

October 2024  
**H.C. Wainwright  
8<sup>th</sup> Annual MASH  
Investor Conference**

**LIPOCINE<sup>®</sup>**  
ENHANCING HEALTH



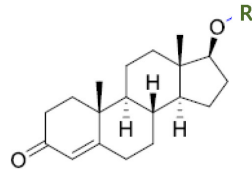
## Forward-Looking Statements

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](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.

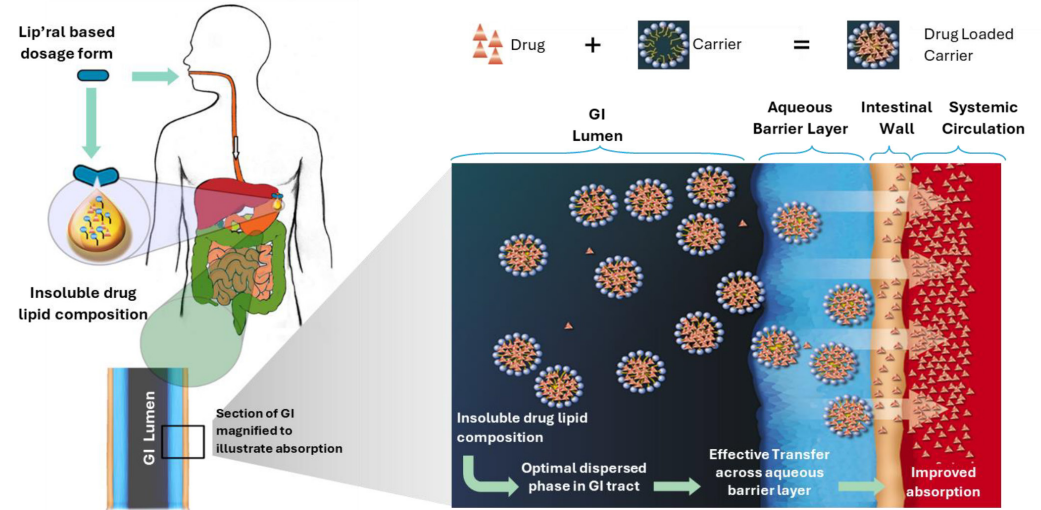
# Lipocine - Enabling Effective Oral Delivery

The Lip'ral platform optimizes GI absorption for faster onset of efficacy

## Testosterone Esters



**Testosterone Esters**  
Highly lipophilic with  $\text{Logp} > 8$



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

## Lip'ral enables development of superior oral products

Improved Solubilization and High Drug-Loading Capacity

Improved Bioavailability

Faster and More Consistent Absorption

Improved Patient Compliance

# LiFT (Liver Fat Intervention with oral Testosterone)\*†

## Phase 2 paired biopsy study in men with MASH (NCT04134091)

### Study Design

- ❑ Biopsy confirmed male MASH subjects with F1-F3  
Three-arm, blinded, placebo-controlled
- Hypogonadal and eugonadal men enrolled
- 1:1:1 randomization
  - TU mono - Oral TU monotherapy
  - TU combo - Oral TU + d-alpha tocopherol
  - Matching placebo
- ❑ Treatment duration of 36 weeks

### Primary Endpoint

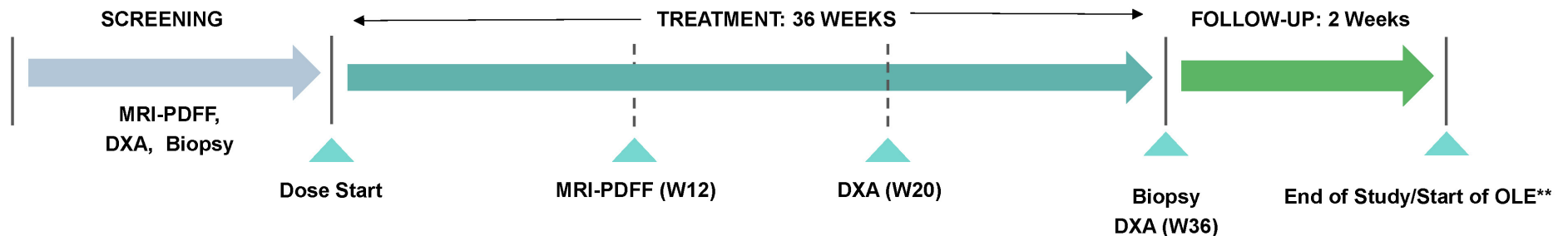
- ✓ Change in hepatic fat fraction via MRI-PDFF (W12)

