Abram THERAPEUTICS

Pioneering first in class Obeisty treatment through
TRANSIENT amino acid starvation

Outline

- Team and vision
- Market and unmet needs
- Rationales and mode of actions
- Differentiation from GLP-1R agonist
- Risks mitigation
- Path to clinical proof of concept data

Company overview

Founders and Management Team

Prof. Thomas Leung
Co-founder

The Hong Kong Polytechnic University 香港理工大學

Imperial College London

University of Oxford

- 20+ year of arginase discovery
- First in the world to create engineered arginase for clinical use
- Modified arginase licensed to two clinical stage companies

Prof. Alisa Shum
Co-founder

CU Medicine 香港中文大學醫學院 Faculty of Medicine The Chinese University of Hong Kong

University of Glasgow

University of Oxford

University of Cambridge

- 20+ years of obesity and metabolism study
- Expert in pre-clinical mouse models in obesity and other metabolic diseases

Dr. Bill Wong
Chief Executive Officer

Abram Therapeutics

Bristol-Myers Squibb

Johnson & Johnson

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- +11 year of drug development experience
- 3 IND submissions
- 3 investment deals closed

Mission and Vision

Mission: Pioneering first in class Obesity treatment through TRANSIENT amino acid starvation

Vision: One drug to treat Obesity inter-related diseases

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Reported concerns over GLP-1R agonist

- Daily appetite suppression using GLP-1R agonist is significantly associated with depression and gastrointestinal discomfort, resulting in discontinuation rates of 26.2%, 30.8%, and 36.5% at 3, 6, and 12 months, respectively[1]

- Reductions in lean mass range between 40% and 60% as a proportion of total weight lost[2]

- Approximately 18% of patients regained all the weight they had lost within one year after discontinuing the medication[3]

1. Do D et al. GLP-1 receptor agonist discontinuation among patients with obesity and/or type 2 diabetes. JAMA Netw Open. 2024;7(5):e2413172-
2. Neeland, I. J., (2024). Changes in lean body mass with glucagon-like peptide-1-based therapies and mitigation strategies. *Diabetes Obesity and Metabolism*, *26*(S4), 16–27
3. https://www.webmd.com/obesity/news/20240124/many-patients-who-stop-weight-loss-drugs-keep-pounds-off-study

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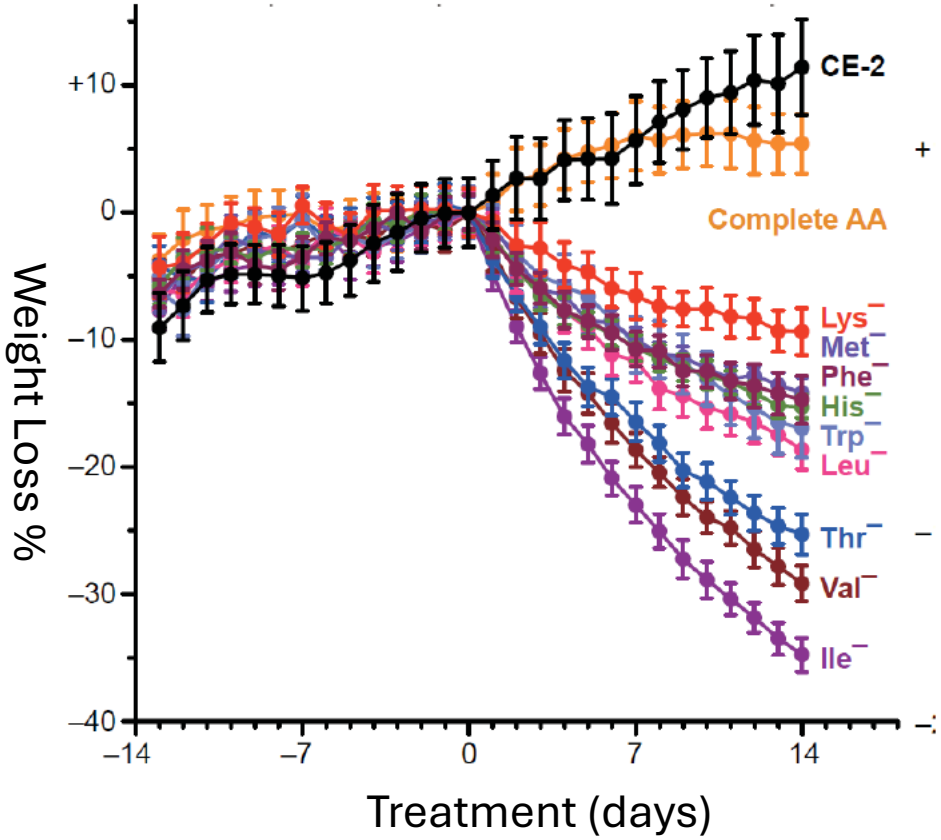
The next wave of weight loss drug

Prior human and animal studies linking ABCD and amino acid metabolism

- High serum levels of arginine, leucine and other amino acids are highly correlated with obesity[1]
- Deficiency of amino acids such as leucine and cysteine in mice have been shown to induce weight loss through utilization of fat mass[2-3]
- Arginine depletion can promote weight loss in mice [4]
- Loss of appetite and insufficient weight gain as drug specific adverse event reported in cancer patients taking arginine depletion agent [5]



