Veru Inc.
Nasdaq:VERU

Focused on metabolic diseases and oncology

Veru Corporate Presentation
Oppenheimer 34th Annual Healthcare Life Sciences Conference
February 13-14, 2024

Forward looking statements and safe harbor

The statements in this document that are not historical facts are "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995. Forward-looking statements in this document include statements regarding: the planned design, enrollment, timing, commencement, interim and full data readout timing, scope, regulatory pathways, and results of the Company's current and planned clinical trials, including the Phase 2b study of enobosarm in combination with a GLP-1 agonist for the treatment of obesity and related muscle wasting, the confirmatory Phase 3 study of sabizabulin for certain COVID-19 patients (if undertaken), the Phase 3 study of sabizabulin in adult hospitalized patients with ARDS (if undertaken), the Phase 2b/3 study of enobosarm in combination with abemaciclib for the 2nd line treatment of AR+ ER+ HER2 metastatic breast cancer, and whether any of such studies will meet any of its primary or secondary endpoints; whether and when the IND for the enobosarm/GLP-1 combination study will be filed with the U.S. FDA, whether the FDA will require any additional studies or any preclinical studies, whether the study, if started, will have the same target patient populations as described in this presentation, and whether and when the planned study will commence enrollment and read out data; whether the historical clinical results showing enobosarm's effect on preventing muscle wasting, increasing or maintaining muscle mass and bone density or assisting with preferential fat loss will be replicated to any significant degree or at all in the planned Phase 2b study or in any future study and whether, if approved, any such results would be seen in commercial clinical use; whether and when any of the planned interim analyses in the planned Phase 3 confirmatory study of sabizabulin for certain COVID patients or in ARDS patients or in any other trial will occur and what the results of any such interim analyses will be; whether the results of any such interim analyses or any completed Phase 3 study or any other interim data will be sufficient to support an NDA for sabizabulin for any indication; whether and when any potential NDA would be granted; whether and when the Company will meet with BARDA regarding any potential partnering opportunities and whether those efforts will be successful, and when the Company might learn the results of any potential partnering efforts with BARDA; whether and how the Company will fund the planned Phase 3 studies of sabizabulin in COVID-19 and ARDS or any other indication; whether the current and future clinical development efforts of the Company, including all studies of sabizabulin in COVID-19, ARDS, or any other infectious disease indications or enobosarm in obesity or oncology indications, and any of their results will demonstrate sufficient efficacy and safety and potential benefits to secure FDA approval of any of the Company's drug candidates; whether the drug candidates will be approved for the targeted line of therapy; whether government and private payors will provide sufficient coverage for enobosarm for obesity or any of the Company's other drugs, if approved in each case; whether the companies that develop and commercialize GLP-1 drugs for obesity will accept the use of enobosarm in combination with their respective products; whether the intellectual property portfolio for enobosarm is sufficient to protect the Company's interest in enobosarm in obesity, breast cancer or any other indication and whether it will prevent competitors from developing SARMs for the same indication or whether the Company will have the resources or be successful in enforcing its intellectual property rights; whether and how long the relative lack of competition in the obesity market for drugs and drug candidates that might help mitigate muscle wasting will continue and what the effects of any such competition might be on the Company's prospects in the sector; whether enobosarm will become a treatment, in combination or alone, for obesity or breast cancer, and whether sabizabulin will become a treatment for broad ARDS or COVID-19; whether the Company's FC2 telemedicine portal sales will grow or replace prior revenue from the U.S. prescription sales of FC2; whether the Company will recover any of the monies owed it by The Pill Club; whether and when the Company will receive the remaining installments from Blue Water in connection with the sale of ENTADFI or will receive any of the potential sales milestones related thereto and whether the Company will ever be able to liquidate the preferred stock that it owns in Blue Water; whether, when and how many shares may be sold under the Lincoln Park Capital Fund equity line; whether the cash raised by any future equity offering will be sufficient for the Company's planned or expected operations; and whether the Company's current cash will be sufficient to fund its planned or expected operations. These forward-looking statements are based on the Company's current expectations and subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to: the development of the Company's product portfolio and the results of clinical studies possibly being unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical studies and the ability to enroll subjects in accordance with planned schedules; the ability to fund planned clinical development as well as other operations of the Company; the timing of any submission to the FDA or any other regulatory authority and any determinations made by the FDA or any other regulatory authority; the Company's existing product, FC2 and any future products, if approved, possibly not being commercially successful; the ability of the Company to obtain sufficient financing on acceptable terms when needed to fund development and operations; demand for, market acceptance of, and competition against any of the Company's products or product candidates; new or existing competitors with greater resources and capabilities and new competitive product approvals and/or introductions; changes in regulatory practices or policies or government-driven healthcare reform efforts, including pricing pressures and insurance coverage and reimbursement changes; risks relating to the Company's development of its own dedicated direct to patient telemedicine and telepharmacy services platform, including the Company's lack of experience in developing such a platform, potential regulatory complexity, and development costs; the Company's ability to protect and enforce its intellectual property; the potential that delays in orders or shipments under government tenders or the Company's U.S. prescription business could cause significant quarter-to-quarter variations in the Company's operating results and adversely affect its net revenues and gross profit; the Company's reliance on its international partners and on the level of spending by country governments, global donors and other public health organizations in the global public sector; the concentration of accounts receivable with our largest customers and the collection of those receivables; the Company's production capacity, efficiency and supply constraints and interruptions, including potential disruption of production at the Company's and third party manufacturing facilities and/or of the Company's ability to timely supply product due to labor unrest or strikes, labor shortages, raw material shortages, physical damage to the Company's and third party facilities, product testing, transportation delays or regulatory actions; costs and other effects of litigation, including product liability claims and securities litigation; the Company's ability to identify, successfully negotiate and complete suitable acquisitions or other strategic initiatives; the Company's ability to successfully integrate acquired businesses, technologies or products; and other risks detailed from time to time in the Company's press releases, shareholder communications and Securities and Exchange Commission filings, including the Company's Form 10-K for the fiscal year ended September 30, 2023 and subsequent quarterly reports on Form 10-Q. These documents are available on the "SEC Filings" section of our website at www.verupharma.com/investors. The Company disclaims any intent or obligation to update these forward-looking statements.

Drug candidate pipeline
Biopharmaceutical company

Program	Mechanism	Indication	2023	2024	2025	2026
Metabolic						
Enobosarm and GLP-1 receptor agonist combination	Selective androgen receptor modulator (SARM) + GLP-1 receptor agonist	Obese or overweight elderly patients receiving a GLP-1 RA		IND; Phase 2b FPI	Phase 2b Protect muscle loss from GLP-1 data; Phase 2b Rescue open-label data	Active
Breast Cancer						
Enobosarm +/- abemaciclib combination (Lilly)	Selective androgen receptor modulator (SARM) + CDK 4/6 inhibitor	Phase 3 ENABLAR-2 AR+ ER+HER2- metastatic breast cancer (2nd line metastatic setting)*	Lilly clinical collaboration and supply agreement	Phase 3 FPI Stage 1- 160	Phase 3 data- stage 1	Open
Infectious Disease- Acute Respiratory Distress Syndrome						
Sabizabulin	Oral microtubule Disruptor Broad host targeted antiviral and anti-inflammatory agent	Phase 3 (902) study- Hospitalized COVID-19 patients at high risk for ARDS	Positive Phase 3 study Fast Track Designation			Completed
		Phase 3 (904) study - Hospitalized patients with viral ARDS**		Phase 3 FPI -408	Phase 3 data	Planned

*Subject to availability of funds **Subject to funding from government grants, pharmaceutical company partnerships, or other similar third-party external sources

Muscle loss significant side effect of GLP-1 receptor agonists weight loss drugs

HEALTH · WEIGHT-LOSS AND DIET CONTROL INDUSTRY

Weight-loss drugs like Ozempic and Wegovy may b risky for older people because they melt away all-important muscles, experts say

BY MADISON MULLER AND BLOOMBERG

September 27, 2023, 3:57 PM CDT

NEWS POLITICS U.S. NEWS WORLD NBC NEWS TIPLINE GRAPEVINE PODCAST BUSINESS HEALTH VIDEO WATCH LIVE

HEALTH NEWS

Weight loss drugs can lead to muscle loss, too. Is that a bad thing?