### Key Secondary Endpoints

- ✓ NASH resolution without worsening of fibrosis (CRN scoring, W36)
- ✓ Change in liver injury markers

### Analysis Sets

- Safety Set: All randomized subjects (ITT)
- NASH Resolution Set: Biopsy set with NAS  $\geq 4$  and at least 1 point in both inflammation and ballooning





# LiFT Study

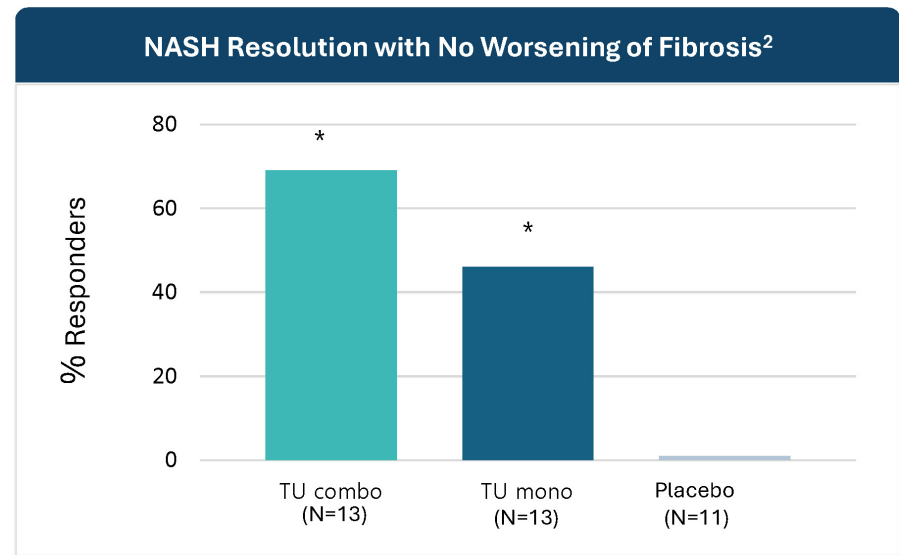
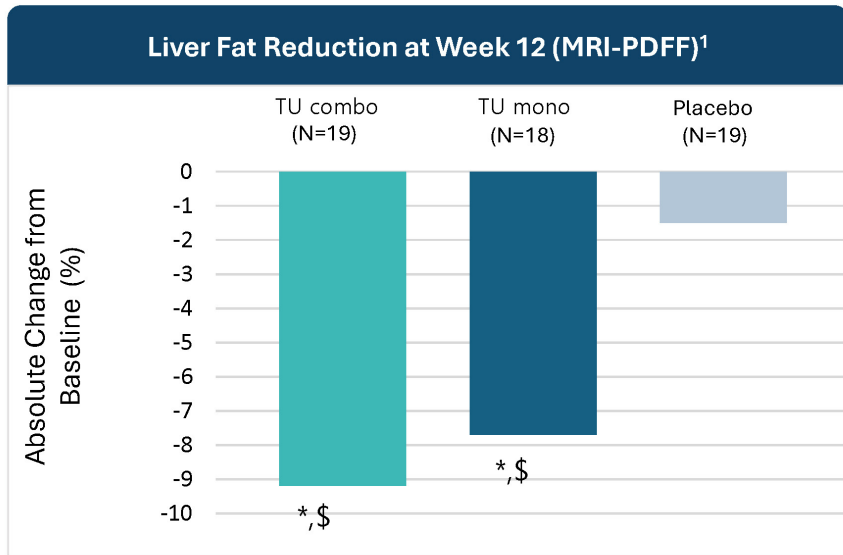
## Baseline characteristics

### Safety Analysis Set<sup>1</sup>

Parameter at Baseline	TU mono (N=18)	TU combo (N=19)	Placebo (N=19)
Mean Age (years)	51.3	53.4	53.6
Mean BMI (kg/m <sup>2</sup> )	36.9	34.5	37.3
Diabetes (%)	72.2	57.9	52.6
Hypertension (%)	66.7	57.9	68.4
Mean NAFLD Activity Score	4.9	4.8	4.7