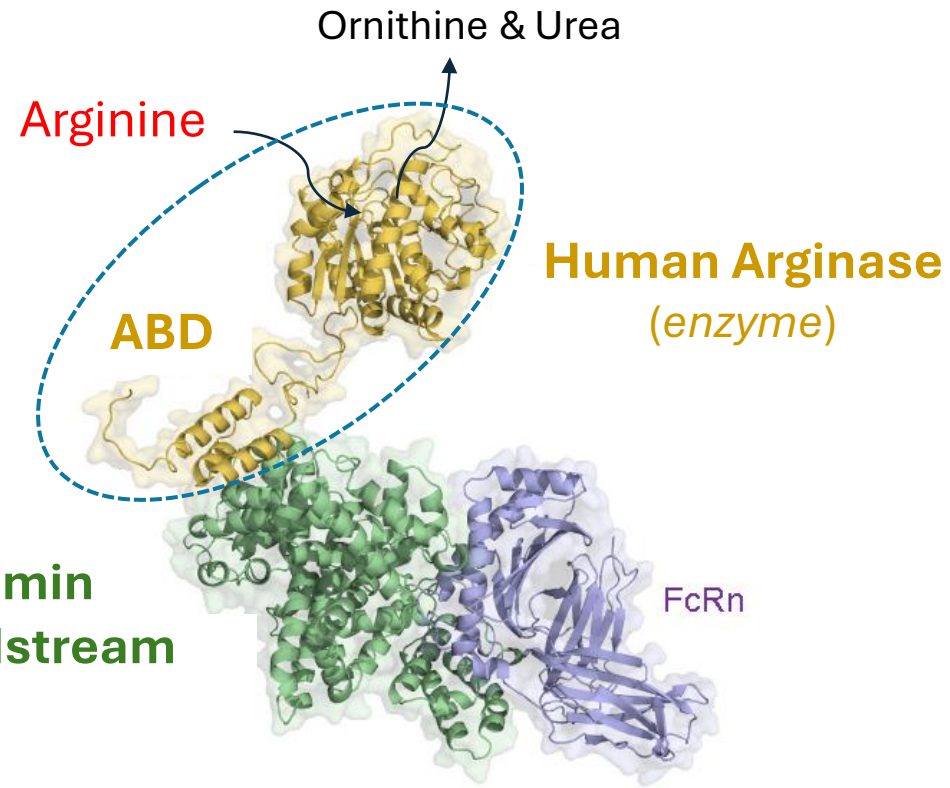
1. Moran-Ramos et al., (2017). An Amino Acid Signature Associated with Obesity Predicts 2-Year Risk of Hypertriglyceridemia in School-Age Children. Scientific Reports, 7(1)
2. Varghese, A., et al., (2024). Unraveling cysteine deficiency-associated rapid weight loss. *bioRxiv (Cold Spring Harbor Laboratory)*
3. Cheng, Y., et al.,(2009). Leucine deprivation decreases fat mass by stimulation of lipolysis in white adipose tissue and upregulation of uncoupling protein 1 (UCP1) in brown adipose tissue. Diabetes, 59(1)
4. Zhang, Y et al. (2022). Pegylated arginine deiminase drives arginine turnover and systemic autophagy to dictate energy metabolism. *Cell Reports Medicine*, *3*(1), 100498
5. https://aacrjournals.org/cancerres/article/78/13_Supplement/CT030/630941/Abstract-CT030-Phase-I-dose-escalation-trial-of

Stress our body with TRANSIENT arginine starvation

- Eliminating a specific amino acid from the diet is impractical, necessitating medical intervention
- The absence of essential amino acids, such as lysine, can have severe consequences, leading to mortality in mice
- Our drug can transiently lower intra-cellular level of arginine to provide a stress signal without the risk of long term depletion

Albumin binding domain (ABD) to extend arginase half life

ABarginase



Circulatory half-life of native human arginase: ~ 30 min

Circulatory half-life of ABarginase extended to 4 days

LONG-ACTING: One dose per week

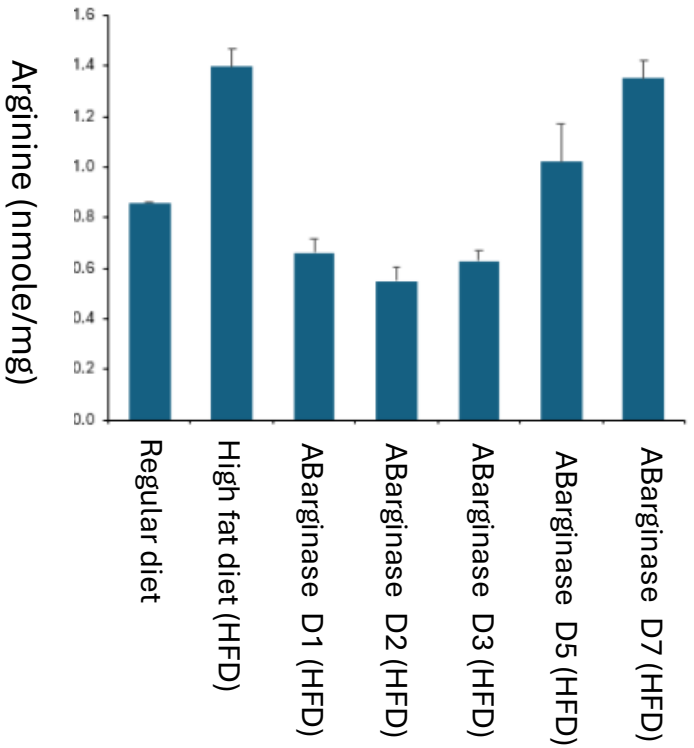
Transient arginine starvation reduces obesity through multiple mechanisms

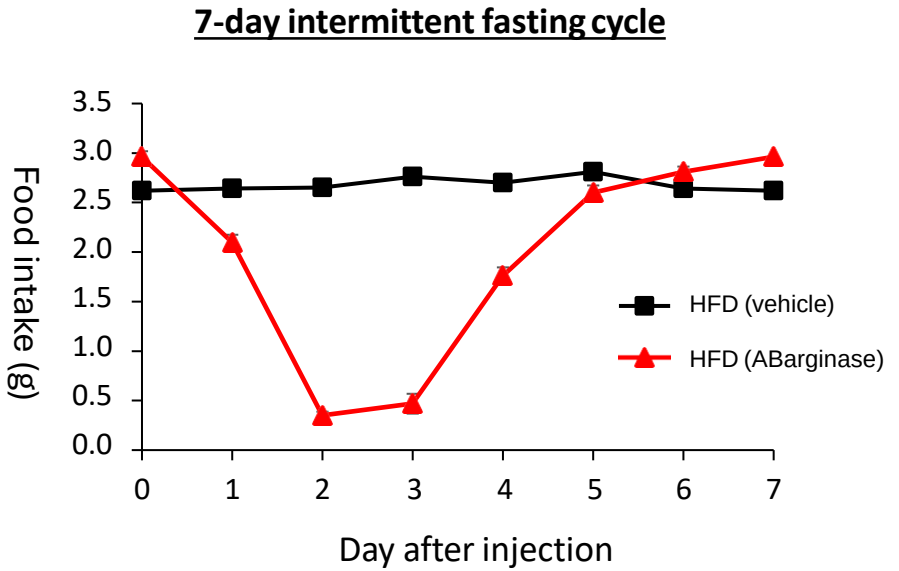
ABarginase

Appetite suppressants	Energy storage Blocker	Exercise mimetics	Muscle perservation
GLP-1 receptor agonist	GIP inhibitor	Apelin receptor agonist	Activin receptor II inhibitor
GLP-2 receptor agonist	INHBE modulator	FGF21 agonist	Myostatin inhibitor
Amylin	**Acc1 inhibitor**	**UCP1 activator**	**Muscle stem cell promoter**
Cannabinoid Agonist	**Fasn inhibitor**	**NLRP3 inhibitor**	
Insulin sensitizer	**Scd1 inhibitor**		
Hypothalamus AMPK inhibitor	**Lipophagy inducer**		
Intermittent fasting			