It's normal to lose lean mass, including muscle, during any type of weight loss intervention, but too much muscle loss can be a problem.

SCIENTIFIC AMERICAN

PHARMACEUTICALS

Ozempic and Other Weight-Loss Drugs Bear Heavy Costs and Questions for Seniors

Limited data on adults age 60 and older raise questions on whether high-priced weight-loss drugs will really help with lowering rates of chronic illness and disability

HEALTH NEWS ✓ Fact Checked

Ozempic Can Cause Major Loss of Muscle Mass and Reduce Bone Density

By Cathy Cassata on May 2, 2023 — Fact checked by Jill Seladi-Schulman, Ph.D.

Weight loss medications like Ozempic and Wegovy can help people drop pounds quickly, but they can also cause a rapid loss of muscle mass and bone density unless lifestyle changes are made. anandaBGD/Getty Images

- **Rapid weight loss from taking GLP-1 medications like Ozempic and Wegovy can cause a decrease in muscle mass, lessen bone density, and lower your resting metabolic rate, leading to sarcopenia.**
- **Sarcopenia is the gradual loss of muscle mass, strength, and function and is typically associated with aging.**
- **Lifestyle changes such as increasing protein intake and incorporating strength and resistance training can help combat muscle and bone density loss while taking GLP-1 medications.**

Currently approved GLP-1 receptor agonist drugs have demonstrated significant loss of both fat and muscle in overweight or obese patients

- **Weight loss drugs GLP-1 receptor agonists demonstrated a 6.2-17% average total weight loss[1,2]**
- **20-50% of the total weight loss is from muscle loss[1,3,4,5]**

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 18, 2021 VOL. 384 NO. 11

Once-Weekly Semaglutide in Adults with Overweight or Obesity

John P.H. Wilding, D.M., Rachel L. Batterham, M.B., B.S., Ph.D., Salvatore Calanna, Ph.D., Melanie Davies, M.D., Luc F. Van Gaal, M.D., Ph.D., Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Barbara M. McGowan, M.D., Ph.D., Julio Rosenstock, M.D., Marie T.D. Tran, M.D., Ph.D., Thomas A. Wadden, Ph.D., Sean Wharton, M.D., Pharm.D., Koutaro Yokote, M.D., Ph.D., Niels Zeuthen, M.Sc., and Robert F. Kushner, M.D., for the STEP 1 Study Group*

	Semaglutide 2.4 mg once weekly (N=1306)	Placebo once weekly (N=655)	Treatment comparison for semaglutide vs. placebo [95% CI]
Co-primary endpoint assessed in the overall population			
Body weight change from baseline to week 68 – %	−16.86	−2.44	ETD: −14.42 [−15.29; −13.55]
Body weight reduction ≥5% – proportion of participants (%) at week 68	92.4	33.1	OR: 37.0 [28.0; 49.0]

Supportive secondary endpoints assessed in the DEXA subpopulation

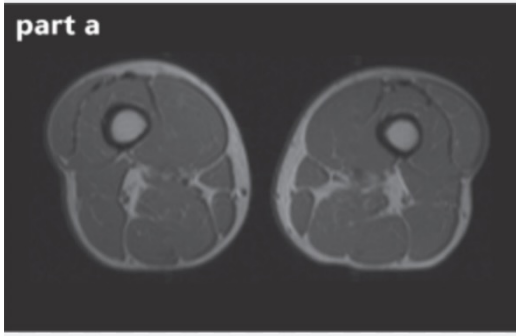
	N=95	N=45	
Body composition change from baseline to week 68 (DEXA)			
Total fat mass			
Kg change	−10.40	−1.17	ETD: −9.23 [−12.72; −5.74]
Percentage-points change in total fat mass proportion§	−4.19	−0.19	ETD: −4.00 [−6.27; −1.73]
Regional visceral fat mass¶			
Kg change	−0.47	−0.03	ETD: −0.45 [−0.60; −0.30]
Percentage-points change in regional visceral fat mass proportion‖	−2.65	0.58	ETD: −3.23 [−5.35; −1.10]
Total lean body mass			
Kg change	−6.92	−1.48	ETD: −5.44 [−7.07; −3.81]
Percentage-points change in total lean body mass proportion§	3.61	0.11	ETD: 3.50 [1.35; 5.64]

[1] Wilding JPH et al. NEJM 384:989-1002, 2021 | [2] Wegovy FDA PI | [3] Sargeant JA et al. Endocrinol Metab 34:247-262, 2019 | [4] Ida S et al. Current Diabetes Rev 17:293-303, 2021 | [5] McGrimmon RJ et al. Diabetologia 63:473-485, 2020 |

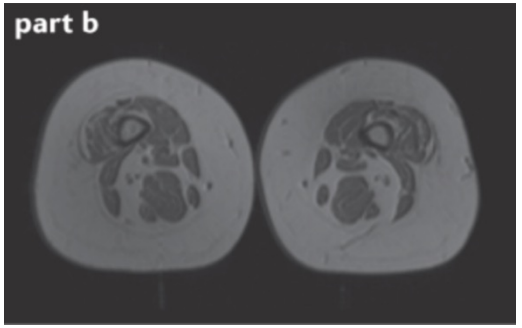
Currently GLP-1 RA drugs result in significant loss of both fat and muscle
The target population is the at risk obese or overweight patients with low muscle reserves

- **Approximately 42% of older adults (>60 yo) have obesity or overweight and could benefit from weight-loss drugs[1]**
- **Subpopulation: older obese or overweight patients with low muscle mass/ functional limitations**
  - 30% of people over 60 years old and more than 50% of those over 80 years old have sarcopenia
  - Patients with sarcopenic obesity, high fat mass with very low muscle mass, have the greatest risk to develop ***muscle weakness*** because of critically low muscle mass with weight-loss drug treatment[2-4]
  - Elderly patients with sarcopenia obesity have a higher risk of frailty/***muscle weakness***, *which can* lead to poor balance, decrease in gait, loss of muscle strength, functional limitations, mobility disability, falls and fractures, higher hospitalization rate, and increased mortality[2-4]

Normal[5]



Sarcopenic obesity[5]



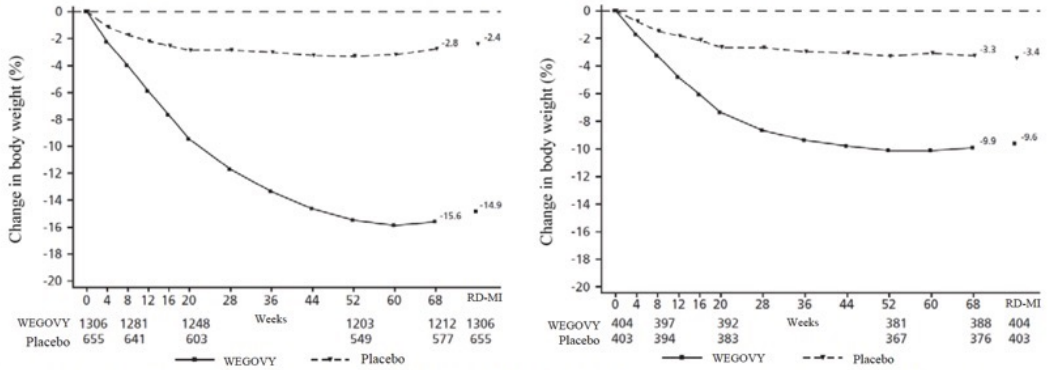
CT scans

[1] CDC | [2] Wennamethee SG et al. Current Diabetes Reports 2023 | [3] Spanoudaki M et al. Life 13:1242, 2023 | [4] Roh E et al. Front Endocrinol 11: 2020 | [5] Batsis J et al. Nature Reviews Endocrinology 14:513-537, 2018

