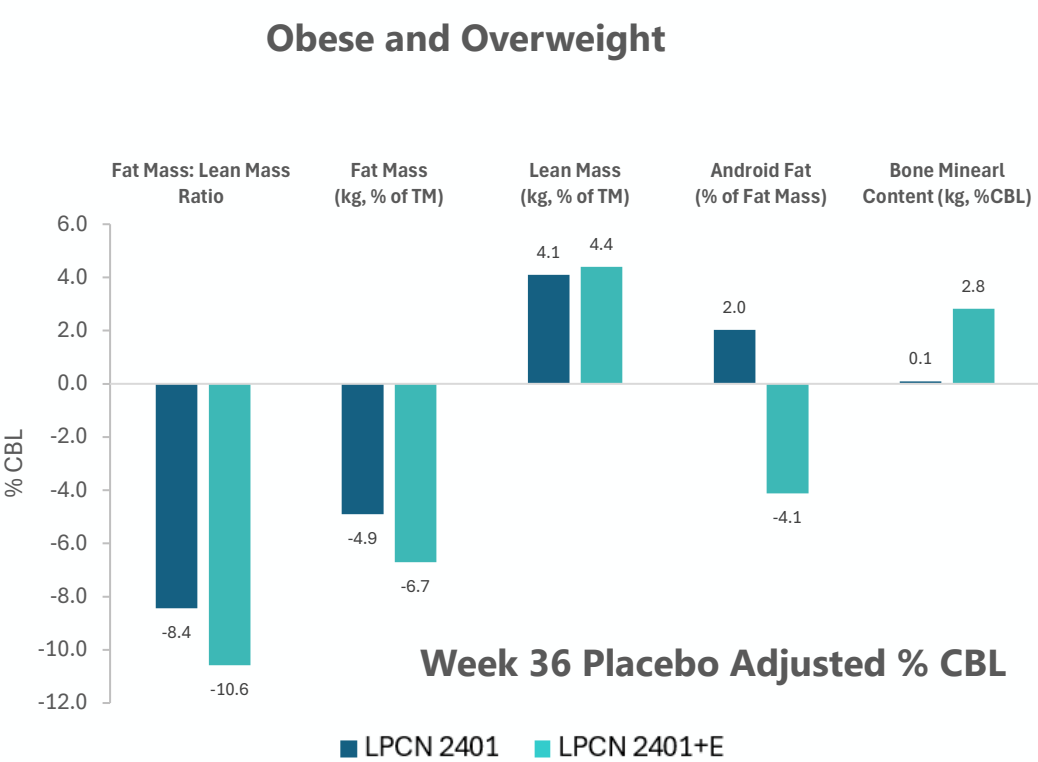
Comparative Efficacy Outcomes in Adults Living with Overweight and Obesity

Drug	Dosing	Δ Total body weight	Δ Total fat mass	Δ Lean body mass	Δ A1C
Bimagrumab n=37	IV Q4W	-6.5%	-20.5%	+3.6%	-0.76%
Semaglutide 2.4 n=1,306	SC QW	-14.9%	-19.3%	-9.7%	-1.6%

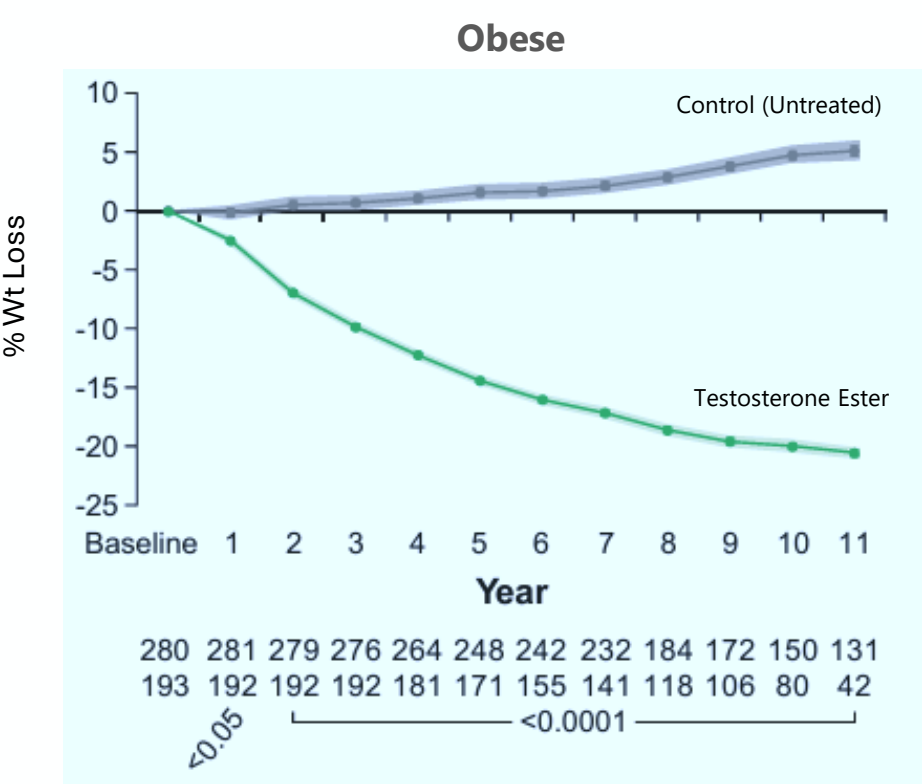
Heymsfield SB, et. al. JAMA. 2021;384(11):989-1002; Wilding JPH, et. al. STEP 1 Body Composition. J Endocr Soc. 2021;5(1):A16-17; Wegovy USPI (STEP2); NA, not available; PO, oral; QW, once weekly; Q4W, once monthly.

1. Heymsfield SB, et al. JAMA Netw Open 2021;4(1):e2033457.
2. Ackerman P, et al. Presented at ObesityWeek 2023. Oct 14-17, 2023; Dallas, TX. Poster 211. 3. Jan J., et al., Nutrients. 2021;13(5):1508. 4. Latres, E. et al, Nat Comm 8, 15153 (2017).

Impact of Testosterone Ester on Body Composition and Weight



Source: Lipocine Corporate Presentation 2024



Saad et al. Int J Obes. 2020; 44:1264-1278

20% Weight loss over 11 yrs compared to lean, Reduction in, BP, lipids, HbA1c, metabolic syndrome and 72% reduction in mortality 85% in MACE over 11 years

Summary

Obesity is excess and abnormal adipose tissue, not just excess weight

GLP-1-associated incretins have demonstrated the ability to reduce total body weight at levels commensurate with bariatric surgery

- ◆ GLP-1 agonists are associated with excess lean mass loss, loss of bone density, and rapid weight regain with dosing interruption compromising long term health
- ◆ We need methodologies in the clinic for accurately measuring body fat loss instead of depending on weight loss
- ◆ Agents that reduce body fat and improve metabolic health, while mitigating against muscle loss, increase muscle strength and decrease bone loss would be ideal