Bolded underlined MOA is observed using ABarginase

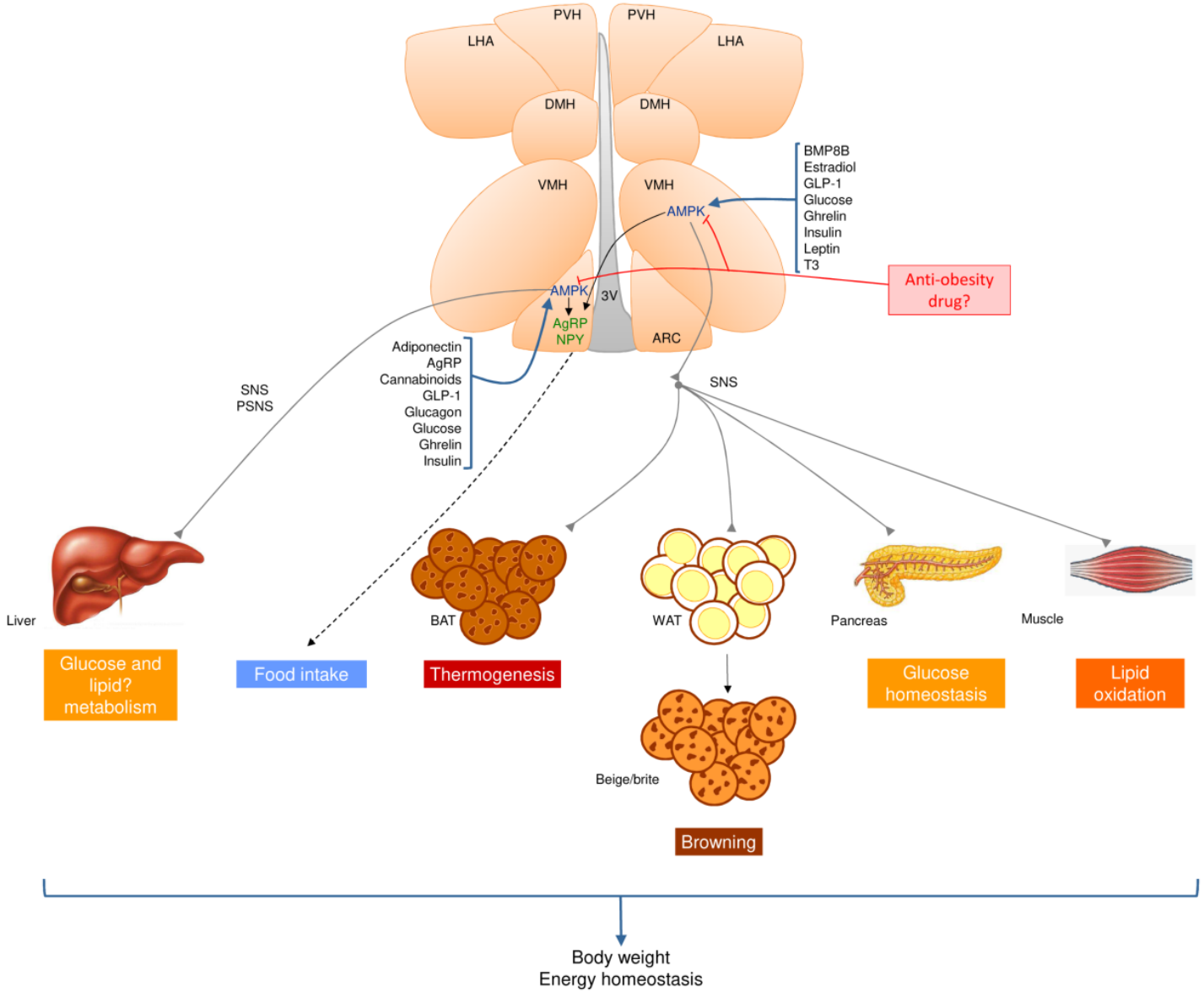
TRANSIENT low level of arginine in hypothalamus contributes to 7 day intermittent fasting cycle



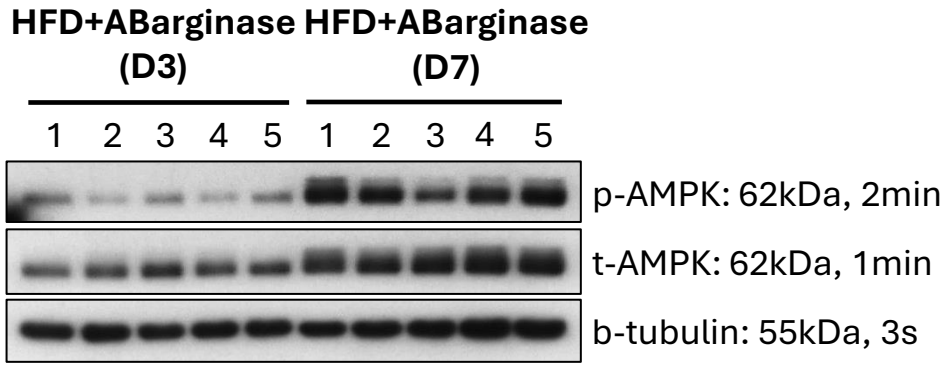


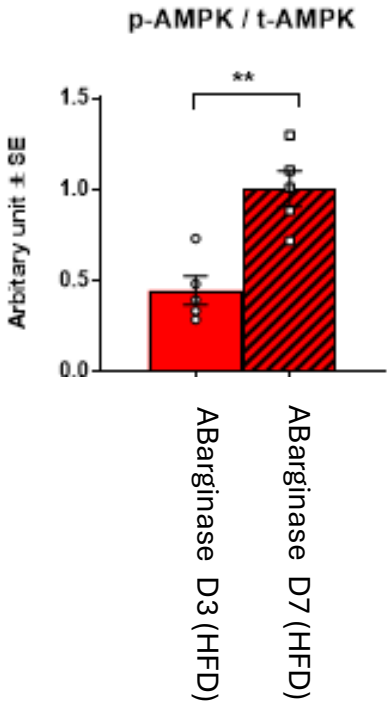
* Mice remain active and burn fat in metabolic cage during the fasting period