Wegovy approval clinical studies[1]: overweight and obese adult patients
Rate of weight loss reaches a plateau

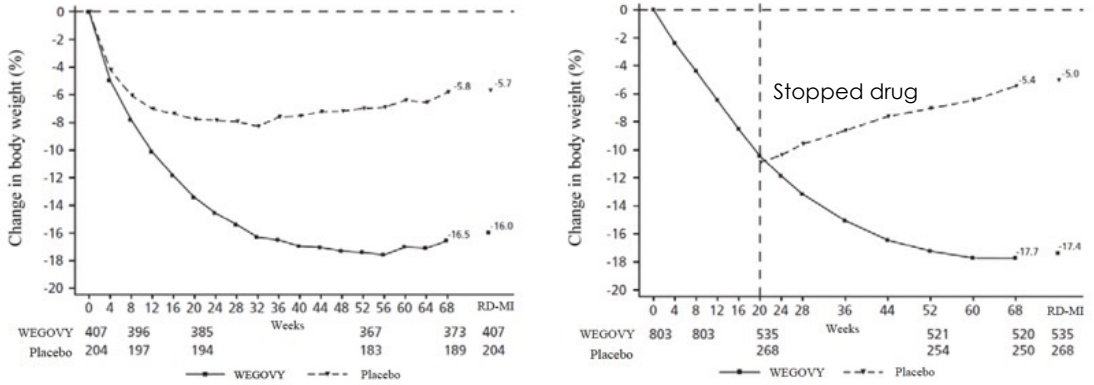
- Greatest amount of absolute total weight loss between weeks 0 and 20
- Patients who discontinued treatment at week 20 had significant weight gain (rebound)
- The reported weight gain was almost entirely fat mass not muscle
- One explanation: deficit in lean body mass (muscle) drives an increase in appetite and fat rebound regain[2,3]

Figure 6. Change from baseline (%) in body weight (Study 1 on left and Study 2 on right)



Observed values for patients completing each scheduled visit, and estimates with multiple imputations from retrieved dropouts (RD-MI)

Figure 7. Change from baseline (%) in body weight (Study 3 on left and Study 4[a] on right)



[1]FDA Wegovy PI | [2] Dulloo AG et al. Eur J Clin Nutrition 71:353-357, 2017; [3] Dulloo A Obesity 25:277-279, 2017

GLP-1 receptor agonist drug seems to have stopped working?
What do I do now and how do I stop?

The Atlantic

HEALTH

The Ozempic Plateau

Everyone hits a weight-loss plateau, but the race is on for next-generation drugs that can help patients lose even more weight.

By Sarah Zhang

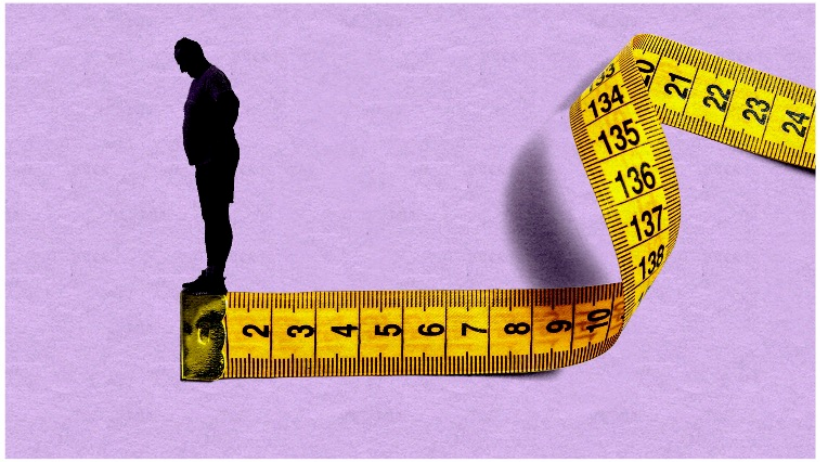


Illustration by The Atlantic. Source: Getty.

JANUARY 17, 2024, 8 AM ET SHARE SAVE

Medscape Medical News > Features

Why Do GLP-1 Drugs Stop Working, and What to Do About It?

Marilynn Larkin
January 12, 2024

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There's no question that glucagon-like peptide 1 (GLP-1) agonists represent a major advance in the treatment of obesity for patients with or without diabetes. In clinical trials, participants lost 15%-20% of their body weight, depending on the drug.

But studies also have shown that once people stop taking these drugs — either by choice, because of shortage, or lack of access — they regain most, if not all, the weight they lost.

Arguably more frustrating is the fact that those who continue on the drug eventually reach a plateau, at which point, the body seemingly stubbornly refuses to lose more weight. Essentially, it stabilizes at its set point, said Fatima Cody Stanford, MD, MPH, MPA, MBA, an obesity medicine physician at Massachusetts General Hospital and associate professor at Harvard Medical School in Boston.

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PROVIDERS

2024 Outlook: Can GLP-1 patients stop taking the drug and keep weight off?

By Noah Tong - Dec 28, 2023 7:00am

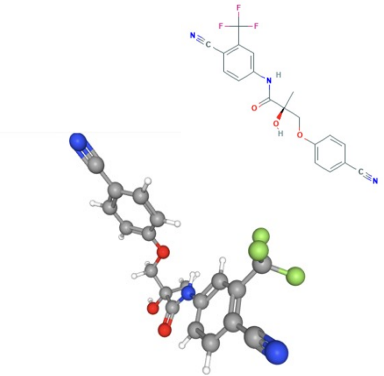
GLP-1 · weight loss · semaglutide · tirzepatide

Enobosarm is a novel oral selective androgen receptor modulator (SARM) designed to reduce fat mass and increase lean mass (muscle and bone)

Enobosarm is a nonsteroidal, selective androgen receptor agonist[1, 2]

Data from clinical trials and preclinical studies support enobosarm's potential:

- Once-a-day oral dosing
- Activates the androgen receptor, a well-established mechanism
- Tissue selective
  - Improves muscle mass and physical function[2,6]
  - Stimulates lipolysis, inhibits lipogenesis, and decreases fat mass[7,8]
  - Builds and heals bone-potential to treat bone loss/osteoporosis[3-5]
- Safety
  - Lack of masculinizing effects
  - Not converted to estrogen or dihydrotestosterone
  - No liver toxicity



Chemical structure of enobosarm

[1] Narayanan R et al. Mol Cell Endocrinol 2017 | [2] Dalton JT et al. Curr Opin Support Palliat Care 7:345-351, 2013 | [3]Kamrakova M et al Calcif Tissue Int 106:147-157,2020 | [4]Hoffman DB et al. J Bone Metab 37:243-255, 2019 | [5]Kearbey JD et al Pharm Res 26:2471-2477, 2009 | [6]Dobs AS et al. Lancet Oncol 14:335-45, 2013 | [7]Dalton JT et al. J Cachexia Sarcopenia Muscle 2:153-161, 2011 | [8] Leciejewska N et al. J Phys and Pharma 70:525-533, 2019

Enobosarm clinical data from 5 clinical trials approx. 1,000 patients conducted by GTx or Merck in subjects with and without muscle wasting