LPCN 2401

P2 Results & Next Steps

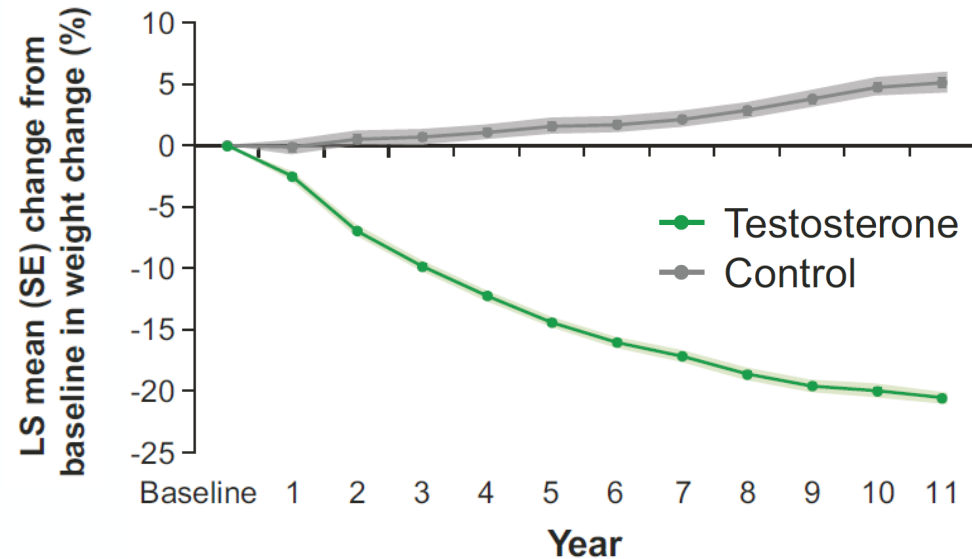
Dr. Ben Bruno
VP of Clinical Development

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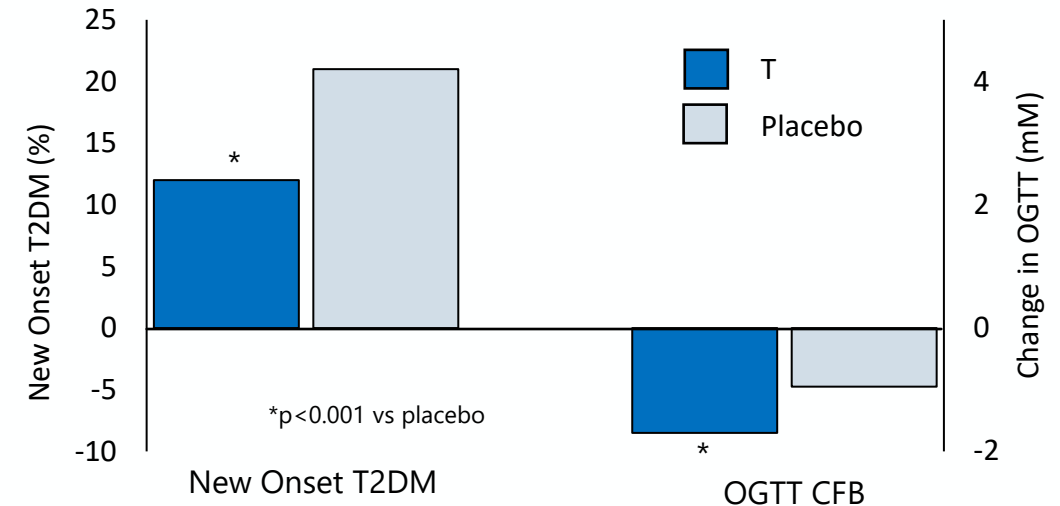
Testosterone Therapy Reduces Weight, Improves Glycemia

T therapy led to continued weight loss over 11-years in obese men with lower T (N=474) ¹



- Weight loss did not plateau, even after 11 years
- Included men with low-normal testosterone (<350 ng/dL)
 - ~50% were diabetic
- Improvement in other cardiometabolic markers including HbA1c, blood pressure, cholesterol
- Significantly fewer deaths and MACE events with T therapy
- Prospective observational study

T therapy prevented or reversed newly diagnosed T2DM in men without hypogonadism (N=1007) ²

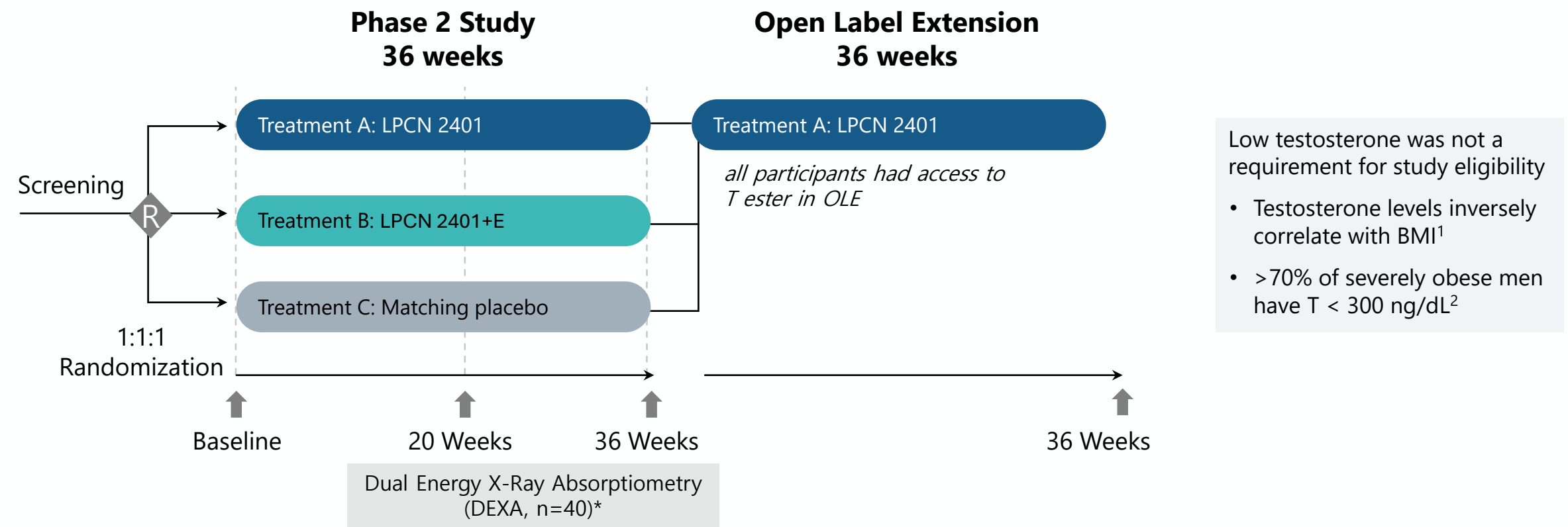


- Included men with low-normal testosterone (average was ~400 ng/dL)
 - Improvements were independent of baseline T level
- Consistent with T therapy class label
 - "In diabetic patients ... androgens may decrease blood glucose"
- Increased bone mineral density to similar extent as antiresorptive drugs³

Phase 2 Study in Patients with Obesity and Overweight

NCT04134091 study design

Three-arm, blinded, placebo-controlled trial in male subjects with metabolic dysfunction associated steatohepatitis (n=56)



Low testosterone was not a requirement for study eligibility

- Testosterone levels inversely correlate with BMI¹
- >70% of severely obese men have T < 300 ng/dL²