# Improvement in Liver Health

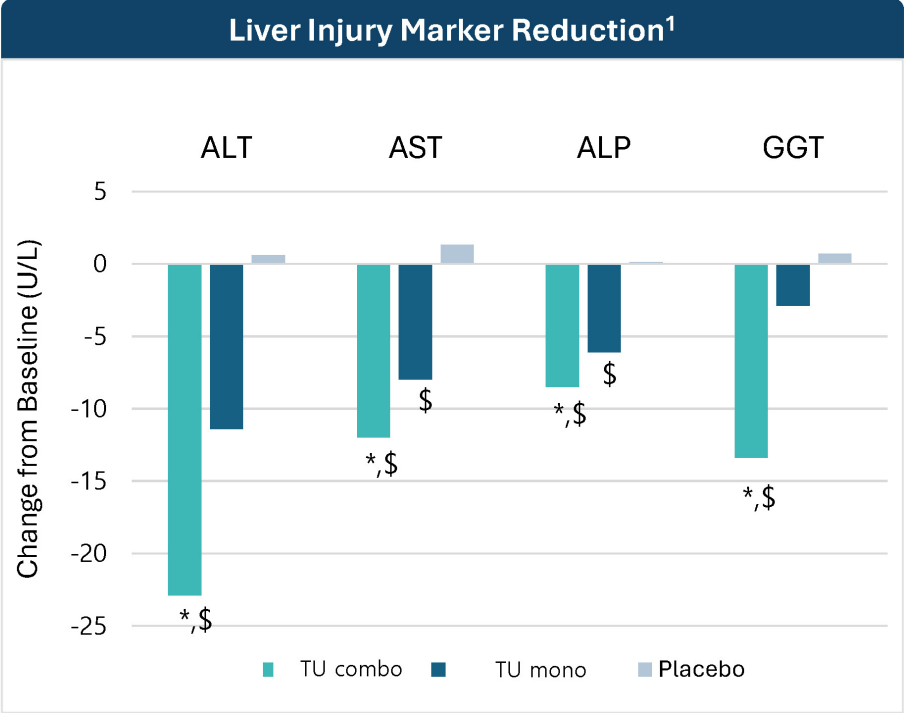
## LPCN 1144 - primary endpoint met



1. All Subjects: ITT Dataset, n = 56, missing data imputed using multiple imputation. \* p < 0.05; vs placebo; \$ p < 0.05 vs baseline.  
2. NASH resolution is defined per FDA guidance. NASH Resolution Set includes those subjects with baseline and EOS biopsy and with NASH at baseline per FDA Phase 3 guidance. \* p < 0.05; vs placebo

# Improvement in Liver Health

LPCN 1144 therapy demonstrated an improvement in liver injury markers



1. Safety set. \* p < 0.05; vs placebo; \$ p < 0.05 vs baseline.  
 2. All Subjects: ITT Dataset, n = 56, missing data imputed using multiple imputation. \* p < 0.05; vs placebo; † p < 0.05 vs baseline.

# Safety profile

## Well-tolerated with no safety signals with up to 72-week exposure

- Frequency and severity of TEAEs, SAEs with TU arms were comparable to placebo
  - 4 subjects discontinued in placebo due to TEAEs vs. 1 subject total in combined TU treatment arms
- GI adverse events (diarrhea, nausea, vomiting) rates and severities similar to placebo
- Androgenic adverse events (edema, BPH, PSA increase, hypertension<sup>†</sup>) similar to placebo
  - No concerning cardiovascular signals
  - These safety data align with recent investigations into long-term testosterone therapy in hypogonadal men (i.e. TRAVERSE study)<sup>1</sup>

## LPCN 1144: Key Attributes

Positive results support further development

### LPCN 1144

- Oral, prodrug of bioidentical hormone
- Liver Health: Positive findings for MASH resolution
- Liver Health: Positive reductions in liver injury markers
- Side effects: Minimal