Subjects (n=)	Phase	Population	Purpose	Muscle (LBM)	Muscle strength/ function	Fat Mass	Duration	Source
120 (24 received enobosarm 3mg)	2	Males over 60 years of age and postmenopausal women (Study G200501)	Dose-finding (0.1mg-3mg) placebo controlled	3mg=1.25 kg increase (p< 0.001 compared to placebo) 3.1% increase from baseline	3mg Increase SCP (p=0.049 compared to placebo)	3mg=0.32 kg decrease (p=0.049 compared to placebo) 2-5% decrease in fat mass	12 weeks	Dalton JT J Cachexia Sarcopenia Muscle 2:153, 2011 and CSR
48 (12 received enobosarm 3mg)	2	Sarcopenic postmenopausal women (Study 003)	Double-blind placebo controlled (3mg)	3mg=1.54 kg increase (p<0.001 compared to placebo) 3.7% increase from baseline.	Bilateral leg press 3mg 21.96 lbs. increase from baseline vs placebo 1.5 lbs. increase from baseline	Not collected	12 weeks	Merck study Clinical study report (on file)
159 (41 received enobosarm 3mg)	2b	Muscle wasting cancer (Study G200502)	Double-blind placebo controlled (1 and 3 mg)	3mg = 1.27 kg (2.8%) increase (p=0.041 compared to baseline)	3mg 16.8 watt increase SCP. (p=0.001 compared to baseline)	3mg= 0.76 kg decrease in total fat mass (p=0.086 compared to placebo) 4% decrease of total fat mass	16 weeks	Dobs AS Lancet Oncology 14:335, 2013 And CSR
321 (160 received enobosarm 3mg	3	Lung cancer muscle wasting receiving cisplatin + taxane chemotherapy (Study G300504)	Double-blind placebo controlled (3mg)	0.8 kg Increase in LBM at Day 84 (p<0.001 from baseline) Higher mean slope of the change from baseline than placebo (p=0.0002 Day 84 and p<0.0001 Day 147)	5.17% Increased in SCP at Day 84 vs. -1.27% in the placebo Higher mean slope of the change from baseline (p=0.0147 at Day 84, p=0.049 at Day 147)	Not collected	21 weeks	Clinical study report (on file)
320 (159 received enobosarm 3mg)	3	Lung cancer muscle wasting receiving cisplatin + nontaxane chemotherapy (Study G300505)	Double-blind placebo controlled (3mg)	0.73 kg Increase in LBM Day 84 and 0.67 kg increase at Day 147 (p=0.013) Higher mean slope of the change from baseline compared to placebo (p=0.0111 at Day 84, and p=0.0028 at Day 147)	SCP N.S.	Not collected	21 weeks	Clinical study report (on file)

Sarcopenic= presence of low muscle mass; LBM= lean body mass; SCP= stair climb power (Watts), power exerted in a 12-step stair climb; CSR=clinical study report ; N.S.=not significant

Healthy elderly men (>60 yo) and postmenopausal women receiving enobosarm in Phase 2 double-blind placebo controlled clinical trial (G200501) demonstrated improved lean body mass and physical function

- 120 subjects enrolled
- 12 weeks of treatment

% Change in lean mass

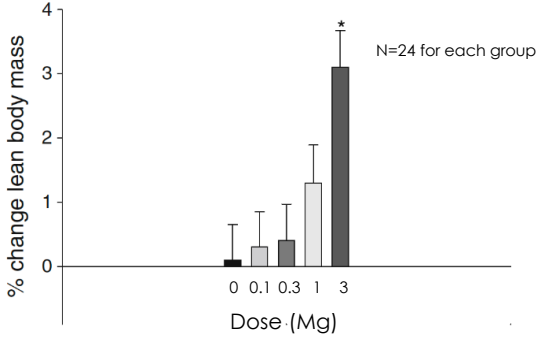


Fig. 1 Percentage change from baseline to day 86/EOS in total lean body mass: evaluable population. *EOS* end of study, *$P<0.001$ 3 mg vs. placebo (*T* test)

% Change in stair climb power

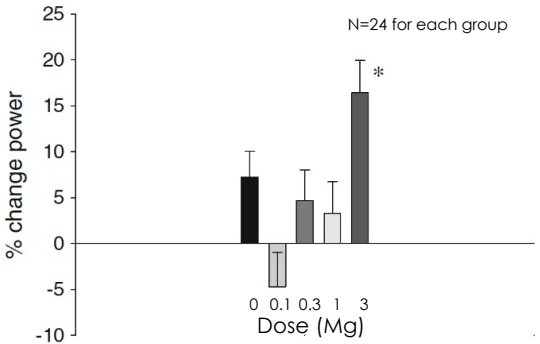
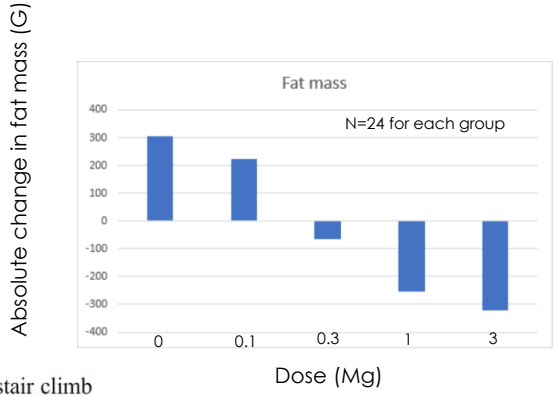


Fig. 2 Percentage change from baseline to day 86/EOS in stair climb power: evaluable population. *EOS* end of study, *$P=0.0133$ mg vs. placebo (*T* test)

Mean change in fat mass



Metabolic changes

Blood glucose was significantly decreased by an average of 6.9 ± 2.5 mg/dL in the enobosarm 3mg versus placebo (n=24; $P = 0.006$)

Blood insulin was reduced by 2.2 ± 1.1 µIU/mL in the enobosarm 3mg versus placebo (n=24; $P = 0.052$)

Insulin resistance (HOMA-IR) was reduced in the enobosarm 1-mg and 3-mg treatment groups (placebo = 2.6% ± 8.6, 1 mg = −9.3% ± 5.5, 3 mg = −27.5% ± 7.6)($P = 0.013$ 3 mg vs. placebo)

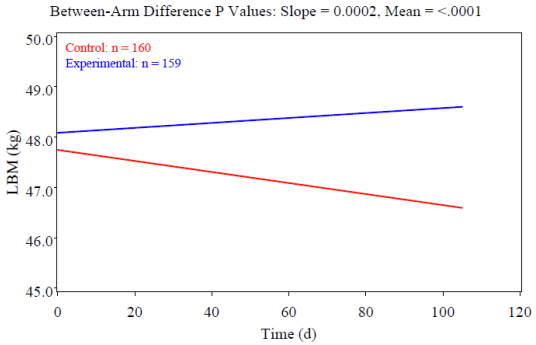
[1] Dalton JT et al. J Cachexia Sarcopenia Muscle 2:153-161, 2011 | [2] G200501 Clinical Study Report

Phase 3 randomized, double-blind, placebo-controlled 504 clinical trial of evaluating the effects of enobosarm on muscle wasting in patients with non-small cell lung cancer on first line platinum plus a taxane chemotherapy[1]

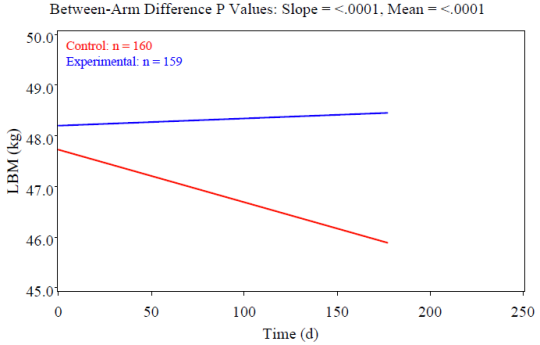
3mg enobosarm treatment in 321 subjects enrolled for 21 weeks

Lean body mass (muscle)