* Prespecified endpoints: change in lean mass and fat mass

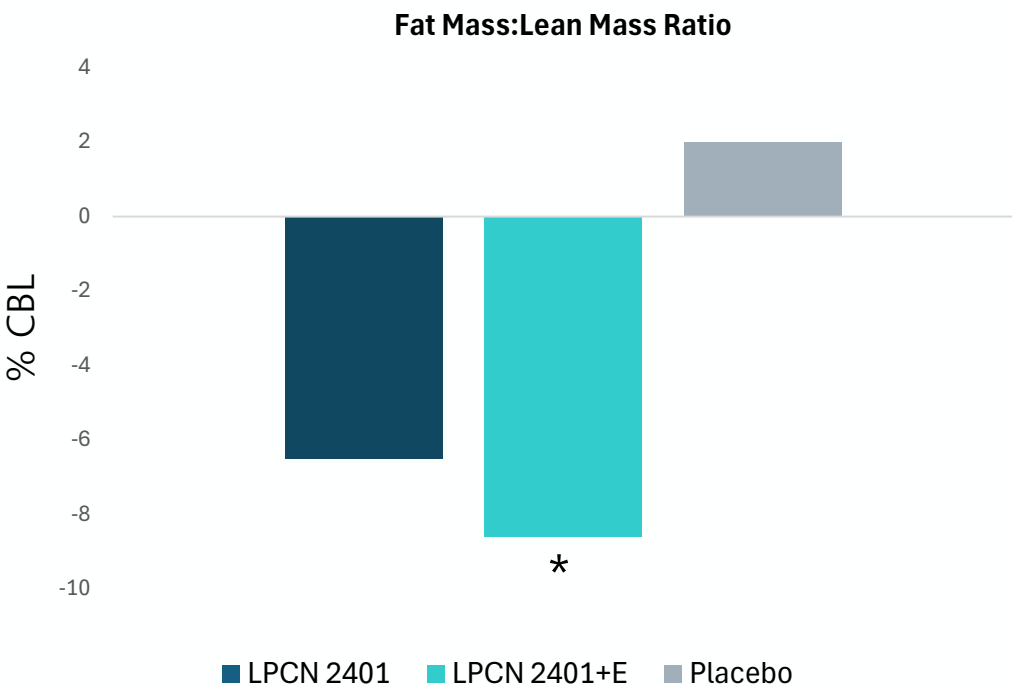
LPCN 2401 - Improvement in Body Composition

Prespecified endpoints met – increased lean mass and decreased fat mass

Body Composition Analysis Set¹

Parameter at Baseline	LPCN 2401 (N=13)	LPCN 2401+E (N=13)	Placebo (N=14)
Mean Age (years)	53.2	53.8	51.1
Mean Weight (kg)	111.3	107.8	118.6
Mean BMI (kg/m ²)	35.9	34.7	37.2
Fat Mass (DXA) % of total mass	39.5	37.2	39.3
Lean Mass (DXA) % of total mass	60.5	62.8	60.7
Fat Mass:Lean Mass Ratio	0.67	0.60	0.66
Android Fat Mass (DXA) % of FM	11.5	11.9	11.2
BMC (DXA), kg	3.1	3.1	3.0

Body Composition Results



All participants met criteria for a weight loss therapeutic*

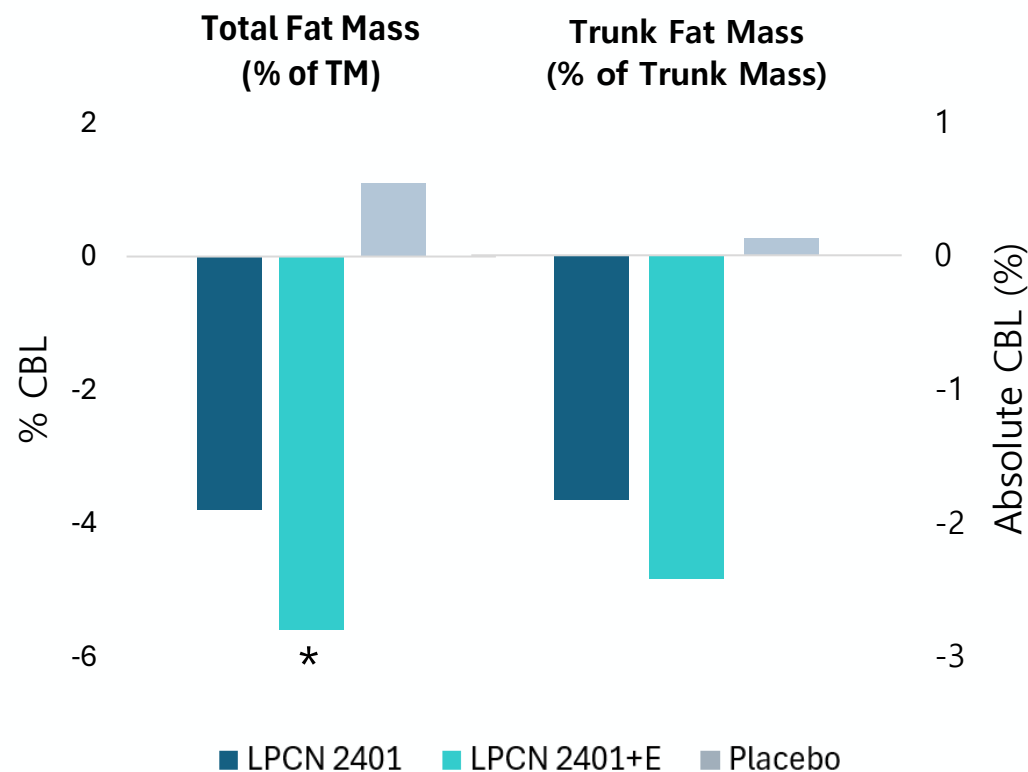
*Population was consistent with FDA’s guidance on developing products for weight management. All Participants had either BMI ≥ 30 (n=36) or BMI ≥ 27 with at least one weight-related comorbid condition (n=4).

1. Patient who completed baseline and at least one post-baseline DEXA. *p<0.05 vs placebo. Body composition analysis set; N=40.

