

# **LPCN 2401 for Obesity Management**

Clinical Study Results

# 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 the development and commercialization of LPCN 2401 and the potential uses and benefits of LPCN 2401 for the improvement of body composition in obesity management. This release also contains statements regarding the potential uses and benefits of our other 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 to treat obesity disorders, 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 non-core 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 2401, 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](http://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.

# LPCN 2401 for Obesity Management

## Potential to Improve Body Composition

### Product Candidate Attributes

Proprietary oral formulation comprising an anabolic androgen receptor agonist (ARA) and  $\alpha$ -tocopherol, an antioxidant and a metabolic modifier

### Targeted MOA

- Stimulates muscle satellite activator, FGF2<sup>1</sup>
- Modulates muscle growth suppressors MRF4, and myostatin (GDF8) expression in skeletal muscle<sup>1</sup>
- Induces lipolysis and lowers lipogenesis<sup>2</sup>
- Anti-oxidant - protects against oxidative stress and maintains membrane fluids<sup>3,4</sup>; counters oxidative stress associated with osteoclasts differentiation<sup>5</sup>
- Anti-inflammatory - decreases the activation of cytokines and adhesion molecules<sup>6</sup>

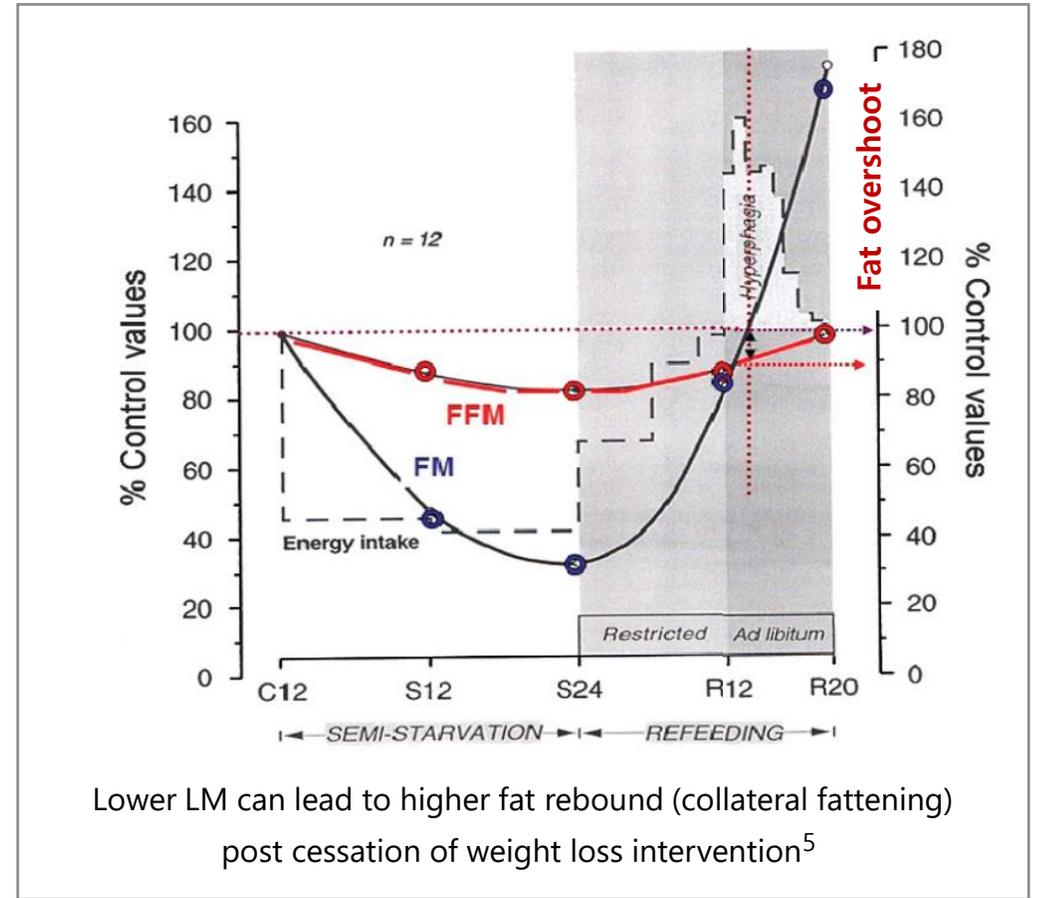


# Importance of Lean Mass (LM)

LM of around 70% for women and 90% for men is considered to be healthy

## Importance of Muscle Mass

- Significant role in metabolic health and disease prevention<sup>1</sup>
  - High caloric demand<sup>2</sup>
- Contributes to physical strength, active lifestyle
- Rapid loss of LM has multiple negative health implications<sup>3</sup>
  - Weakness/fatigue, lowered metabolism, declines in neuromuscular function, potential effects on emotion and psychological states, and increased risk of injury<sup>4</sup>