Up to Day 84 visit

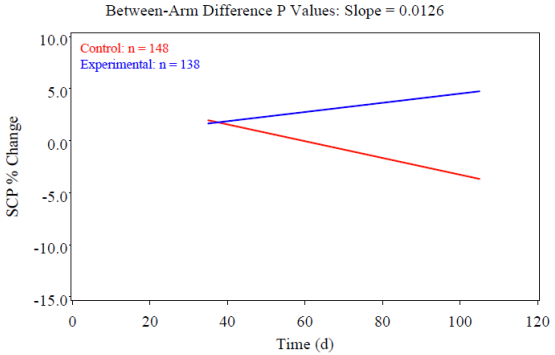


Up to Day 147 visit

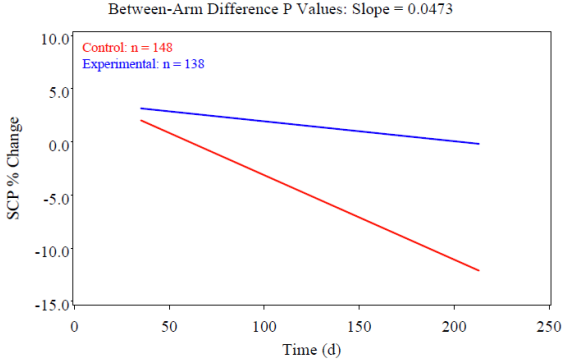


Stair climb power

Up to Day 84 visit

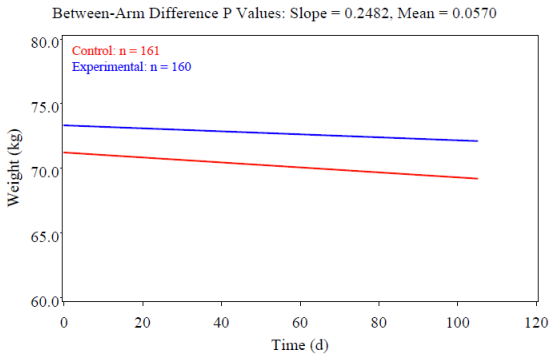


Up to Day 147 visit

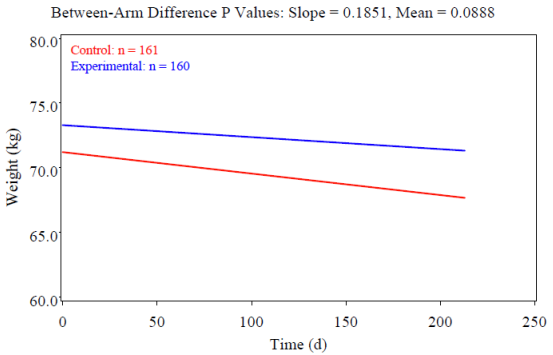


Body weight

Up to Day 84 visit



Up to Day 147 visit

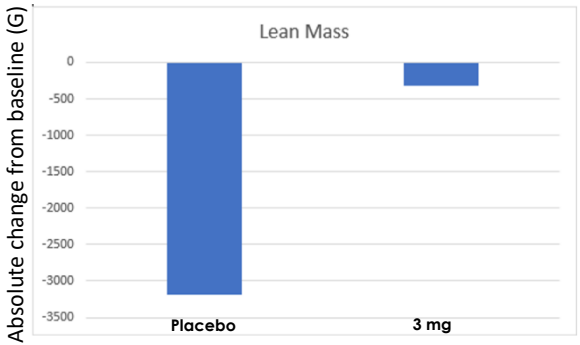


[1] Study G300504 CSR data on file Veru

Phase 3 randomized, placebo-controlled 504 clinical trial of evaluating enobosarm on muscle wasting in patients with non-small cell lung cancer on first line platinum plus a taxane chemotherapy[1]

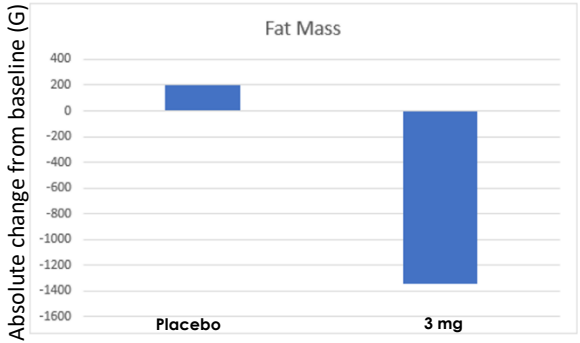
Post-hoc analysis of obese subpopulation (BMI ≥ 30)

Total lean body mass
Up to Day 84 visit



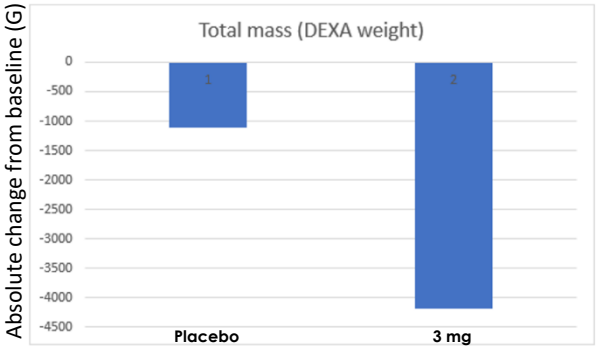
Placebo N=15, Treated N=14
Placebo corrected % change = +4.96%

Total fat mass
Up to Day 84 visit



Placebo N=15, Treated N=14
Placebo corrected % change = -5.77%

Total body weight
Up to Day 147 visit



Placebo N=12, Treated N=12
Placebo corrected % change = -4.51%

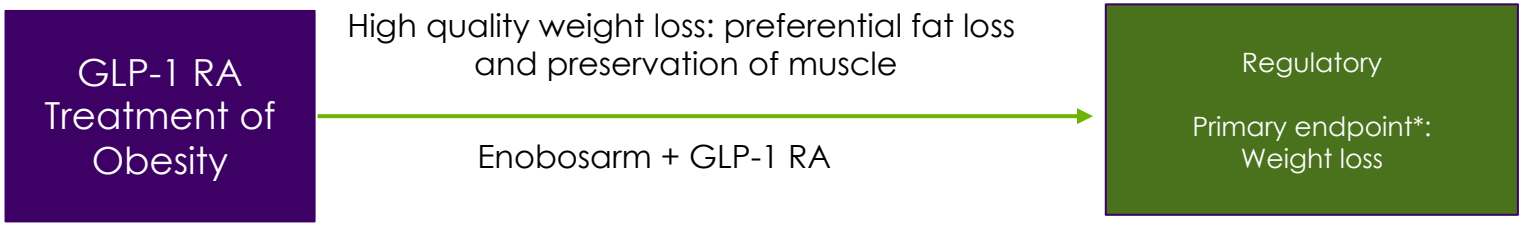
[1] Study G300504 CSR data on file Veru

Enobosarm +/- GLP-1 RA for the treatment of obesity
Clinical and regulatory strategy

Enobosarm potential direct effects:

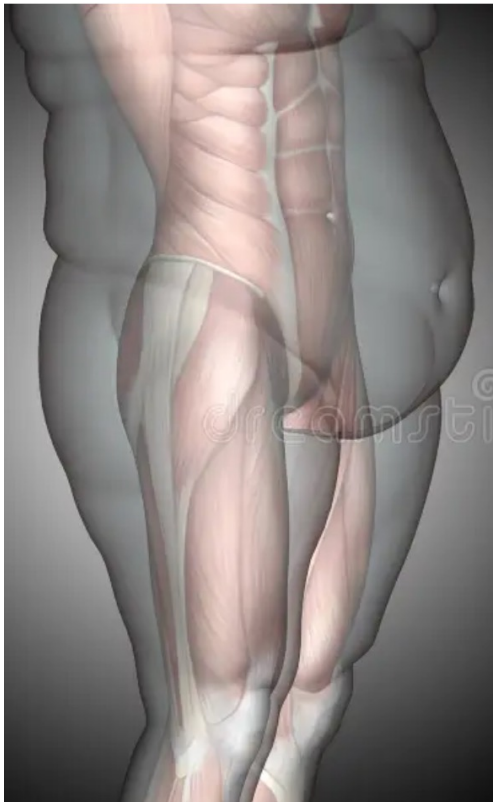
- Prevents muscle loss: active protein synthesis in muscle
- Increases fat loss: increase in lipolysis and decrease in lipogenesis

Strategy 1 - Entire obesity population



If muscle is preserved, can there still be significant weight loss?