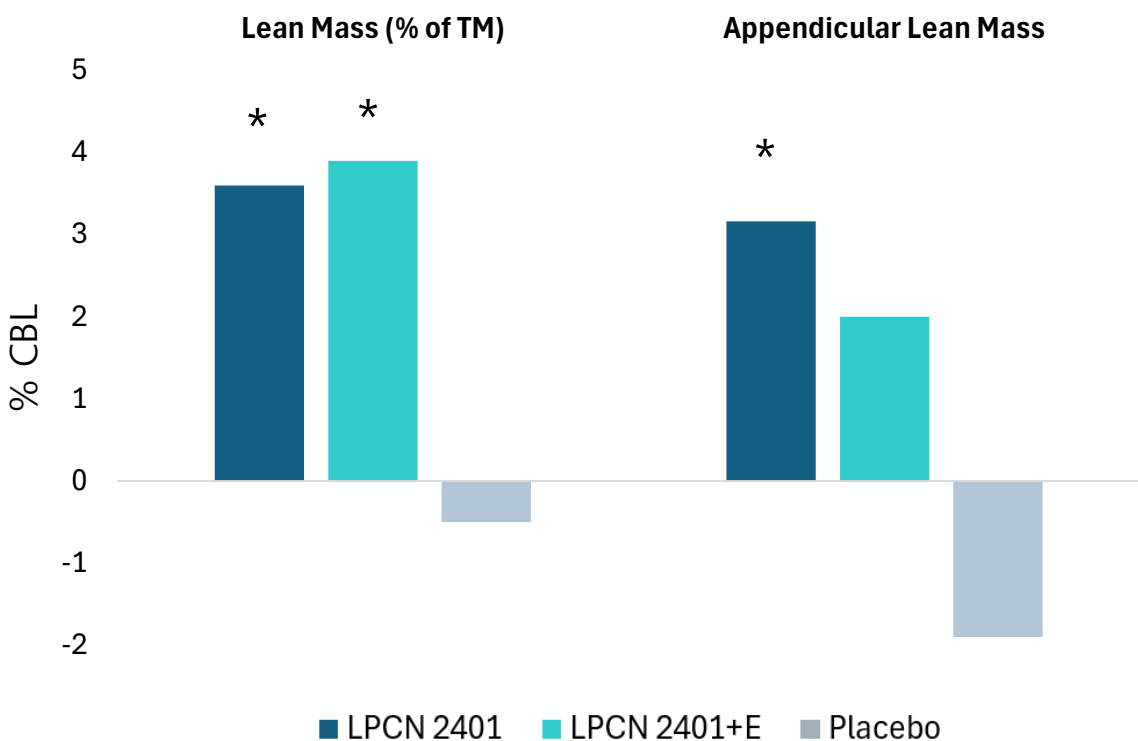
LPCN 2401 - Improvement in Body Composition

Prespecified endpoints met – increased lean mass and decreased fat mass

Fat Mass



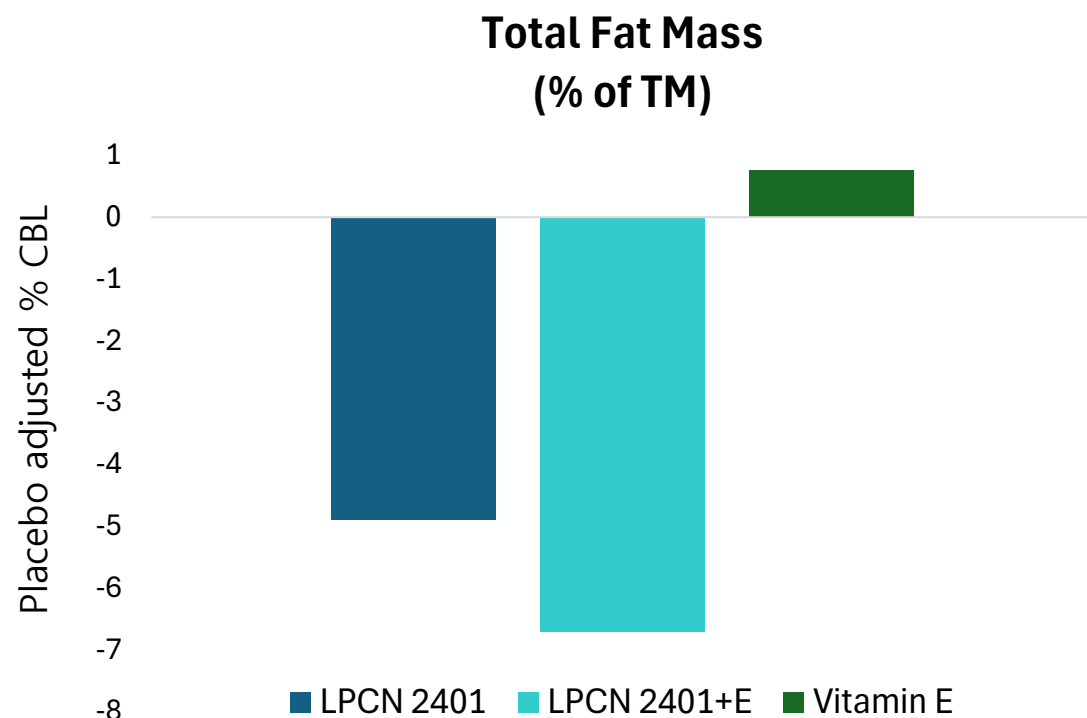
Lean Mass



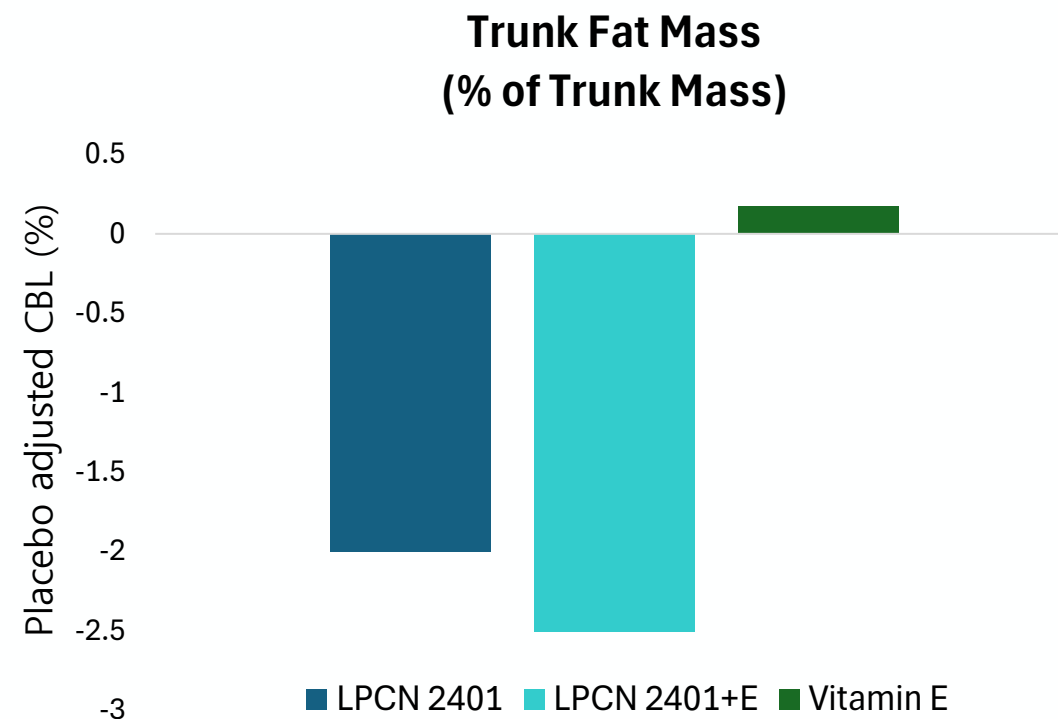
Impact of LPCN 2401, LPCN2401+Vitamin E, and Vitamin E on Fat mass