# Consequences of Excess Total Body Fat (TBF)

**Excess TBF** increases the risk of death and major comorbidities such as type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease, osteoarthritis of the knee, sleep apnea, and some cancers<sup>1,2</sup>

Having excess fat in the **android region, AF (fat in the area roughly between the pelvis and ribs)**, is more strongly associated with negative health outcomes than TBF% or BMI<sup>3</sup>

---

**Visceral fat** (~10% of TBF) refers to fat that is stored within the abdominal cavity<sup>4</sup>

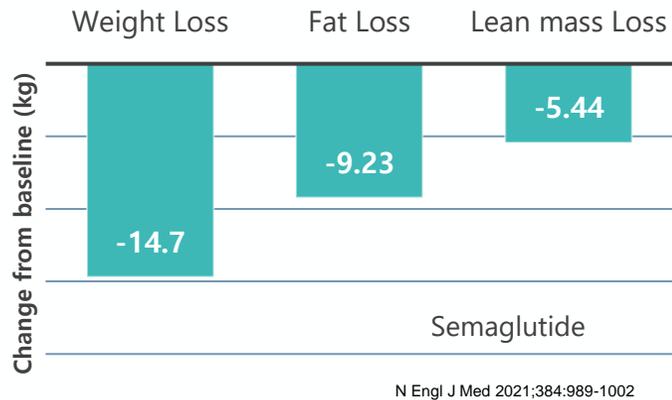
Men have more visceral fat than women<sup>5</sup>

Can increase the risk of certain health conditions, such as diabetes, prediabetes, and heart disease

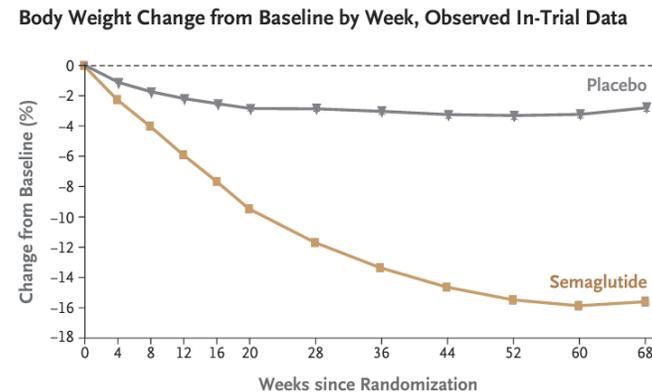
# Limitations of Incretin Mimetics (GLP-1 agonists)

## Significant loss of lean mass and fat rebound potential upon cessation

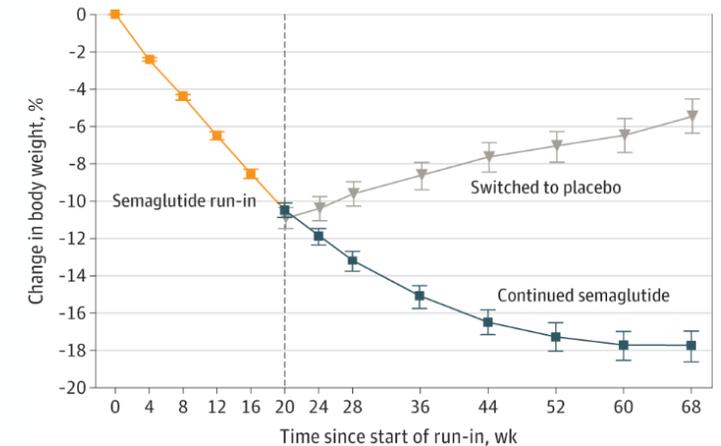
### Loss of lean mass



### Plateauing of weight loss



### Rebound weight gain



GLP-1 agonist treatment led to 15-21% rapid weight loss with unwanted LBM loss of up to 40% of the total weight lost<sup>1</sup>