Inhibition of AMPK activation accounts for the low food intake

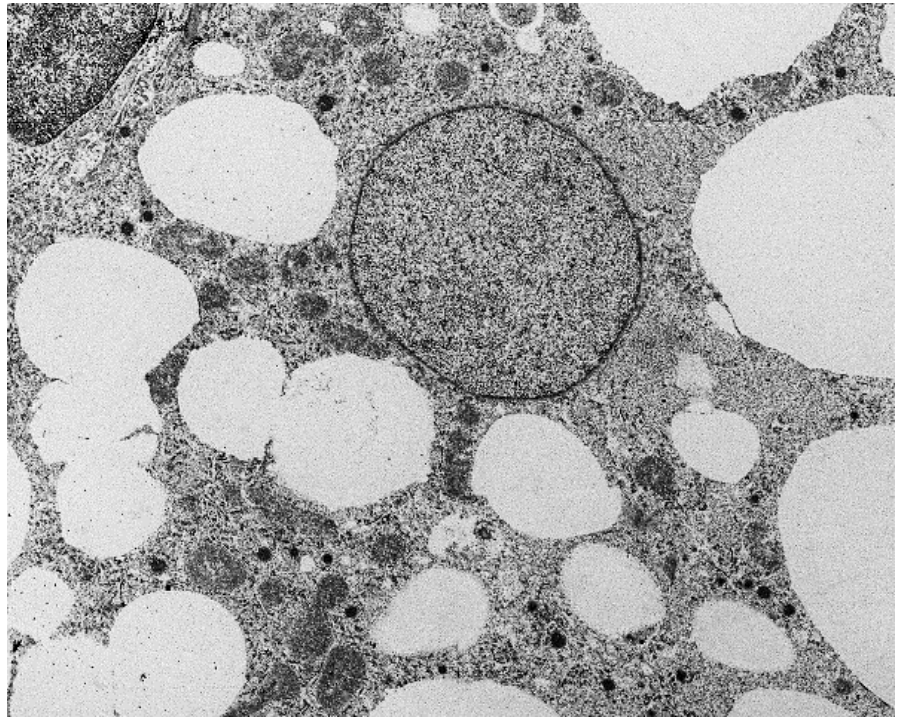


López, M. (2017). EJE PRIZE 2017: Hypothalamic AMPK: a golden target against obesity? *European Journal of Endocrinology*, *176*(5)



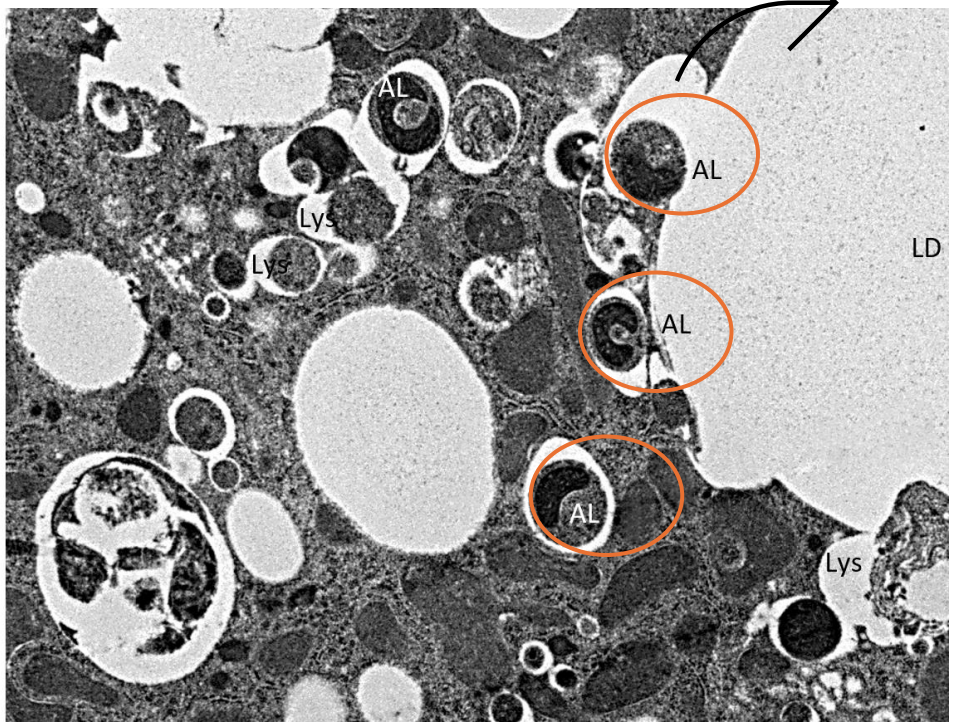


Lipophagy inducer



Fatty Liver in obese mice

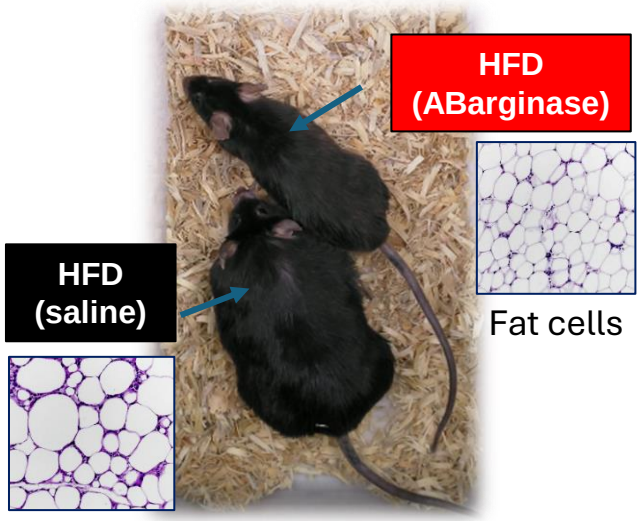
Large number of autolysosome degrading lipid droplet