Fat loss amplification of ARA in conjunction with Vitamin E

Whole Body Fat

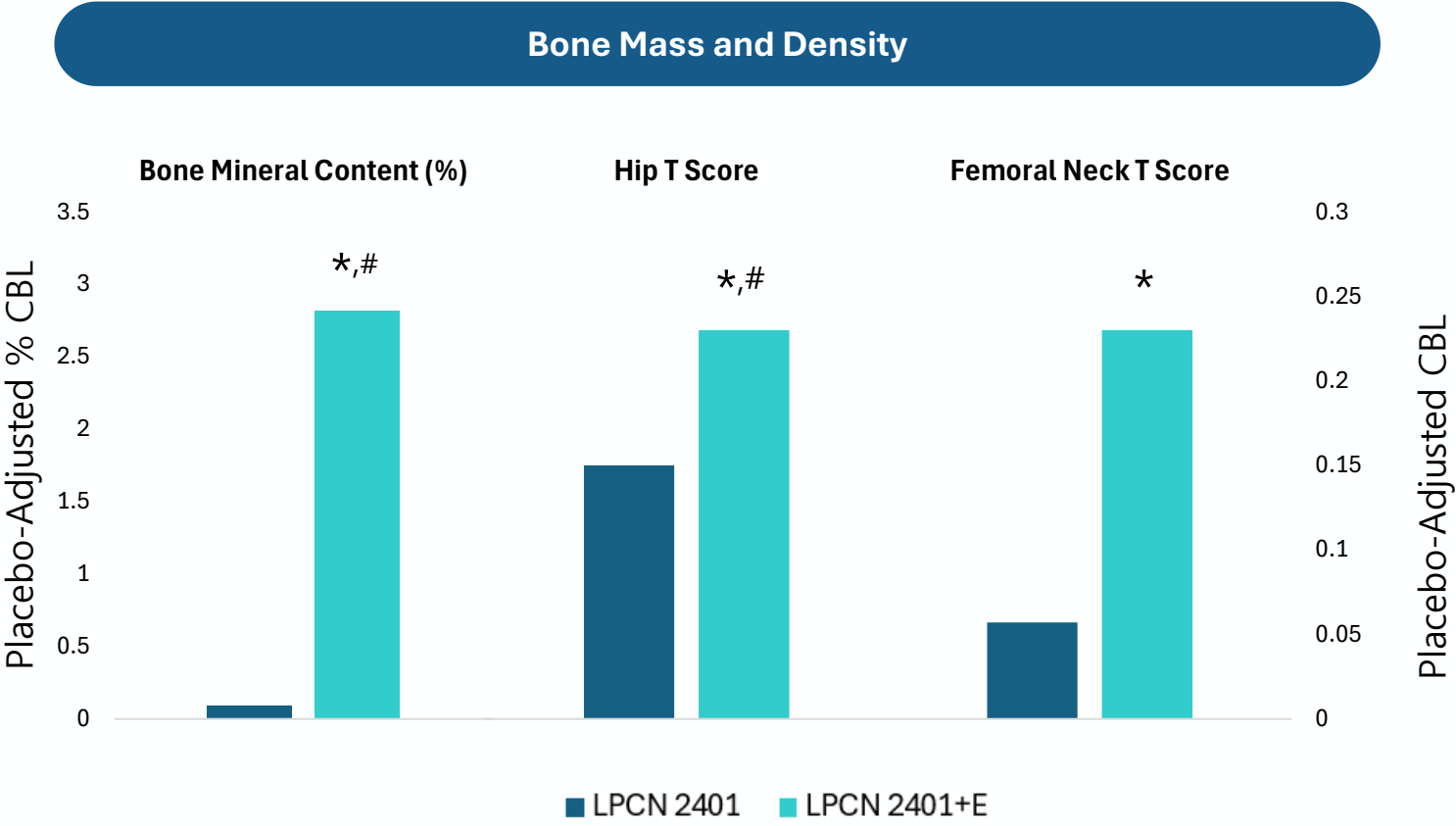


Trunk Fat



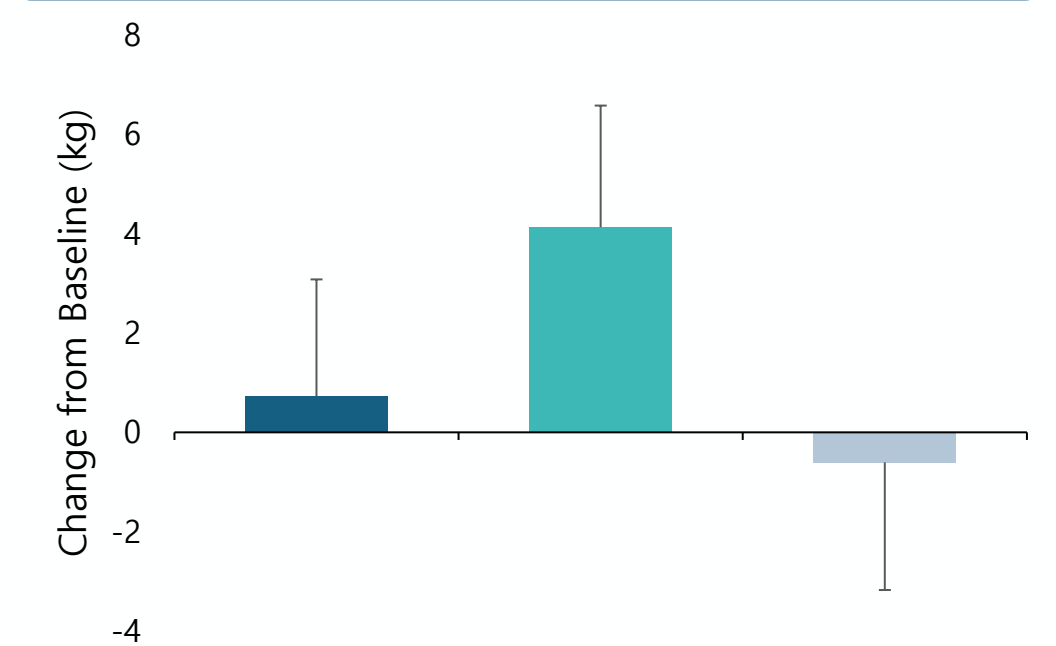
LPCN 2401 - Improvement in Body Composition