**Muscle wasting at an alarming rate**

Greatest amount of weight loss is by week 20  
Rate of weight loss reaches a plateau<sup>1</sup>

Patients who discontinued treatment at week 20 had significant weight gain<sup>2</sup>

# Unmet Need in Incretin Mimetic Based Chronic Weight Management

## Oral agent with improved benefit to risk profile:



- Ameliorate the loss of lean mass loss due to GLP-1/GIP treatment (a higher quality weight loss)
- Improve body composition, lose more fat while preserving, or even gaining, muscle



- **Provide long-term option to maintain weight upon cessation of GLP-1 therapy**
  - Prevent rebound “fat overshoot” and minimize weight gain
  - Accelerate muscle recovery
  - Prevent collateral fattening and progression to sarcopenic obesity

# **LPCN 2401**

## **Preclinical and Clinical Results**

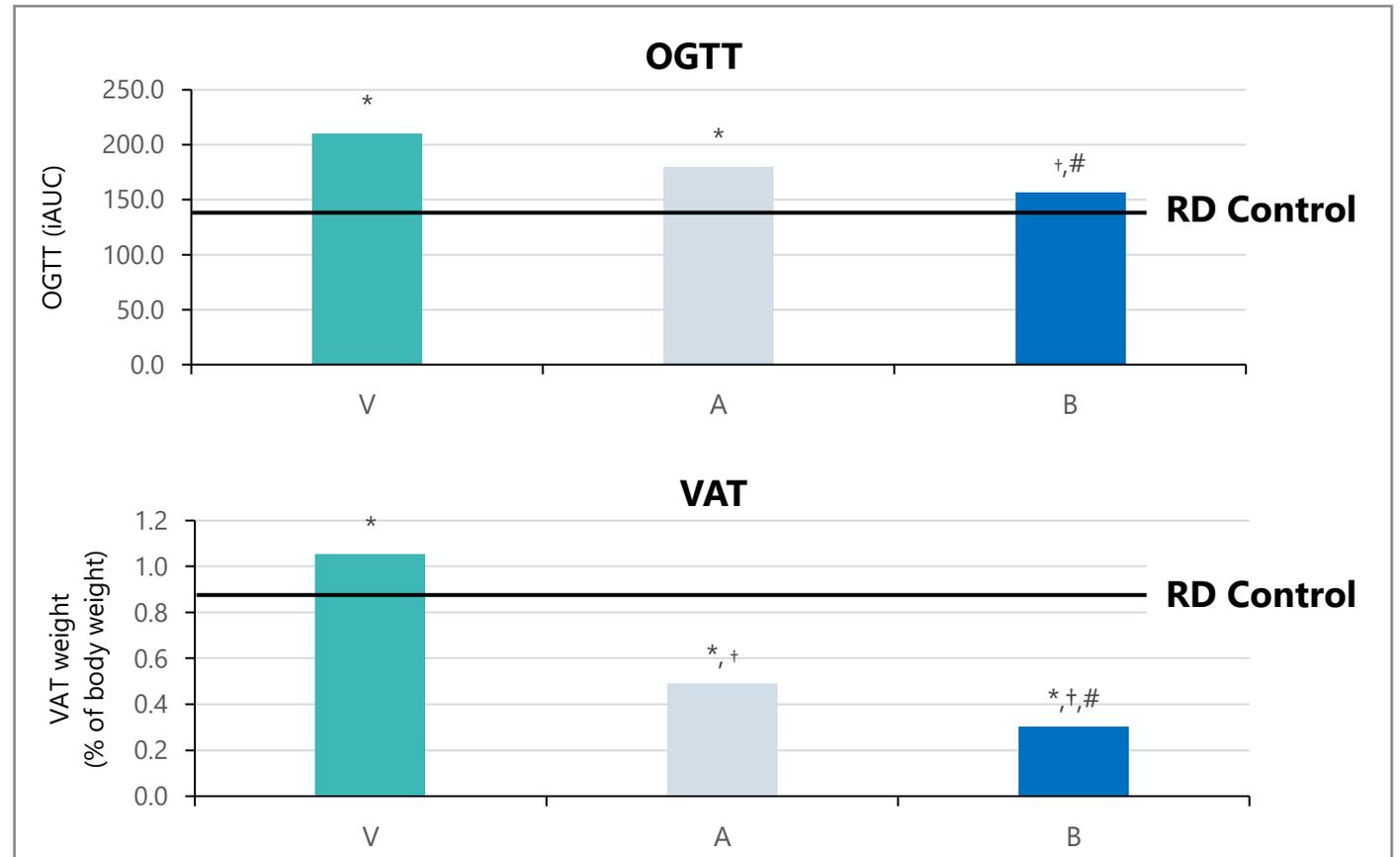
# Summary of Preclinical Results in Diet Induced Model