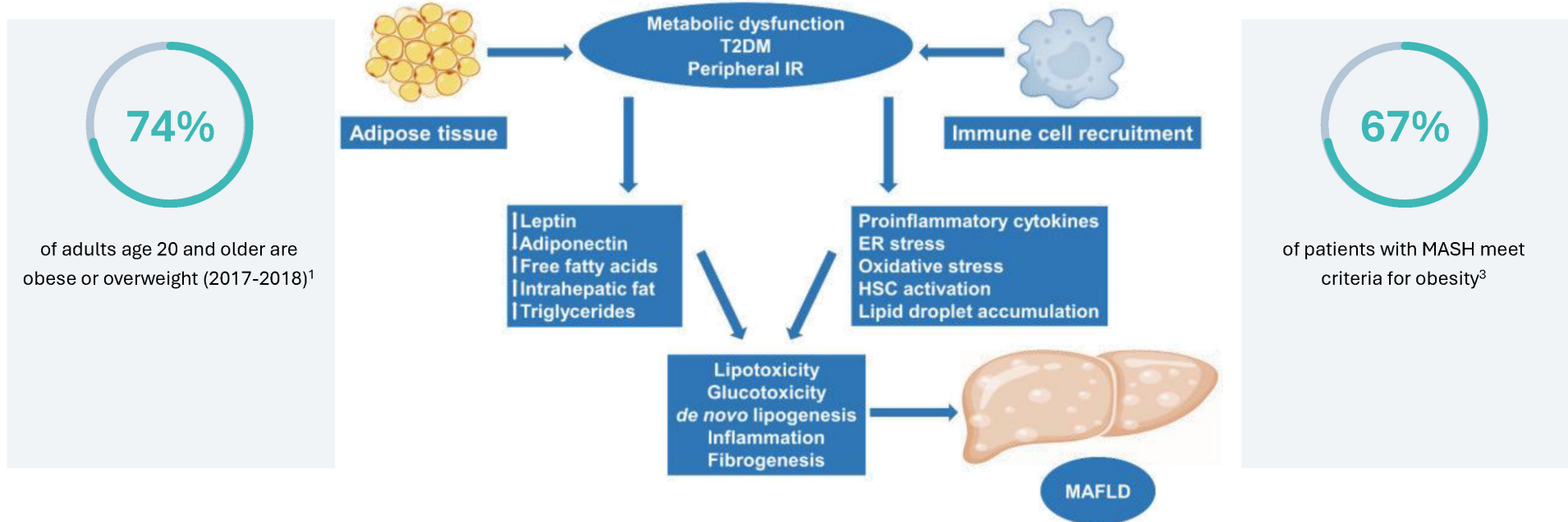
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Addressing the role of obesity

# Obesity - A Growing Epidemic in US

Obesity is a major risk factor for the development and progression of MASH



Phase 2 clinical trials with incretin mimetics have demonstrated improvements in MASH outcomes<sup>4,5</sup>

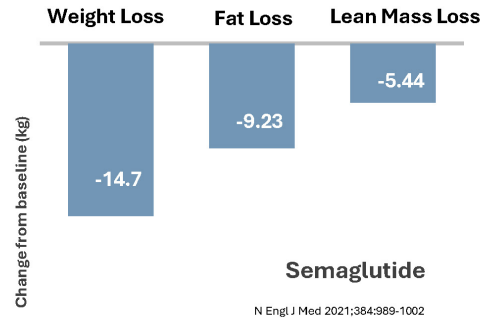
1. <https://www.cdc.gov/nchs/fastats/obesity-overweight.htm>  
 2. Figure from Arvanitakis et al. 2023, Int J Mol Sci  
 3. Tapper et al. 2023, BMC Gastroenterology

4. Newsome et al. 2021, N Engl J Med  
 5. Loomba et al. 2024, N Engl J Med

# Limitations of Incretin Mimetics (GLP-1 Receptor Agonists)

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

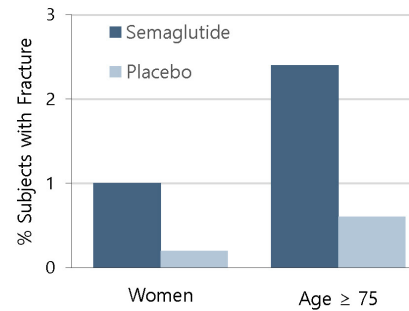
### Loss of Lean Mass



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>

Lean mass/muscle wasting at an alarming rate and extent

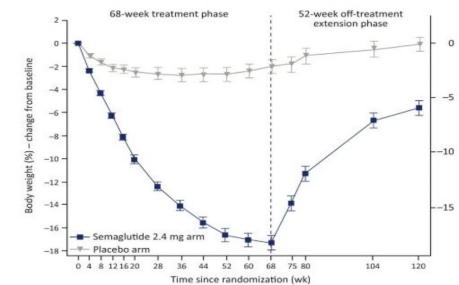
### Increased Fracture Risk



Patients on semaglutide had significantly more fractures of the hip and pelvis<sup>2</sup>