Improvement in bone mass and bone density compared to placebo



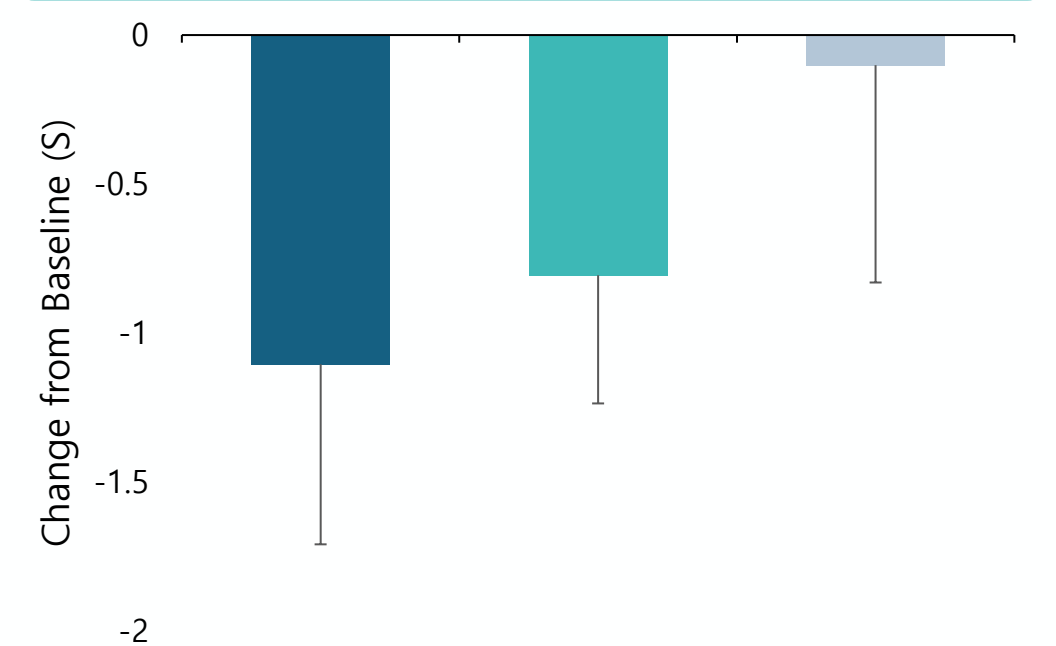
LPCN 2401 - Changes in Functional Tests

Hand Grip Strength



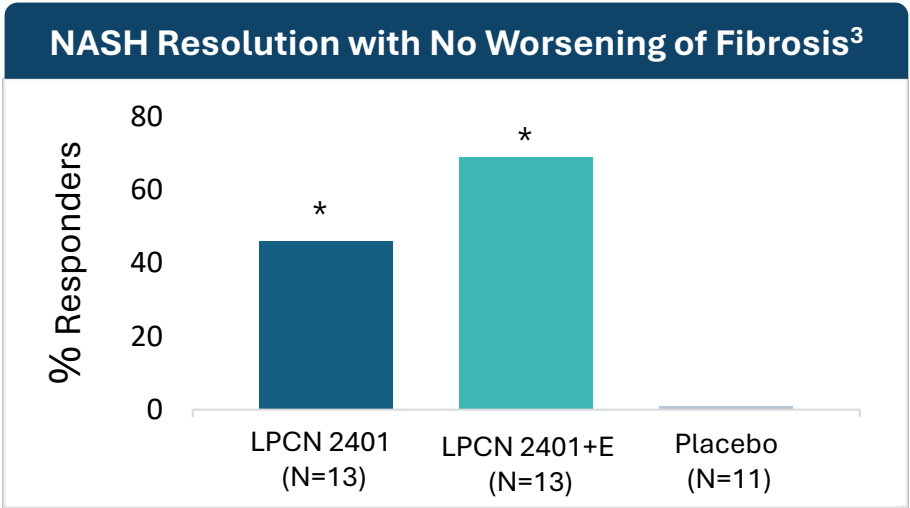
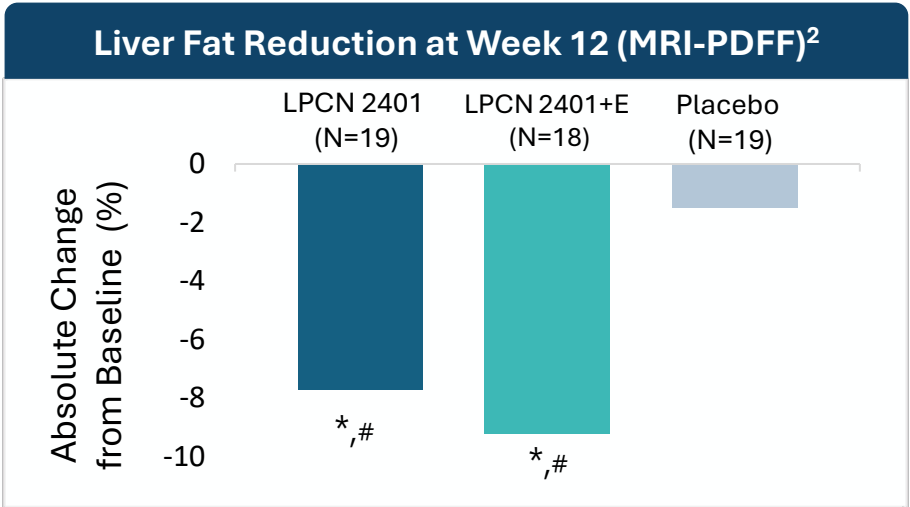
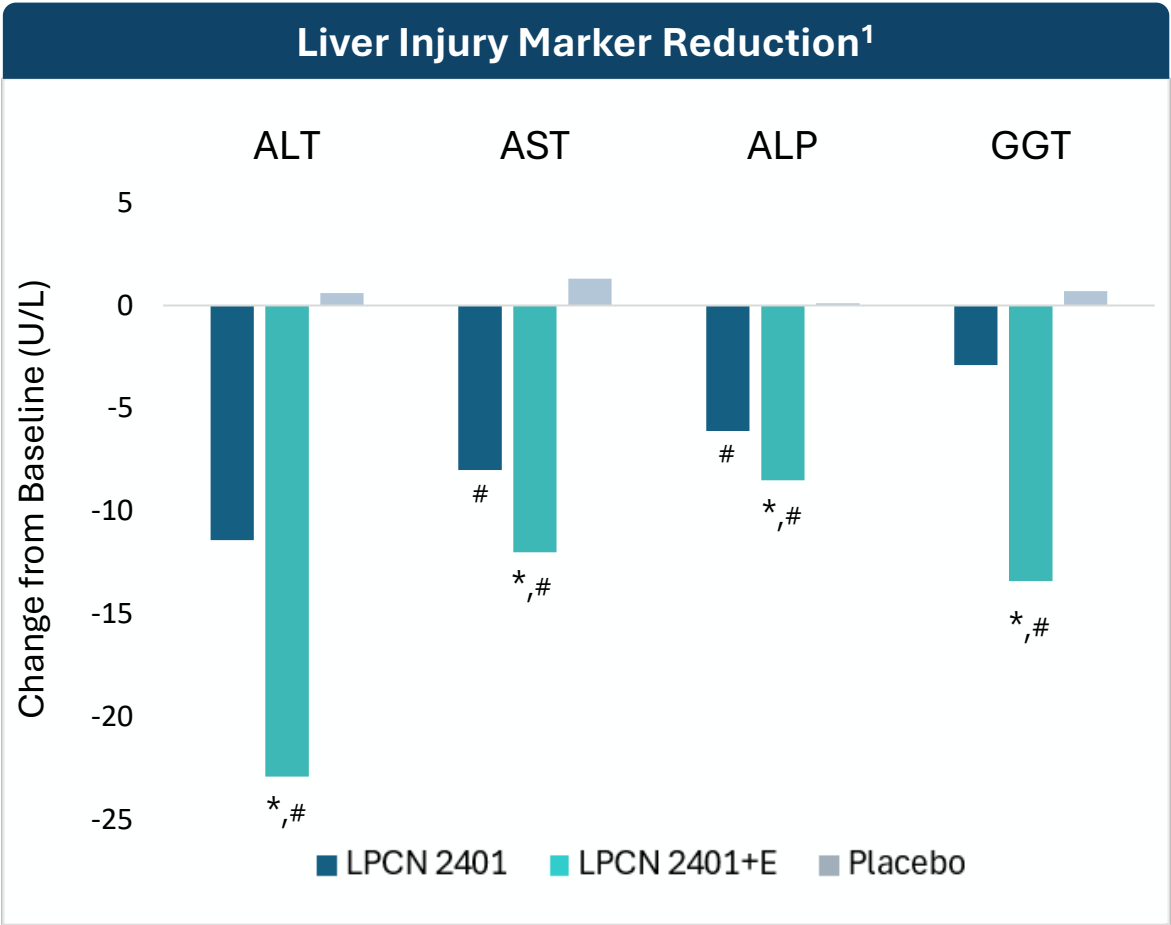
Baseline	Grip Strength (kg)	Walk Time (s)
LPCN 2401	84.4	10.33
LPCN 2401+ E	88.5	8.67
Placebo	82.1	8.60