## LPCN 2401 significantly improved oral glucose tolerance test and reduced VAT

12-week study in male rabbit model of metabolic syndrome

- Regular Diet (RD control), n=10
- High Fat Diet (HFD), n=10
- HFD + vehicle (**V**), n=7
- HFD + TU monotherapy (**A**), n=8
- HFD + LPCN 2401 (TU +  $\alpha$ -tocopherol) (**B**), n=8

LPCN 2401 resulted in a significantly improved OGTT and reduced VAT not only compared to vehicle, but was also superior to Treatment A (monotherapy)



\* p<0.05 vs RD; † p<0.05 vs vehicle; # p<0.05 vs Trt A

# Phase 2 Study in Patients with Obesity

## NCT04134091 study design

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

- High prevalence of obesity and weight related comorbid conditions such as dyslipidemia, T2DM, and hypertension
- 1:1:1 randomization across three oral treatment arms; Treatment duration of 36 weeks
  - Treatment A: T undecanoate monotherapy capsule
  - Treatment B: T undecanoate +  $\alpha$ -tocopherol capsule (LPCN 2401)
  - Treatment C: Matching placebo
- Dual Energy X-Ray Absorptiometry (DEXA, n=40) at baseline, 20 weeks, and 36 weeks
  - Prespecified endpoints: change in lean mass and fat mass
- Low testosterone was not a requirement for study eligibility