The amount of fat mass compartment is greater than the muscle mass one



Preventing muscle loss (FFM deficit) blocks the trigger to increase in appetite[1]

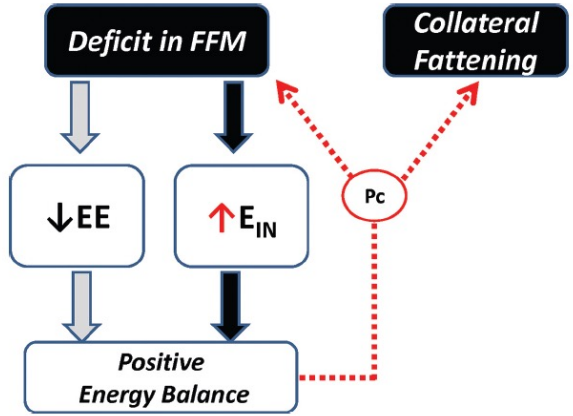
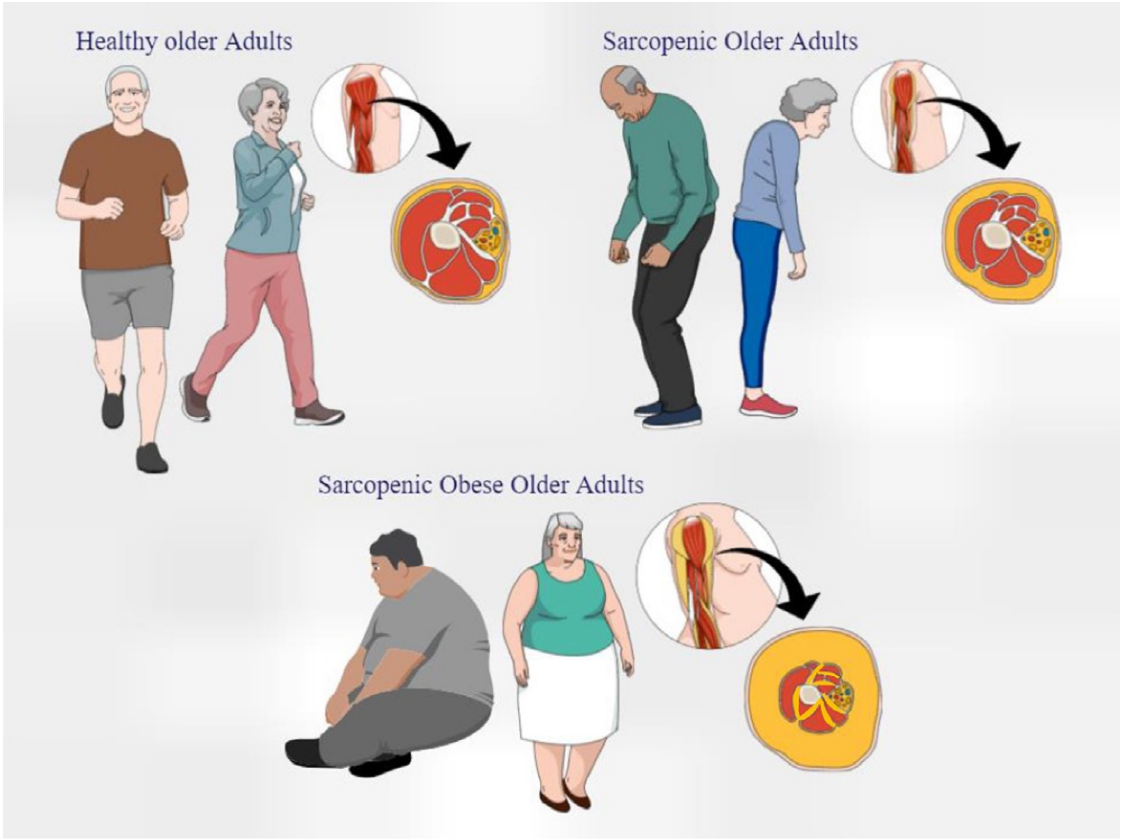


Figure 2 Concept of collateral fattening. A deficit in fat-free mass (FFM) results not only in a lower energy expenditure (EE) and hence lower energy needs for weight maintenance, but also in the activation a feedback loop that drives energy intake (E_{IN}) in an attempt to restore FFM through the lean-to-fat partitioning characteristic (Pc) of the individual (4).

[1] Dulloo A Obesity 25:277-279, 2017

Sarcopenic obese or overweight elderly patients at risk for developing muscle weakness and functional limitations when receiving GLP-1 RA for weight loss



[1] Taken from Malandrino N et al. Endocrinol Metab Clin N Am 52 (2023) 317–339

Enobosarm +/- GLP-1 RA for the treatment of obesity
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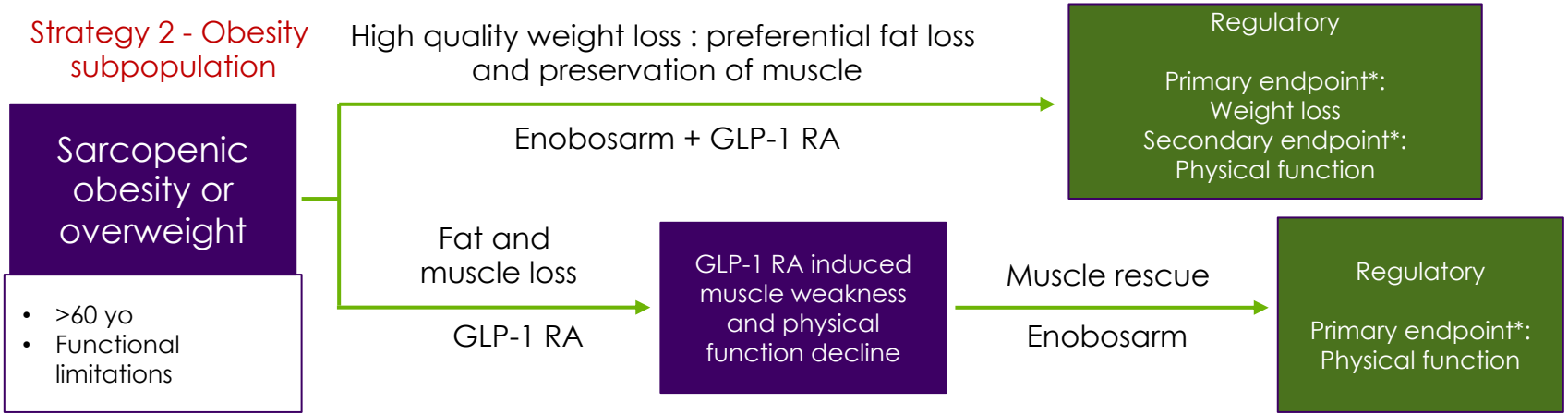
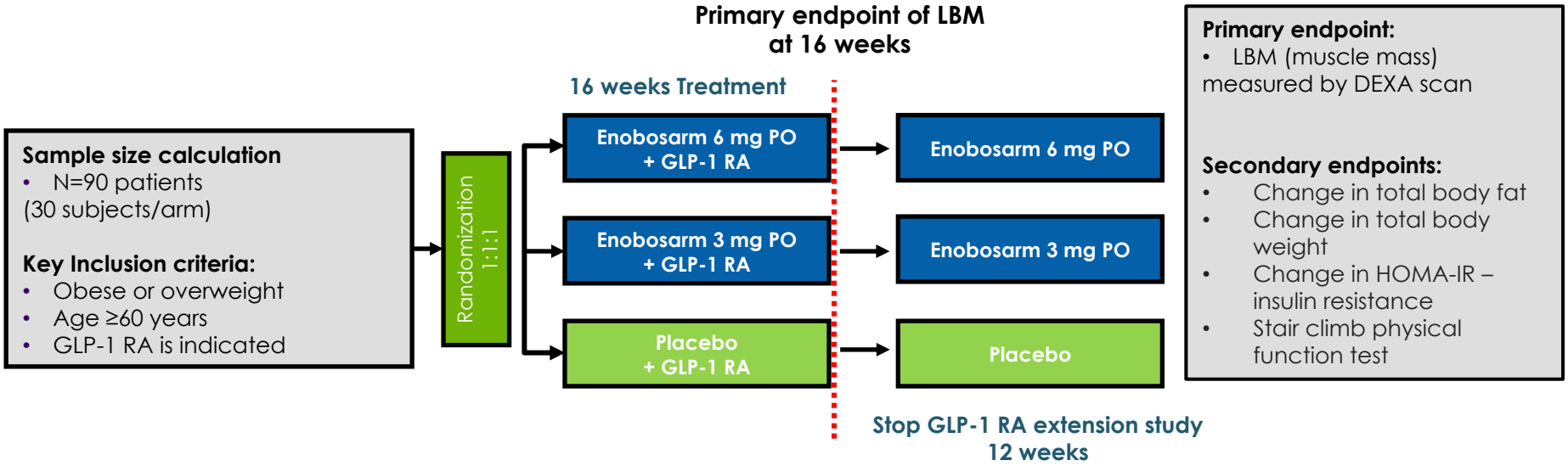