Patients who had received semaglutide were 7x more likely to require additional surgery within 1-year post lumbar fusion (TLIF)<sup>5</sup>

### Plateauing of Weight Loss/ Rebound Weight Gain



Greatest amount of weight loss is by week 20; weight loss plateaus<sup>1</sup>

68% discontinue within 1 year<sup>7</sup>

Patients who discontinued treatment had significant weight gain<sup>3,6</sup> and HbA1c increase<sup>4</sup>

# 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

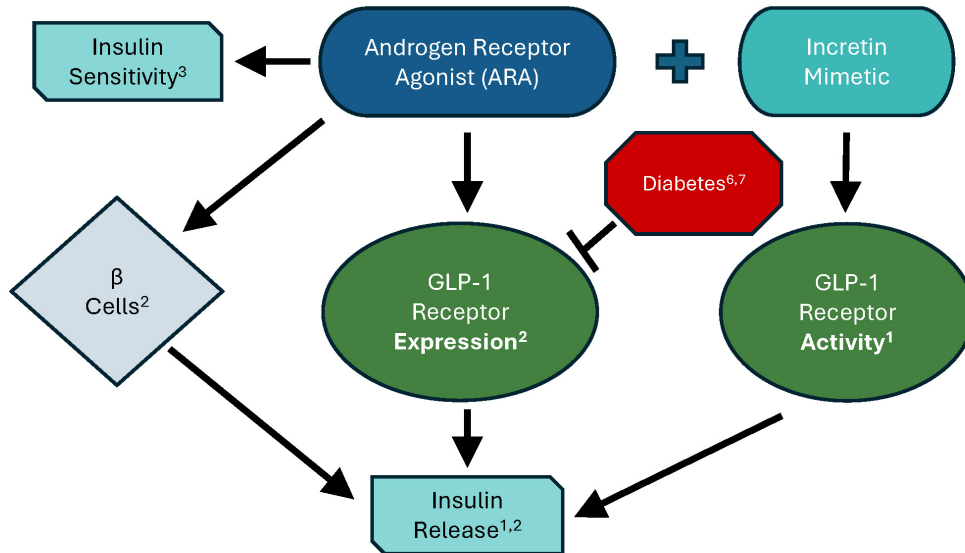
- Proprietary androgen receptor agonist (ARA)
- Proprietary androgen receptor agonist (ARA) with  $\alpha$ -tocopherol

## Targeted Mechanism of Actions

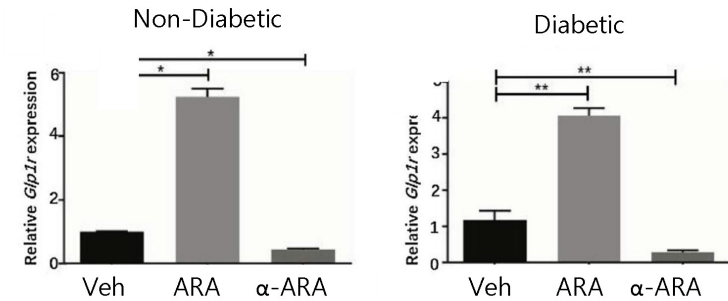
	<b>Fat</b>	<b>Muscle</b>	<b>Bone</b>
<b>Androgen Receptor Agonist</b>	<ul style="list-style-type: none"><li>• Induces lipolysis<sup>1</sup></li><li>• Lowers lipogenesis<sup>1</sup></li><li>• Inhibits expression of adipocytokines (e.g., leptin, TNF-<math>\alpha</math>, IL-6, IL-1)<sup>2</sup></li></ul>	<ul style="list-style-type: none"><li>• Stimulates muscle satellite activator, FGF2<sup>3</sup></li><li>• Modulates muscle growth suppressors MRF4 and myostatin (GDF8) expression in skeletal muscle<sup>3</sup></li></ul>	<ul style="list-style-type: none"><li>• Acts directly on osteoblasts and consequently promotes bone formation<sup>4</sup></li><li>• Increases AR expression level in osteoblasts<sup>4,5</sup></li></ul>