Ten Meter Walk Time



■ LPCN 2401 ■ LPCN 2401+E ■ Placebo

LPCN 2401 Improved Liver Health



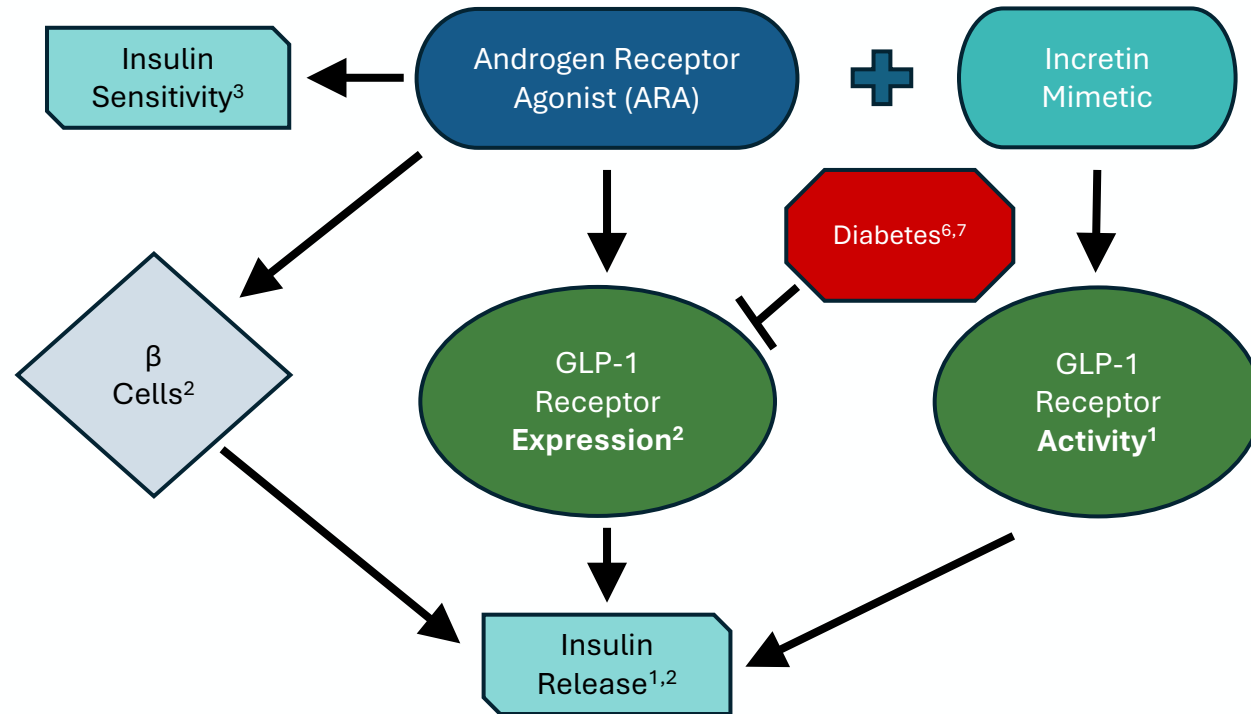
LPCN 2401 - Differentiated Obesity Management Option

Well-tolerated with no safety signals upon 36-week exposure

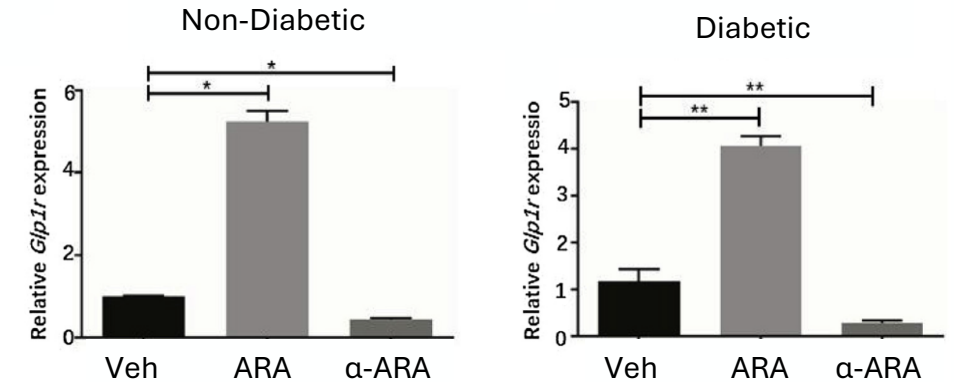
- POC study in relevant obese and overweight population
- Frequency and severity of TEAEs, SAEs with LPCN 2401 were comparable to placebo
 - 4 subjects discontinued placebo due to TEAE vs. 1 subject total in combined T ester treatment arms
- GI adverse events (diarrhea, nausea, vomiting) rates and severities similar to placebo
- Androgenic adverse events (edema, BPH, PSA increase, hypertension) similar to placebo
 - No concerning BP signals (declines in SBP, DBP with LPCN 2401+E)
- No muscle spasms
- Well-tolerated with up to 72 weeks of exposure in open-label extension study (LPCN 2401)

LPCN 2401: Potential to Amplify Effects of Incretin Mimetics

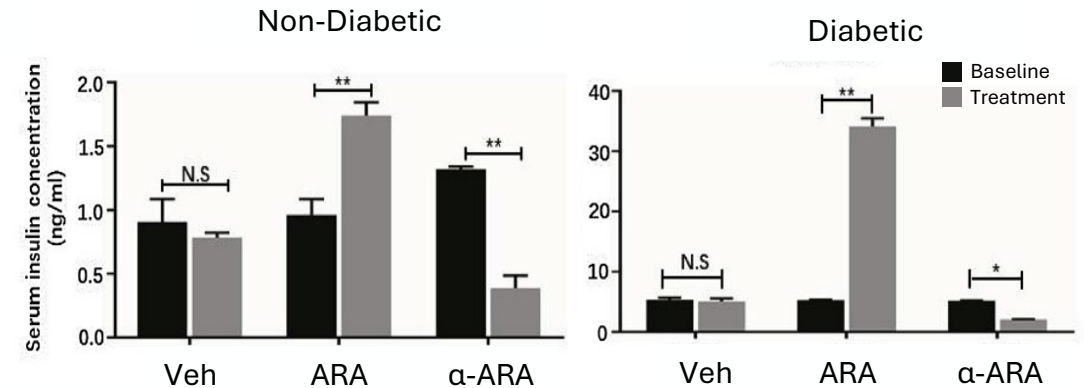
ARA may increase weight loss through increased expression and activity of GLP1R ^{4,5}