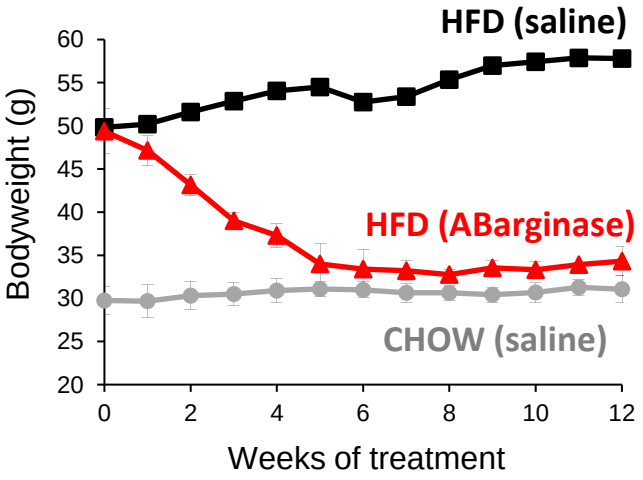
After drug treatment

AL: autolysosome
LD: lipid droplet

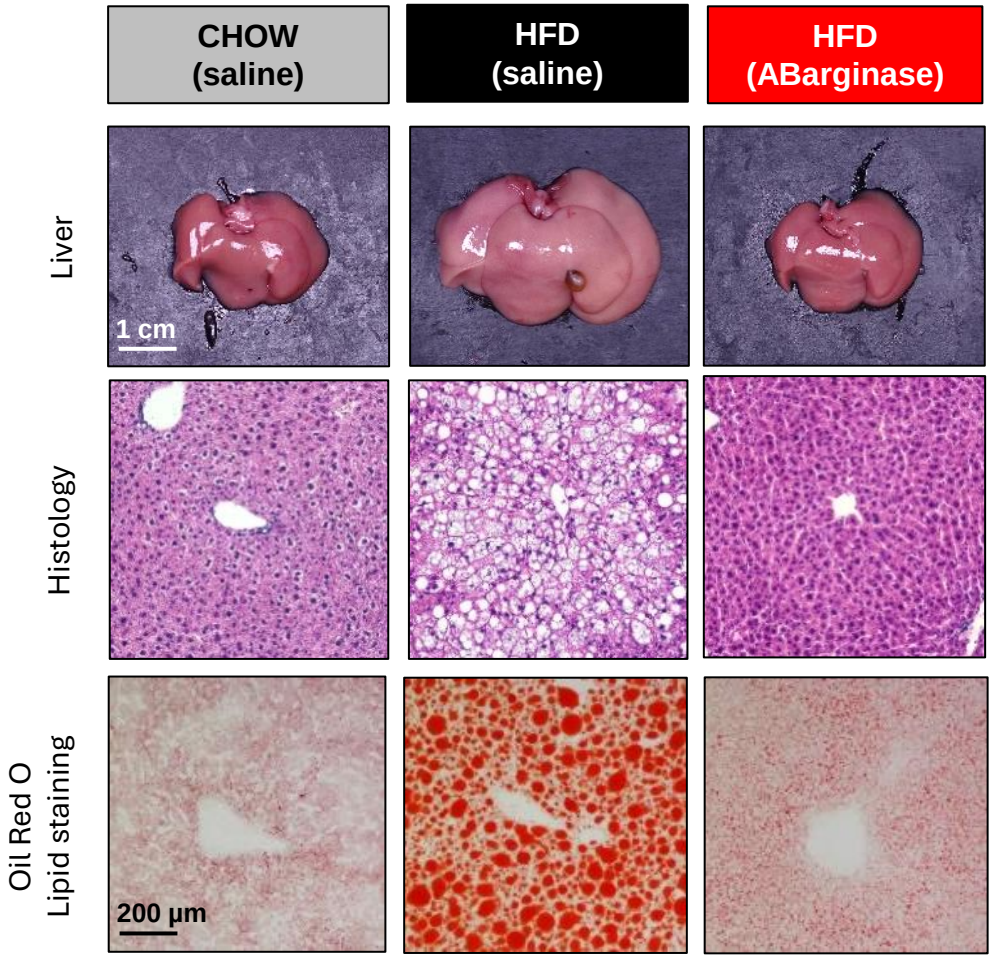
Reverse obesity



High-Fat Diet (HFD) induced obese mice

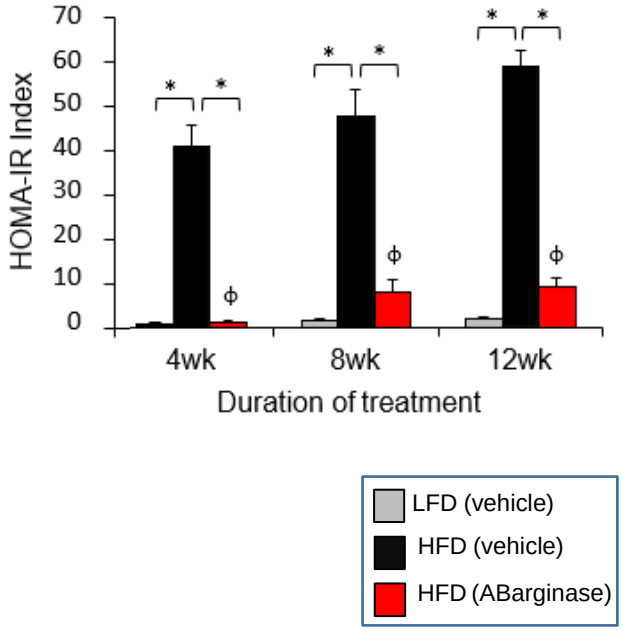


Reverse fatty liver