Phase 2 double-blind, placebo controlled, randomized, dose finding trial of enobosarm in preventing muscle loss and increasing fat loss in patients receiving a GLP-1 RA for weight loss

Enobosarm and GLP-1 RA combination study



- **Semaglutide treatment for obesity[1]**
  - **6.92 kg of lean body mass lost by 68 weeks (40% of total weight loss)**
  - **49% of total weight loss at 68 weeks occurred by 16 weeks**

- **Study Power Assumptions**
  - **α=0.05 (two-sided), power = 80%**
  - **1.6 kg loss in lean mass at 16 weeks in placebo group**
    - **Expect between 1.6 and 3.4 kg lean mass loss**
  - **0.3 kg loss in lean mass at 16 weeks in enobosarm groups**
    - **Expect between 0.3 kg loss and 0.4 kg gain in lean mass**

[1] Wilding JPH et al. NEJM 384:989-1002, 2021

Enobosarm has an extensive safety database

Combined Safety data from 5 Phase 2 and 3 clinical trials in cancer and healthy subjects and Phase 1 studies

Percentage of healthy and cancer subjects in all 5 clinical and Phase 1 clinical trials reporting a treatment-emergent adverse event with a frequency of ≥0.5%

MedDRAPreferred Term	Enobosarm (N=896)	Placebo (N=437)	All subjects (N=1333)
	n(%)	n(%)	n(%)
Any treatment related adverse event	*219 (24.4)*	*73 (16.7)*	*292 (21.9)*
Headache	51 (5.7)	10 (2.3)	61 (4.6)
Nausea	27 (3.0)	12 (2.7)	39 (2.9)
Alanine aminotransferase increased	19 (2.1)	2 (0.5)	21 (1.6)
Diarrhoea	19 (2.1)	12 (2.7)	31 (2.3)
Dizziness	18 (2.0)	2 (0.5)	20 (1.5)
Back pain	13 (1.5)	2 (0.5)	15 (1.1)
Constipation	12 (1.3)	3 (0.7)	15 (1.1)
Vomiting	12 (1.3)	4 (0.9)	16 (1.2)
Pain In extremity	11 (1.2)	4 (0.9)	15 (1.1)
Hyperhidrosis	9 (1.0)	1 (0.2)	10 (0.8)
Pruritus	9 (1.0)	3 (0.7)	12 (0.9)
Somnolence	9 (1.0)	0 (0)	9 (0.7)
Dyspnoea	8 (0.9)	0 (0)	8 (0.6)
Fatigue	8 (0.9)	5 (1.1)	13 (1.0)
Abdominal Pain	7 (0.8)	2 (0.5)	9 (0.7)
Hot Flush	6 (0.7)	2 (0.5)	8 (0.6)
Muscle Spasms	6 (0.7)	1 (0.2)	7 (0.5)
Myalgia	6 (0.7)	1 (0.2)	7 (0.5)
Dizziness Postural	5 (0.6)	0 (0)	5 (0.4)
Insomnia	5 (0.6)	1 (0.2)	6 (0.5)
Rash	5 (0.6)	0 (0)	5 (0.4)

Percentage of healthy and cancer subjects in all 5 clinical and Phase 1 clinical trials reporting a treatment-emergent serious adverse event with a frequency of ≥ 1%

MedDRAPreferred Term	Enobosarm (N=896)	Placebo (N=437)
	n(%)	n (%)
Any serious adverse event	*157 (17.5)*	*145 (33.2)*
Disease progression	34 (3.8)	45 (10.3)
Anaemia	18 (2.0)	14 (3.2)
Pneumonia	15 (1.7)	11 (2.5)
Neutropenia	14 (1.6)	14 (3.2)
Malignant neoplasm progression	12 (1.3)	8 (1.8)
Febrile neutropenia	10 (1.1)	6 (1.4)
Thrombocytopenia	10 (1.1)	6 (1.4)
Pulmonaryhaemorrhage	4 (0.4)	5 (1.1)
Dehydration	3 (0.3)	7 (1.6)

[1]Taken from GTx Investigator Brochure 2017

Enobosarm has an extensive safety database

- **Evaluated in 27 clinical trials comprising >1580 subjects dosed (235 subjects dosed at ≥ 9mg)**

- **Data reported from 12 Phase 1 studies:**
  - No QT effects
  - No significant drug-drug interactions[2]
  - No significant food effect
  - No significant renal or hepatic effects
  - Major metabolites analysis and route of elimination- renal elimination and only metabolite is enobosarm glucuronide
  - Cytochrome P450 3A4- enobosarm is not an inhibitor

Safety of special interest:

Elderly healthy volunteers G200502 Phase 2 study conducted by GTx[1]

	Baseline	SD	Absolute change	SD	*P* value
Total cholesterol (mg/dL)					
Placebo	195.9	35.83	4.8	17.46	
0.1 mg	197.8	27.31	−6.3	20.03	0.088
0.3 mg	204.4	29.84	−14.3	19.88	0.004*
1 mg	197.1	29.87	−19	26.34	<.001*
3 mg	203.1	35.1	−15.3	26.95	0.003*
HDL (mg/dL)					
Placebo	49.9	10.2	0	4.88	
0.1 mg	50.9	9.49	−4.3	4.72	0.027*
0.3 mg	55.3	13.99	−6.3	4.86	0.001*
1 mg	52.1	10.44	−8.9	6.18	<.001*
3 mg	52.8	10.99	−14.7	10.58	<.001*
LDL (mg/dL)					
Placebo	130	34.02	7.5	13.95	
0.1 mg	128	22.91	5.5	16.48	0.734
0.3 mg	130.7	31.57	−0.2	15.67	0.206
1 mg	125.2	23.83	3.9	27.16	0.564
3 mg	130.6	29.68	4.6	27.44	0.629
Triglycerides (mg/dL)					
Placebo	114.8	39.66	7.2	34.43	
0.1 mg	137.4	76.17	5.8	46.96	0.952
0.3 mg	126	80.69	2.4	50.18	0.838
1 mg	112.9	49.14	−12.8	31.14	0.4
3 mg	153.5	182.89	−36.6	155.64	0.06

HDL changes are similar to what has been observed for testosterone replacement

[1]Dalton JT et al. J Cachexia Sarcopenia Muscle 2:153-161, 2011 | 2: Enobosarm has not been evaluated for adverse drug-drug interactions in combination with GLP-1

Clinical drug candidates to prevent muscle loss with GLP-1 RA for obesity
Competitive Landscape

Drug	Class	Delivery	Clinical stage with GLP-1 RA	Data expected	Company	Comments
Enobosarm	Selective androgen receptor modulator	Oral	Phase 2b	2H 2024	veru	GLP-1 RA combo and GLP-1 RA rescue
Bimagrumab	Anti-myostatin Activin receptor Type 2 antagonist	IV	Phase 2	5/2025	Versanis	Acquired by Lilly for $2 billion July 2023
Apitegromab	Anti-myostatin Selective anti-latent myostatin	IV	Phase 2	Mid 2025	ScholarRock	
Taldefgrobep	Anti-myostatin	SubQ	Phase 2	Study initiating in 2Q 2024	biohaven pharmaceuticals	
KER-065	Selective activin receptor ligand trap Anti-myostatin	SubQ	Phase 1	Q1 2025	KEROS THERAPEUTICS	
Trevogrumab	Anti-myostatin	Injectable	Initiating Phase 2	Not specified	REGENERON	
Azelaprag (BGE-105)	Apelin receptor agonist	Oral	Phase 2	Study initiating in 2024	BioAge Labs (Private)	Doing study with Lilly (Mounjaro)