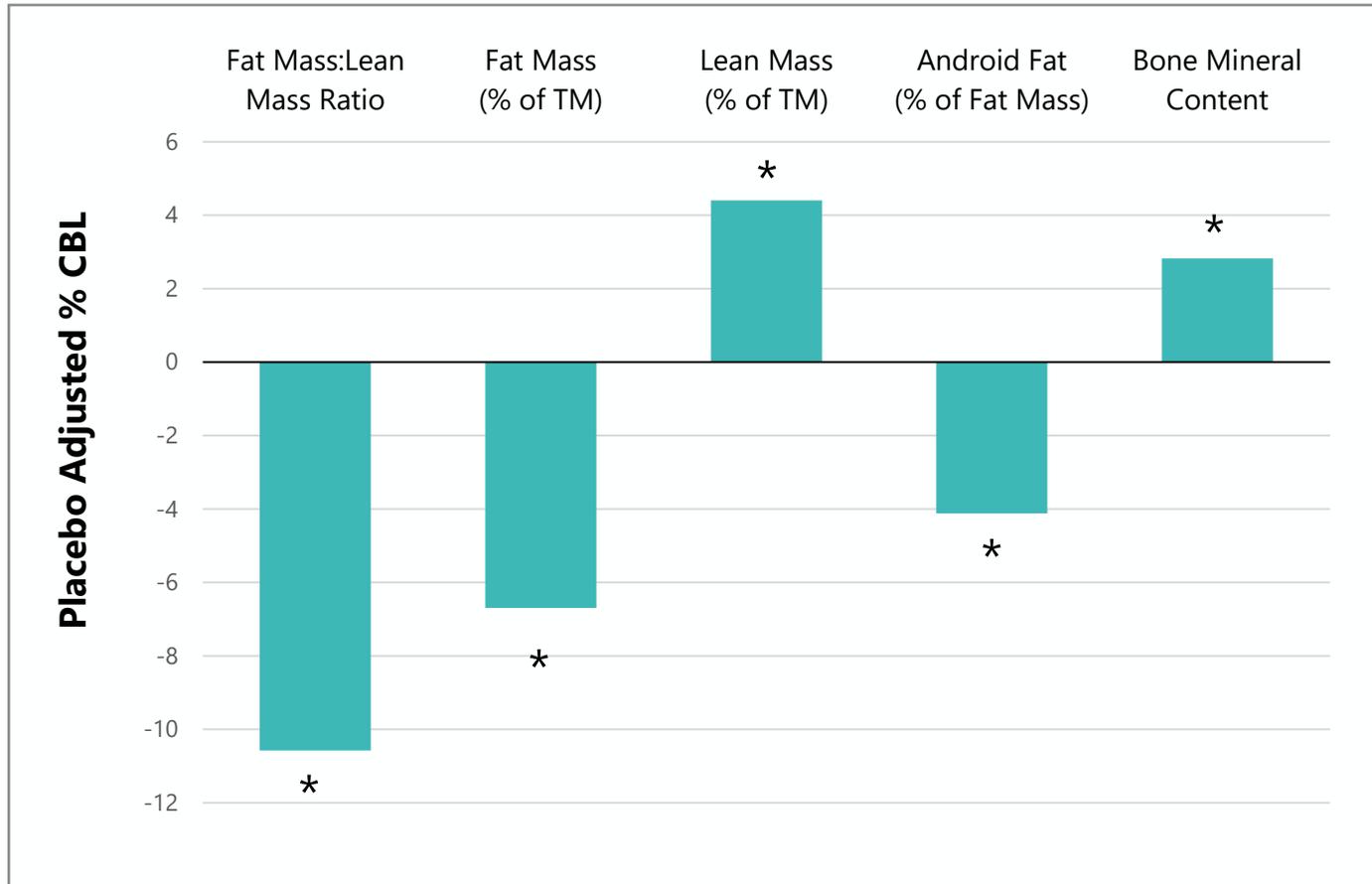
# Baseline Demographics

## Body composition analysis set\*

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

# LPCN 2401 Body Composition Results

Significantly increased lean mass and decreased fat mass

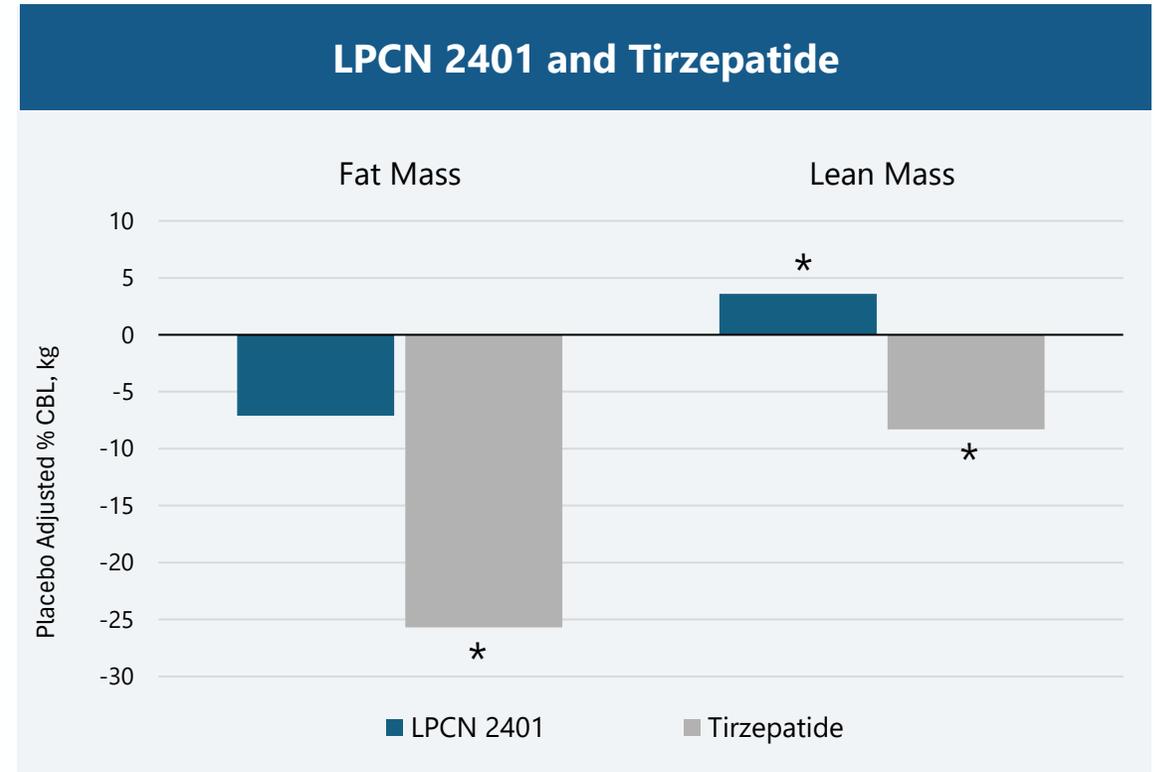
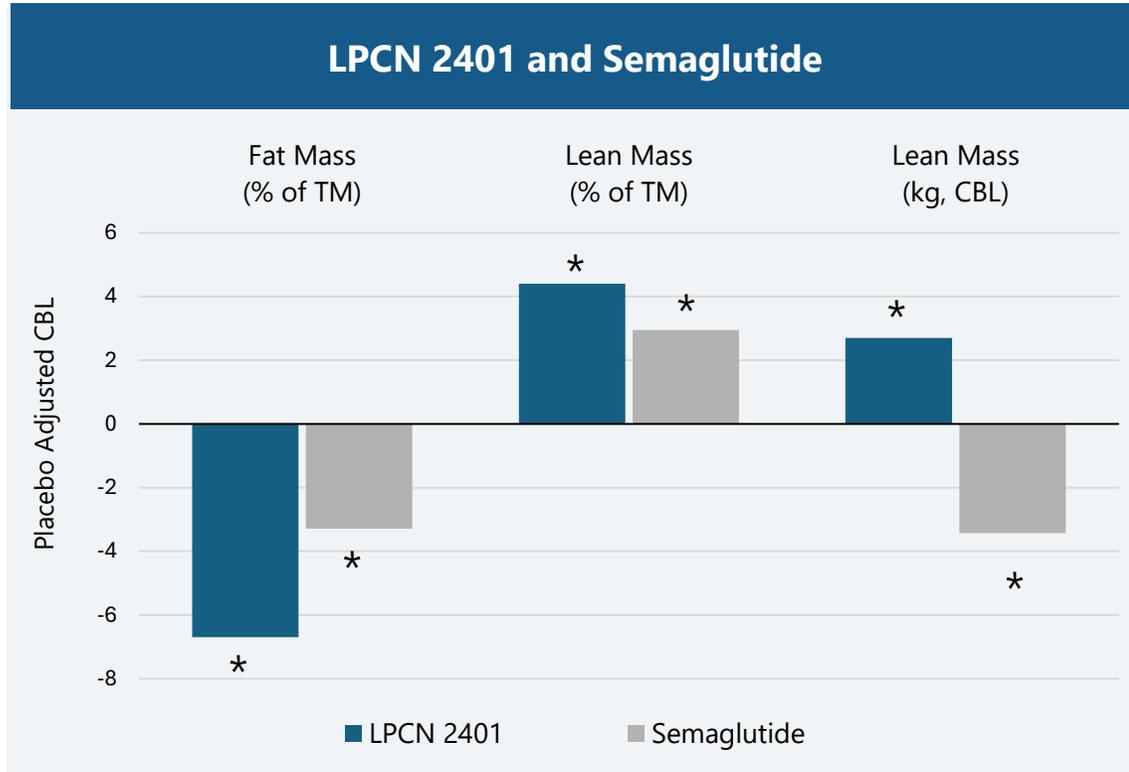


\* p<0.05 vs placebo. Body composition analysis set; N=27.

- ✓ **Improvement in fat:lean ratio**
  - Reduction of fat mass
  - Increase in lean mass
- ✓ **Reduction in android fat**
  - Correlated with whole body visceral fat
- ✓ **Increase in bone mineral content**
- ✓ **Weight neutral**
  - Fat mass lost offset by lean mass gained