After 12 weeks of once-weekly treatment

Reverse insulin resistance



12 weeks of once-weekly treatment

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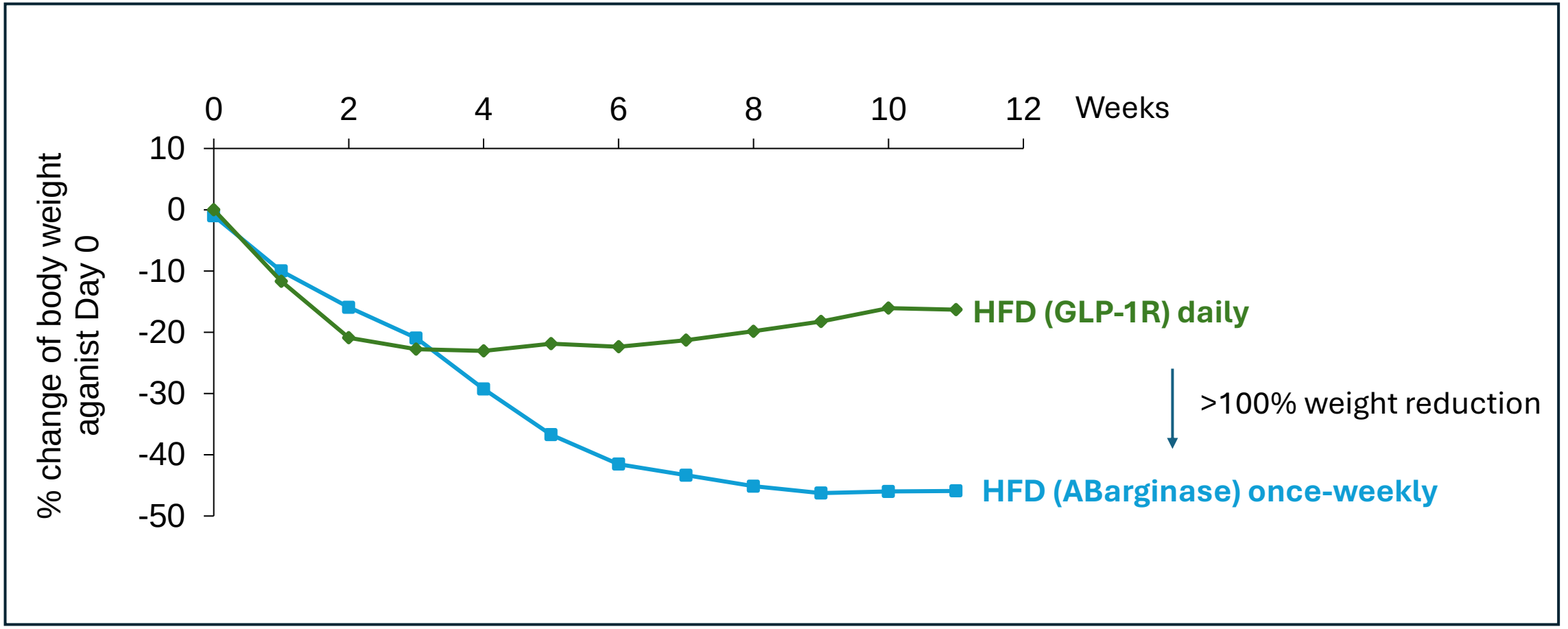
ABarginase

vs

novo nordisk®

Semaglutide
(GLP-1R agonist)