Enobosarm and GLP-1 receptor agonists
Target product profile

- **Enobosarm is a nonsteroidal, selective androgen receptor agonist that targets the androgen receptor, a well-established mechanism of action[1,2]**

- **Data from clinical trials and preclinical studies support enobosarm's potential:**
  - Administration: Once-a-day oral dosing
  - Efficacy
    - Avoidance of muscle loss - improves muscle mass and physical function[2,6]
    - Reduction of fat mass - stimulates lipolysis and inhibits lipogenesis[7,8]
    - Metabolic effects- decrease glucose, lowers insulin, and reduces insulin resistance
    - Builds and heals bone-potential to treat bone loss/osteoporosis[3-5]
  - Safety
    - Large safety database
    - Not converted to estrogen or dihydrotestosterone
    - Lack of masculinizing effects in women
    - No liver toxicity
    - Minimal GI side effects: frequency of nausea, vomiting, and diarrhea are similar to placebo[9]

[1] Narayanan R et al. Mol Cell Endocrinol 2017 | [2] Dalton JT et al. Curr Opin Support Palliat Care 7:345-351, 2013 | [3]Kamrakova M et al Calcif Tissue Int 106:147-157,2020 | [4] Hoffman DB et al. J Bone Metab 37:243-255, 2019 | [5] Kearbey JD et al Pharm Res 26:2471-2477, 2009 | [6]Dobs AS et al. Lancet Oncol 14:335-45, 2013 | [7]Dalton JT et al. J Cachexia Sarcopenia Muscle 2:153-161, 2011 | [8] Leciejewska N et al. J Phys and Pharma 70:525-533, 2019 | 9: Taken from GTx Investigator Brochure 2017

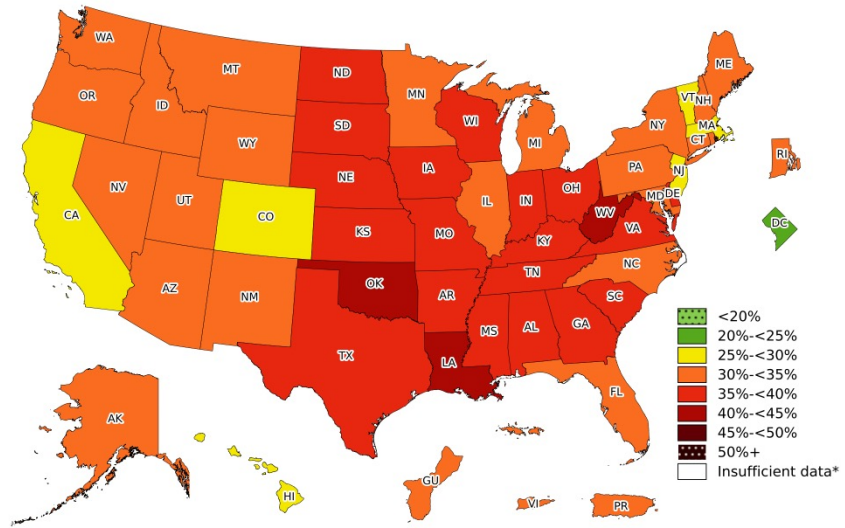
Preventing muscle loss with weight-loss drugs
Global obesity and overweight market projected to be $100 billion by 2030 (Barclays)

US obesity market[1-3]

- 45.9% of adult men aged 40-59 yo
- 38.4% of adult men aged 60+ yo
- 42.8% of adult women aged 40-59 yo
- 44.2 of adult women agreed 60+ yo
- 41.5% of adults > 60 yo
  - 34.4% also have sarcopenia

Overall obesity[1]

Prevalence† of Obesity Based on Self-Reported Weight and Height Among U.S. Adults by State and Territory, BRFSS, 2022



Source: Behavioral Risk Factor Surveillance System

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

†Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

[1]CDC 2022 | [2] Malenfant J J Glob Health Rep 3:e2019045, 2019 | [3]Lutski M et al. Prev Chronic Dis 17:200167, 2020

Financial highlights

Fiscal Year 2023 Results of operations	
FYTD 2023 Net Revenues	$ 16.3 mm
FYTD 2023 Gross Profit	$ 7.6 mm
FYTD 2023 Operating Loss	$ 93.7 mm

Q1 Fiscal Year 2024 Results of operations	
Q1 FY 2024 Net Revenues	$ 2.1 mm
Q1 FY 2024 Gross Profit	$ 1.2 mm

Balance Sheet as of December 31, 2023	
Cash	$ 40.6 mm
US/UK NOL carryforward	$140.5/63.0 mm
Common Shares Outstanding[1]	146.4 mm

[1] An aggregate of 17.2 million stock options and stock appreciation rights are outstanding and are, or could potentially be, dilutive in excess of the 146.4 million common shares above

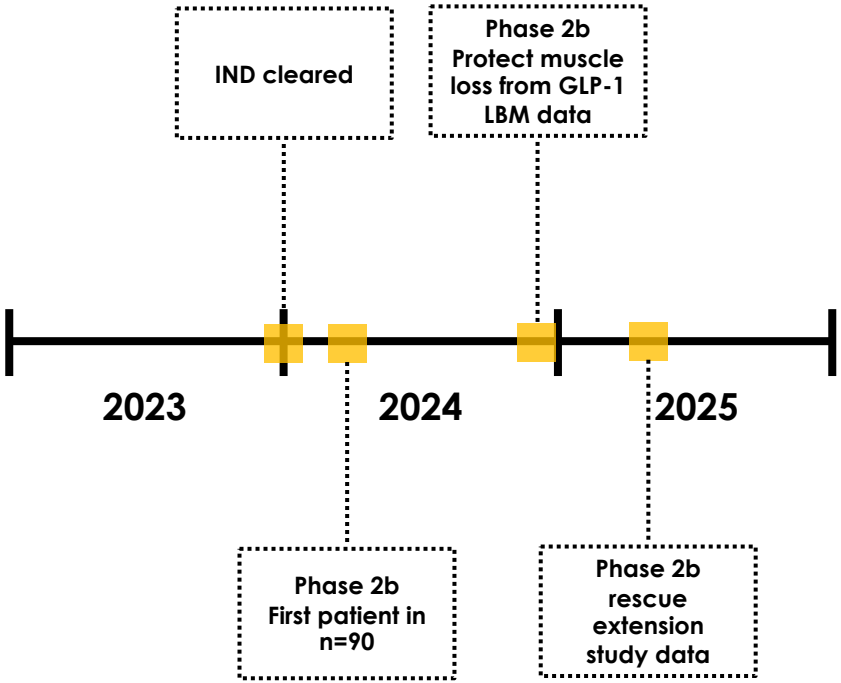
Metabolic diseases program
Clinical milestones

Obesity Program

Drug candidates
Enobosarm and GLP-1 receptor agonist combination

Mechanism
Selective androgen receptor modulator (SARM) + GLP-1 Receptor agonist

Indication
Prevent muscle loss in obese or overweight elderly patients receiving a GLP-1 RA



Enobosarm for weight loss–IP portfolio and regulatory protection create significant barriers to entry

- Enobosarm is a new chemical entity
- Enobosarm issued specific molecule composition of matter patents and issued specific molecule composition of matter polymorphs patents – Last expiry patent term (6 patents) 2028-2029 (latest is US 7,968,603 directed to composition of matter of enobosarm polymorph form)
- Enobosarm and SARMS pending methods of use (combination with GLP-1 receptor agonist / use in chronic weight management) – Last patent expiry (1US provisional) 2044
- Enobosarm – USPTO/FDA – May qualify for 5 additional years patent term extension
- Japan - enobosarm new chemical entity (NCE) exclusivity - May qualify for 7.5 Years from registration (NDA approval)
- Europe - enobosarm as a new chemical entity - May qualify for 10 years market exclusivity term
- Composition of matter formulation patent: New modified release tablet development in process