GLP-1 expression increase with ARA²



Insulin activity increase with ARA²



ARA: Androgen receptor agonist; α-ARA: Androgen receptor antagonist

LPCN 2401 in Women

Potentially safe and effective intervention to improve body composition

Women have ~1/15th the levels of testosterone compared to men

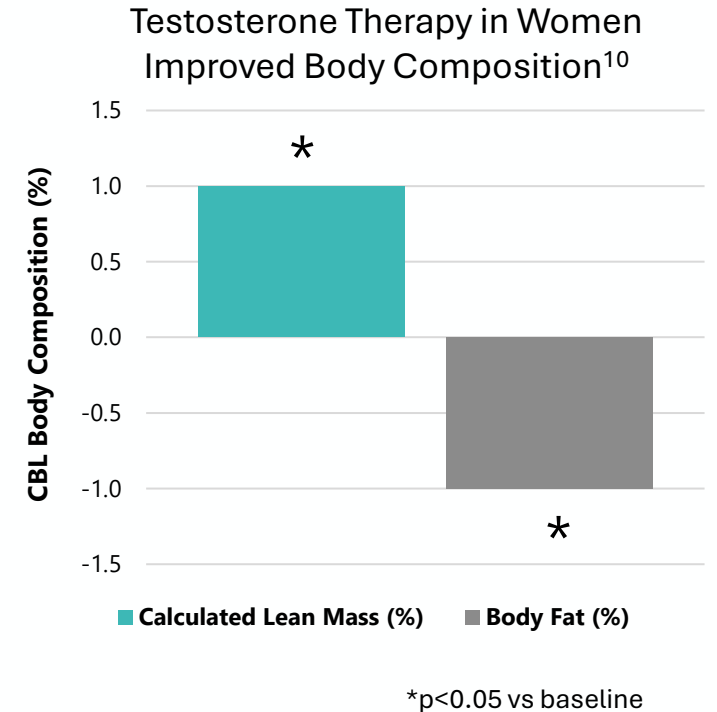
- Typically, women have ~10x higher testosterone levels than estrogen levels
- Testosterone is an important hormone for female health

T administration resulting in **normal T levels** has been shown to increase muscle mass in pre- and post-menopausal women^{1,2, 10}

- Treatment duration up to >6 months and some ≥1 year in both pre- and postmenopausal women^{1, 2}
- Physiologic levels of testosterone were shown to avoid 'masculinizing' effects^{1, 2, 3}

Safety

- Numerous interventional clinical trials of T administration to pre- and post-menopausal women with treatment duration ≥ 1 year (including Androfeme, Libigel, and Intrinsa,) ^{4, 5, 6, 7, 11}
- Clinical and pre-clinical data do not indicate increased risk of breast cancer, CV events in women receiving testosterone ^{8, 9, 11}



Next Steps

POC Clinical Development Objectives

Investigate combination of LPCN 2401 (+/- Vitamin E) + incretin mimetic in proof-of-concept study

- Potential additional fat/weight loss and less lean/bone mass loss with the combination compared to either monotherapies

Determine impact of prior/continued/new LPCN 2401 therapy after discontinuation of incretin mimetic

- Potentially reduce rebound in fat, weight, HbA1c, and other markers of cardiometabolic health

LPCN 2401

Concluding Remarks

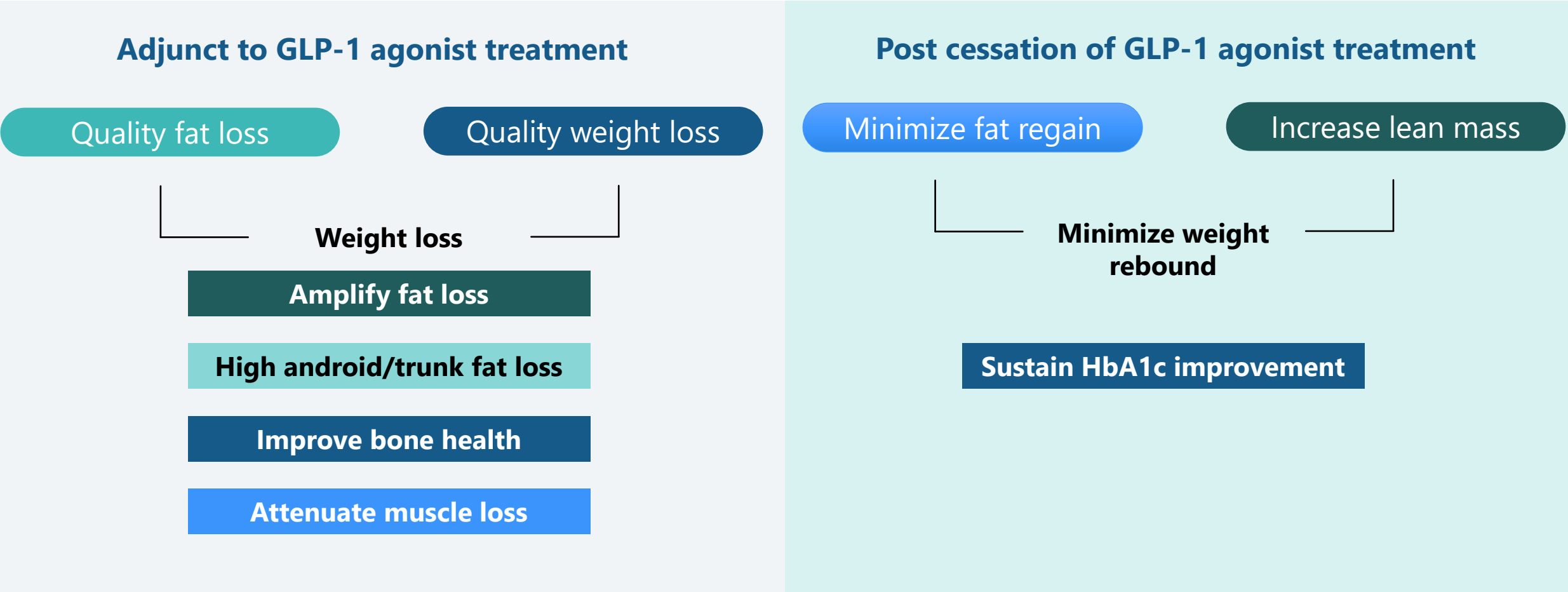
Dr. Mahesh Patel
President and CEO

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LPCN 2401 - A New Paradigm in Oral Treatment for Obesity Management

Target benefits to improve body composition



LPCN 2401 - Potential for Differentiated Benefit to Risk Profile

Key takeaways

LPCN 2401

- Oral, QD, prodrug of bioidentical hormone
- Fat loss amplification
 - Lower fat mass (preferably VAT and android fat)
- Improve/preserve lean mass
 - Muscle mass, quality, and functionality
 - Bone health
- GLP amplification: genomic and non genomic
- GI side effects: minimal
- Muscle spasm AE: none observed
- Liver Health: beneficial effects (MASH resolution, injury markers)
- Serum Alkaline phosphatase: lowers (no increase)
- Impact on sex hormone (FSH, LH, and Estradiol): minimal

Competitive Landscape*

- **Myostatin /activin receptor modulators** (e.g. bimagrumab, taldefgrobep, KER-065, and trevogrumab)^{1,2}
 - Invasive - IV/SC
 - Moderate to high GI side effects ^{2,3}
 - Reports of muscle spasms ^{2,3}
 - Increased serum Alkaline Phosphatase ³
 - Sex hormone changes (FSH/LH) ⁴
 - Unclear muscle functionality improvement
 - Long term exposure risks unknown
- **SARM** (e.g. Enobosarm) ⁵
 - Oral
 - Bone health concerns (estradiol suppression?)
 - Liver toxicity concerns

*select list with reported body composition improvement P2 results

LPCN 2401

Q&A

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