Enhanced body weight reduction

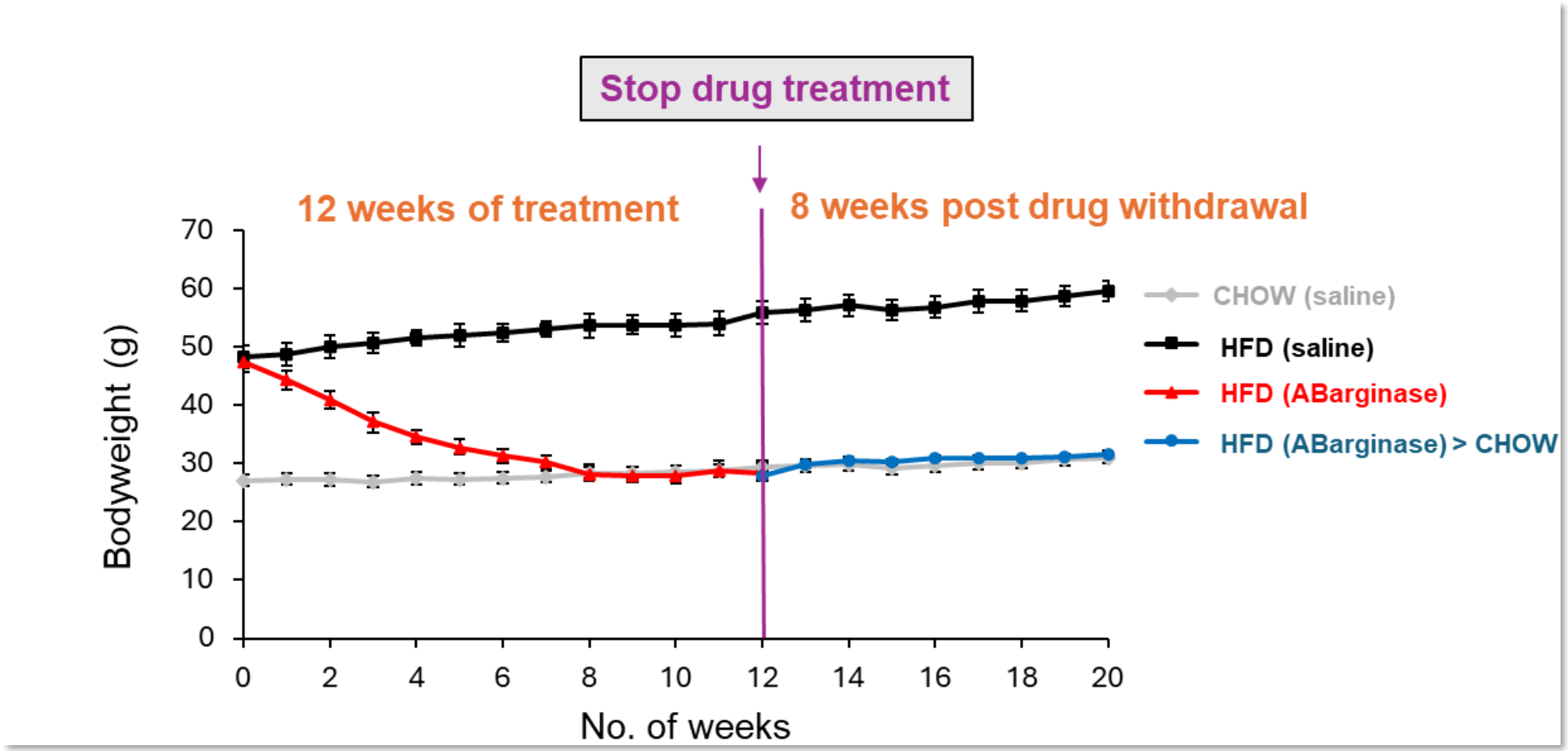


Normalization of body composition

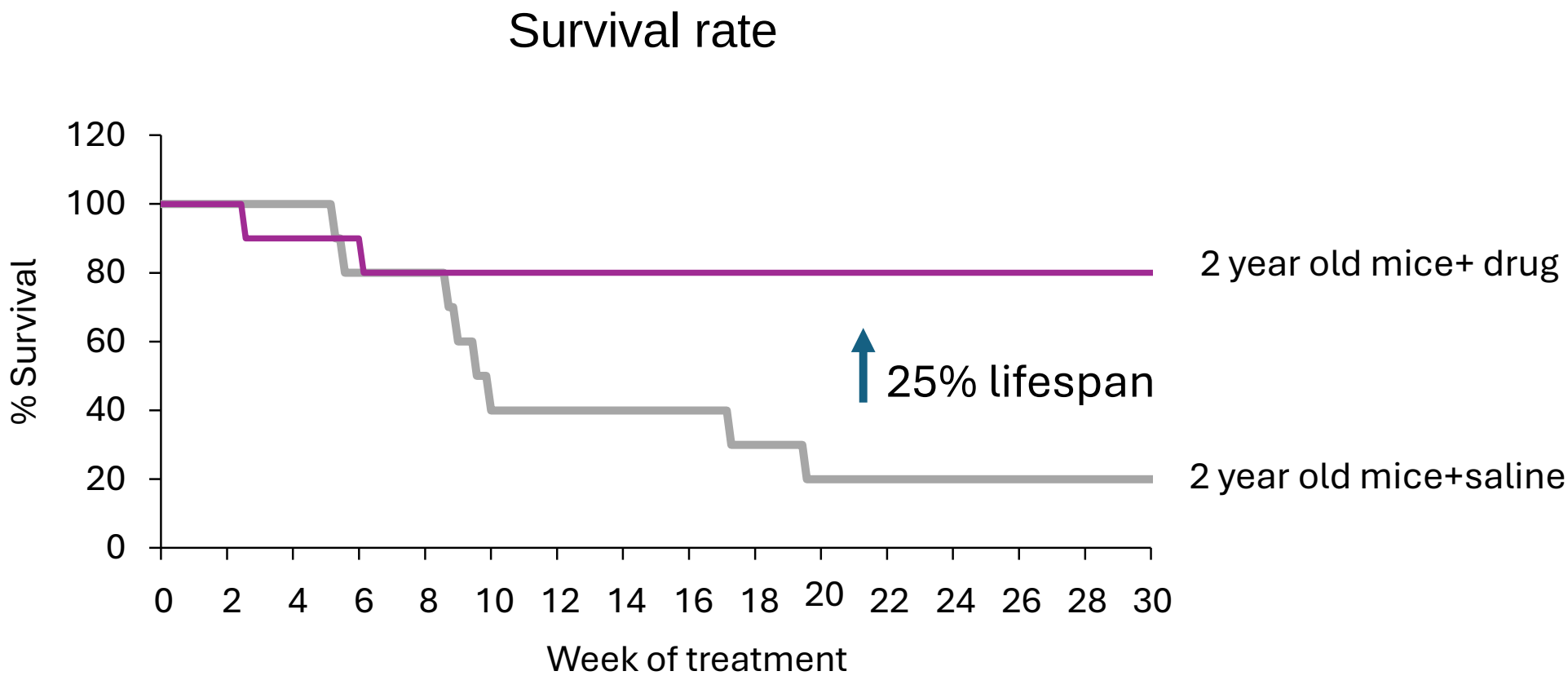
0 week	ABarginase	Semaglutide
Fat composition (%)	39	41
Lean mass composition (%)	50	49

9th week treatment	ABarginase	Semaglutide
Fat composition (%)	21 ↓	39
Lean mass composition (%)	70 ↑	50

No bodyweight rebound



Extended Lifespan



Differentiation from GLP-1R agonist

	ABarginase (Preclinical)	GLP-1R agonist (Preclinical and Human)
Weight loss	Weight loss close to 50%	Weight loss close to 23% (Preclinical)
Body composition	21% fat and 70% lean mass	39% fat and 50% lean mass (Preclinical)
Lipophagy	Liver	Not being reported
Appetite suppression	Intermittent fasting	Daily suppression (Preclinical and Human)
Pancreatitis	No enlargement of pancreas	Enlargement of pancreas (Preclinical) 146% higher risk of pancreatitis (Human)
Insulin	Improved insulin sensitivity	Increased insulin production (Preclinical and Human)
Bodyweight rebound	No rebound of bodyweight	Rebound of bodyweight in 18% of the patients (Human)
Lifespan	Extended lifespan by a minimum of 25%	Not being reported
Cancer risk	Prevent HCC occurrence	Black box warning: increased risk of thyroid cancer (Preclinical and Human)

Strong IP position

- Composition and application patents filed in 14 jurisdictions, including USA and Europe
- 5 Patents granted including EU
- Patents expire in 2039
- Broad claims covering over 20 disease indications