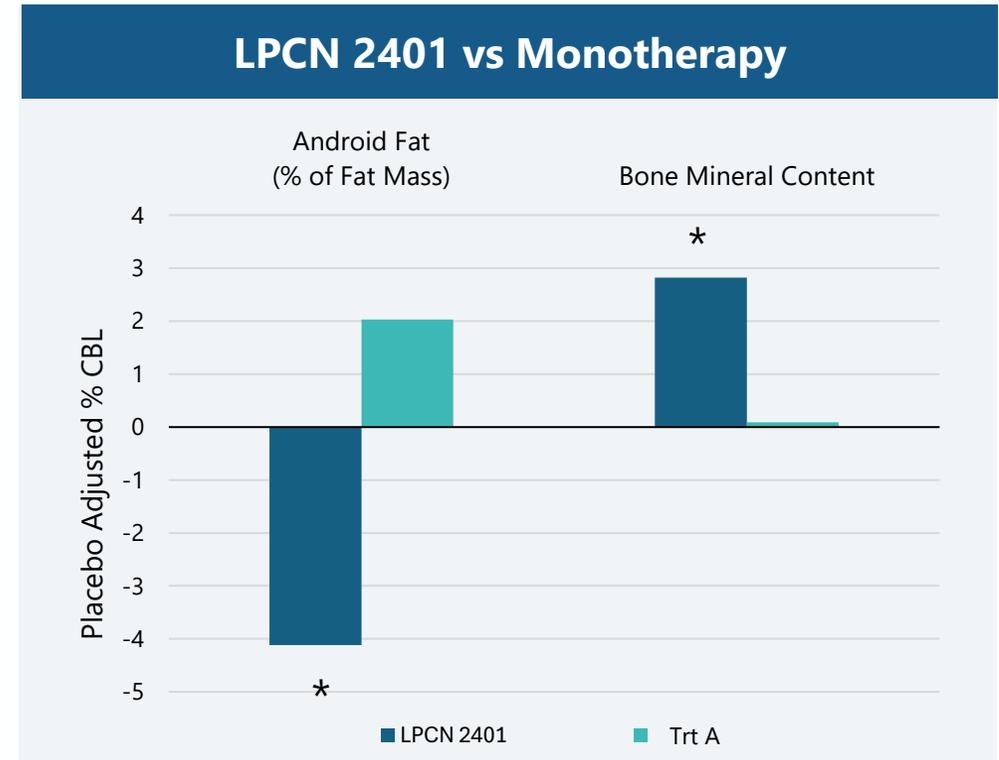
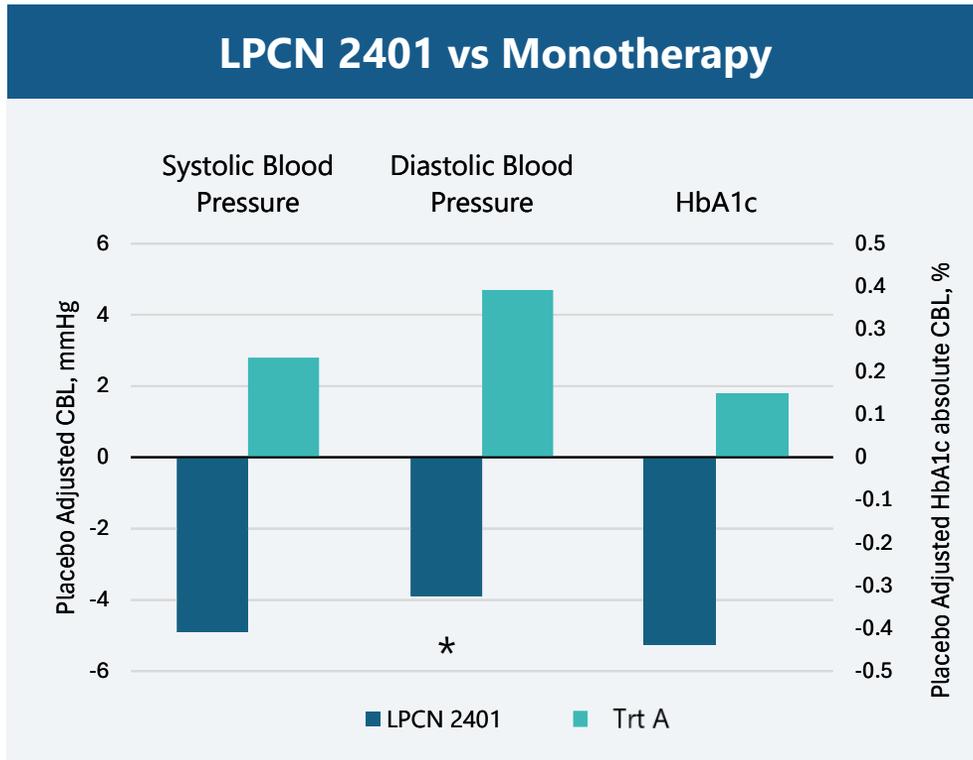
# Changes in Body Composition