# LPCN 2401: Potential to Amplify Effects of Incretin Mimetics

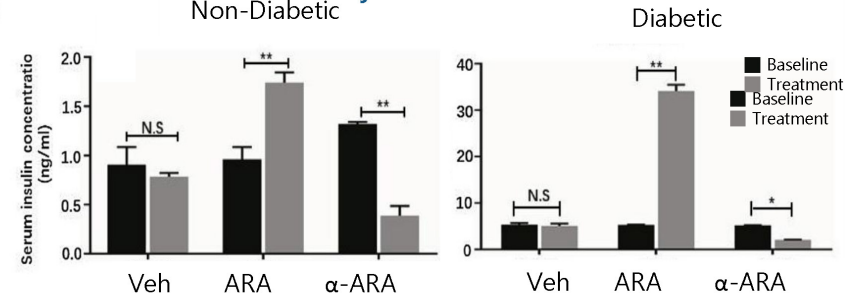
ARA may increase weight loss through increased expression and activity of GLP1R<sup>4,5</sup>



GLP-1 expression increase with ARA<sup>2</sup>



Insulin activity increase with ARA<sup>2</sup>



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



# Phase 2 Study in Patients with Obesity and Overweight

## NCT04134091 study design

### Three-arm, blinded, placebo-controlled trial in male subjects with MASH (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
  - TU mono - Oral TU monotherapy
  - TU combo - Oral TU + d-alpha tocopherol
  - 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
  - Testosterone levels inversely correlate with BMI<sup>1</sup>
  - > 70% of severely obese men have T < 300 ng/dL<sup>2</sup>

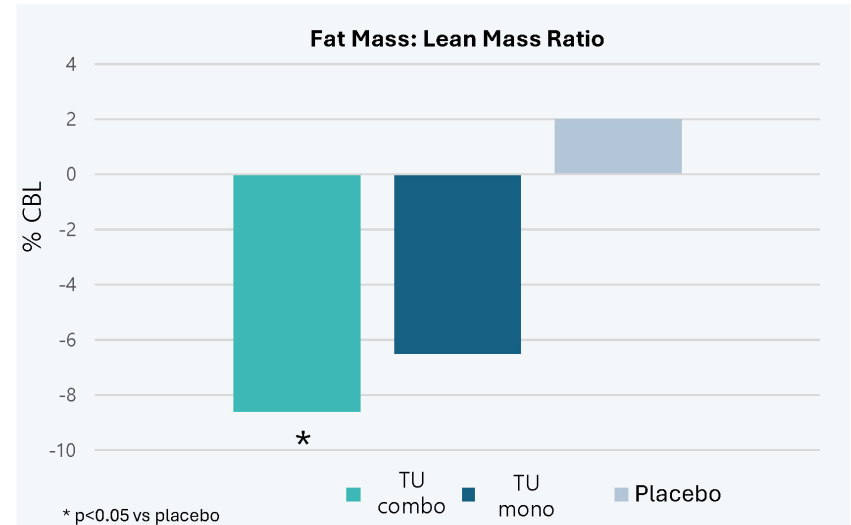
# LPCN 2401: Significant Improvement in Participants' Body Composition

Prespecified endpoints met – increased lean mass and decreased fat mass

## Body Composition Analysis Set<sup>1</sup>

Parameter at Baseline	TU combo (N=13)	TU mono (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

## Body Composition Results

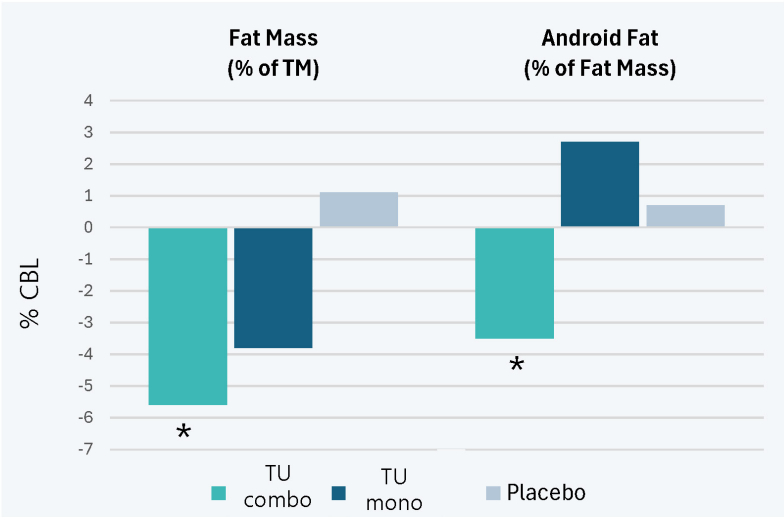


- **Significant improvement in fat to lean ratio**

# LPCN 2401 - Significant Improvement in Participants' Body Composition

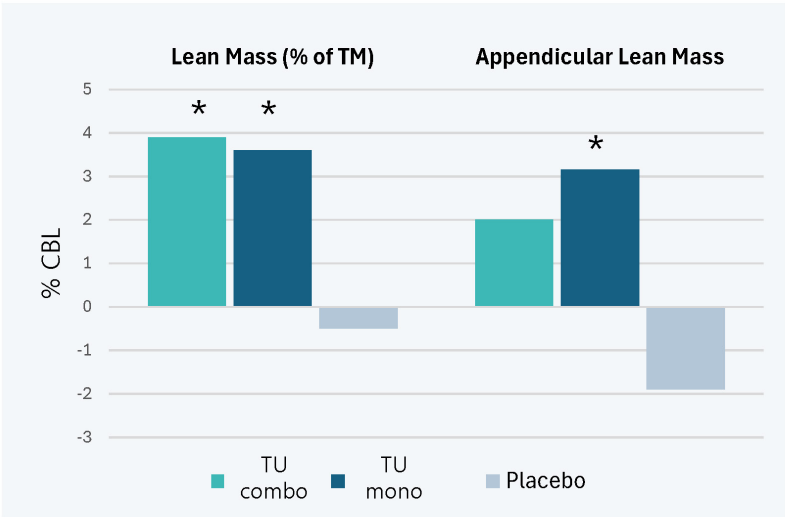
Prespecified endpoints met – increased lean mass and decreased fat mass

## Fat Mass



Significant reductions in fat mass

## Lean Mass

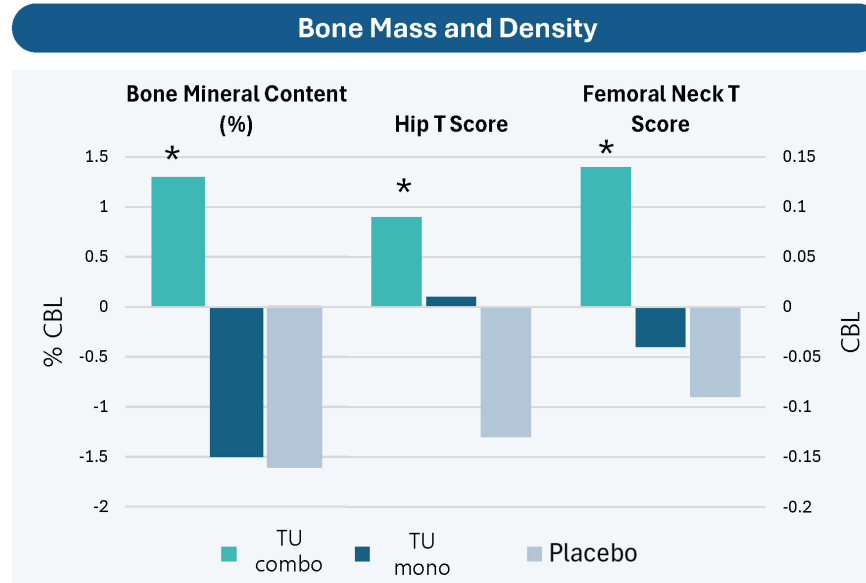


Significant increases in lean mass

- ~1.8 kg increase in whole body lean mass
- ~1.2kg increase in appendicular lean mass