## Comparison† of LPCN 2401 to injectable incretin mimetics clinical data



# Comparison of LPCN 2401 and T Monotherapy (Treatment A)

## Differentiated impacts



Baseline	N	SBP	DBP	HbA1c
Placebo	14	127	80	7.3
LPCN 2401	13	124	78	7.2
Trt A	13	128	79	7.0

\*p<0.05 vs Treatment A

# Safety Overview of LPCN 2401 Through Week 36

## Well-tolerated with an overall safety profile comparable to placebo

### Adverse Events – Safety Set

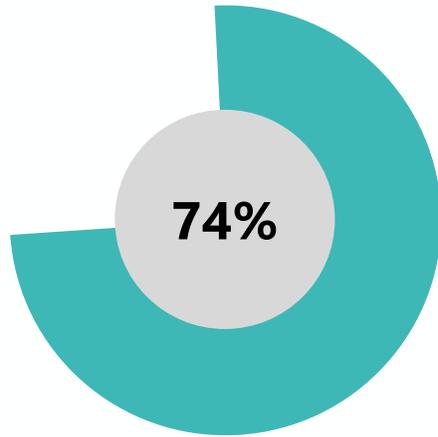
Preferred Term	Placebo N=19	LPCN 2401 N=19
Diarrhea	2 (10.5%)	0 (0%)
Nausea	1 (5.3%)	0 (0%)
Vomiting	none	none
Muscle Spasms	none	none
BPH	1 (5.3%)	0 (0%)
PSA Increased	none	none
Hypertension <sup>†</sup>	1 (5.3%)	0 (0%)
Peripheral Edema	2 (10.5%)	1 (5.3%)

- Frequency and severity of TEAEs with LPCN 2401 were comparable to placebo
- Frequency of SAEs with LPCN 2401 were comparable to placebo
- Discontinuance of study drug due to TEAEs: 0 subjects on LPCN 2401, 4 subjects on placebo
- No cardiovascular events with LPCN 2401
- No reported cases of hepatocellular carcinoma or Drug Induced Liver Injury (“DILI”)
- Changes in lipids comparable to placebo

BPH = Benign prostatic hyperplasia; PSA = Prostate-Specific Antigen; † New or worsening hypertension

# Obesity and Overweight: A Growing Epidemic in US

Increases the risks of heart disease, stroke, type 2 diabetes and certain types of cancer<sup>1,2</sup>



of adults age 20 and older  
are obese or overweight  
(2017-2018)<sup>3</sup>

- The est. annual medical cost of obesity was ~ \$173 B in 2019<sup>3</sup>
- Diabesity population (~110mn adults)<sup>4</sup>
  - ~24M obese elderly, group most vulnerable to losing muscle mass<sup>3,4</sup>
- GLP-1 users in the US projected to reach 30 million by 2030<sup>5</sup>
- 38% of men and 51% of women would be interested in taking a prescription drug for weight loss<sup>6</sup>

# Recent Trends and Complications in Weight Management

## Current clinical use prioritizes weight loss over healthy body composition

### Recent Trends

#### US Obesity (2017-March 2020)<sup>1</sup>

- Increased from ~31% to ~42%
- Prevalence of severe obesity increased from 4.7% to 9.2%

#### Incretin mimetics are widely used in chronic weight management

- GLP-1 agonist (e.g. semaglutide, Wegovy<sup>®</sup>, liraglutide, Saxenda)
- Dual GLP-1/GIP agonist (e.g. tirzepatide, Zepbound<sup>®</sup>)

### Issues with Incretin Mimetics

Substantial lean mass loss

Rebound weight gain upon cessation<sup>2</sup>

Potential for “fat overshoot” upon discontinuation of therapy<sup>3</sup>

Unclear long term use challenges

# LPCN 2401 – Novel Oral Treatment for Obesity and Weight Management

## Key Take Aways

### Significant body composition improvement in men with at least one weight-related comorbidity

---

Decreased fat mass (FM)

Increased lean mass (LM)

Reduced android fat

Increased bone mineral content (BMC)



Potential for improved body composition in combination with GLP-1 agonists:

- Ameliorate muscle loss
- Amplify fat loss



Potential to maintain weight, prevent “fat overshoot,” and accelerate muscle rebound after GLP-1 discontinuation



Well-tolerated, with AE rates and severities similar to that of placebo



Clinical and preclinical data support further testing as an aid in quality weight loss while preserving lean mass