# LPCN 2401 - Significant Improvement in Bone Health

Significant increase in bone mass and density

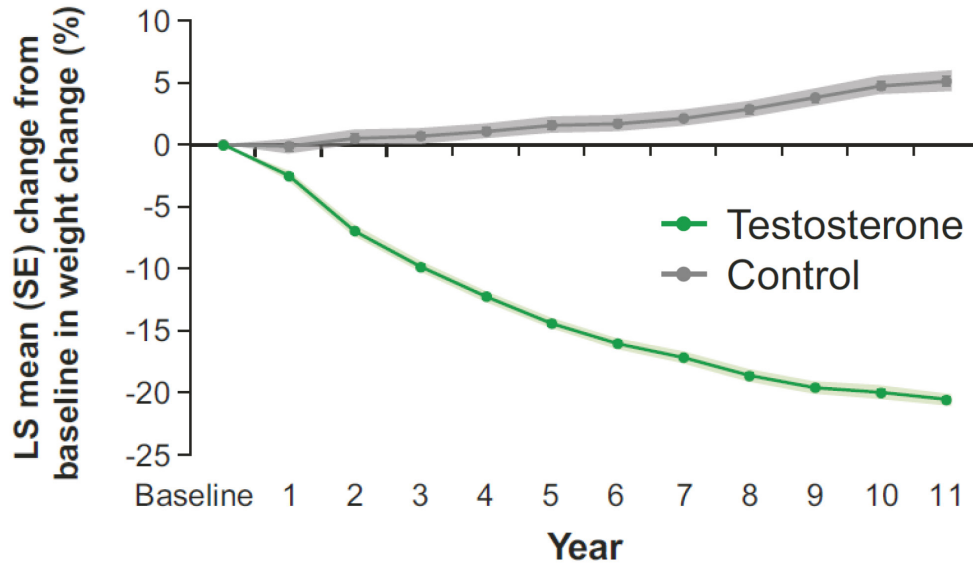


### Increase in bone mineral content

- Significant increase in hip and femur T scores

# Testosterone Therapy Reduces Weight

Continued weight loss after initial slow period



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

- 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



# 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

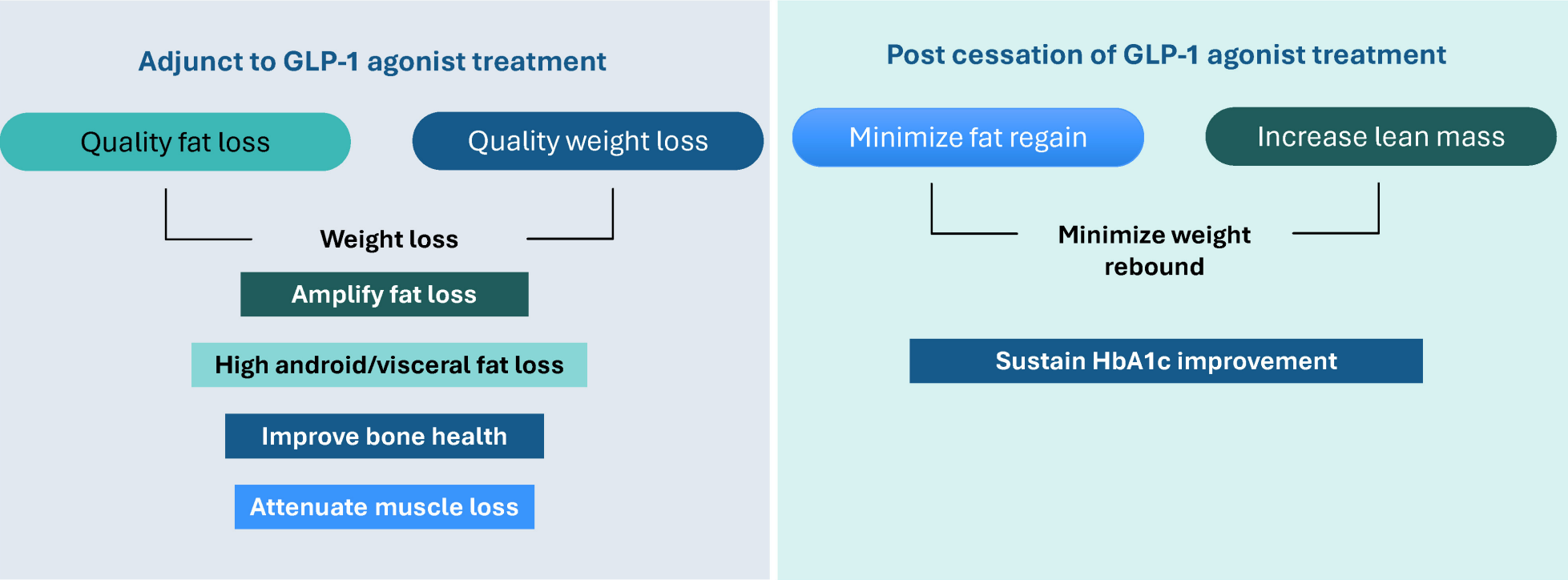
### Competitive landscape\*

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

\*select list with reported body composition improvement P2 results

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

Target benefits to improve body composition



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