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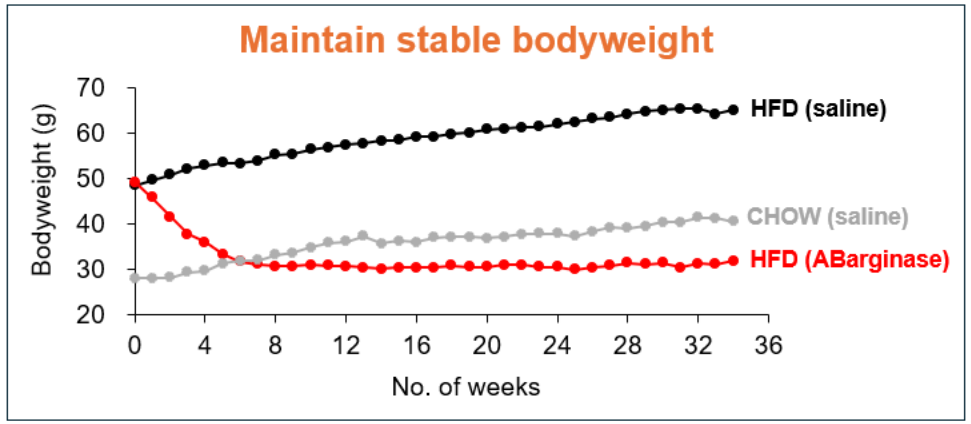
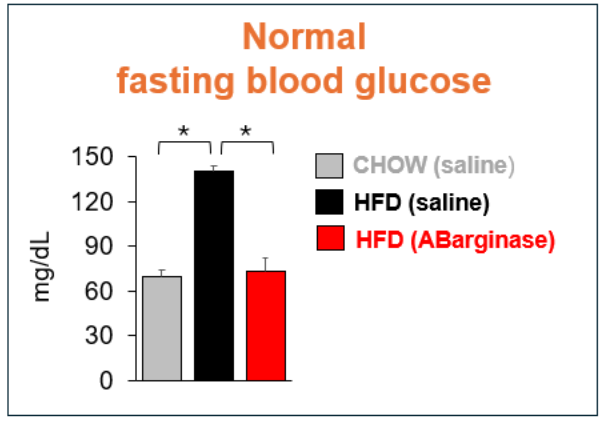
Risks mitigation

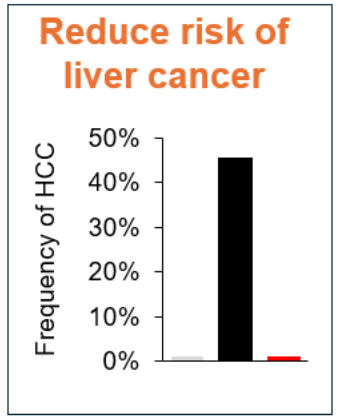
Risks	Mitigation measures
Safety: Long term arginine depletion may lead to cardiovascular problems and other health issues	Administration of ABarginase at efficacious levels over the course of a year did not cause any observable toxicity and cardiovascular problems
Efficacy: Generation of neutralizing antibody may lead to drug resistance	No drug resistance observed over a year of treatment
Efficacy: Efficacy in mice does not translate in human setting.	Weight loss in animal models is positively correlated with the weight loss observed in humans[1]
Patient compliance: Intravenous drug administration may restrict patient compliance	Subcutaneous formulation has been developed and validated
Production scale up: Compromised protein yield and purity from 2L to 30L culture	We have achieved production of over 2.0 g/L purified protein in 30L fermenter

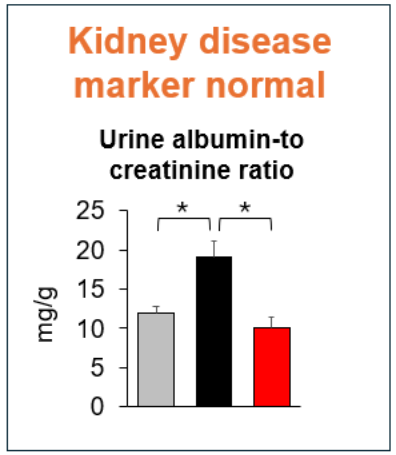
1. Anti-obesity drug discovery: advances and challenges *Nat Rev Drug Discov* 2022, 21(3):201-223.

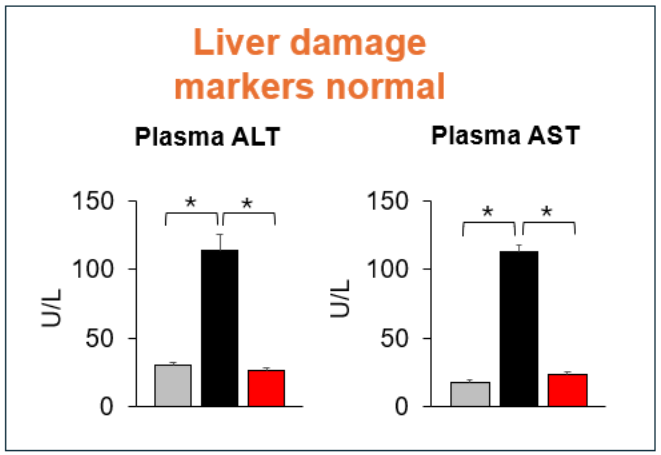
8-month safety data

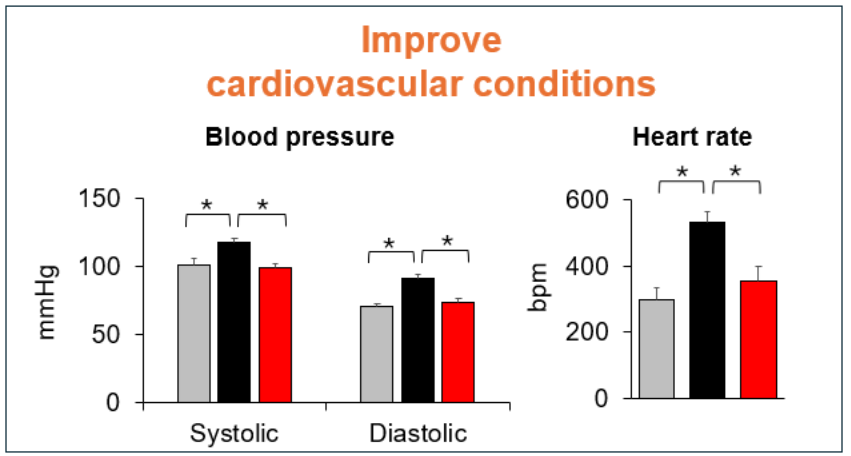












*p < 0.05, one-way ANOVA followed by Tukey's test

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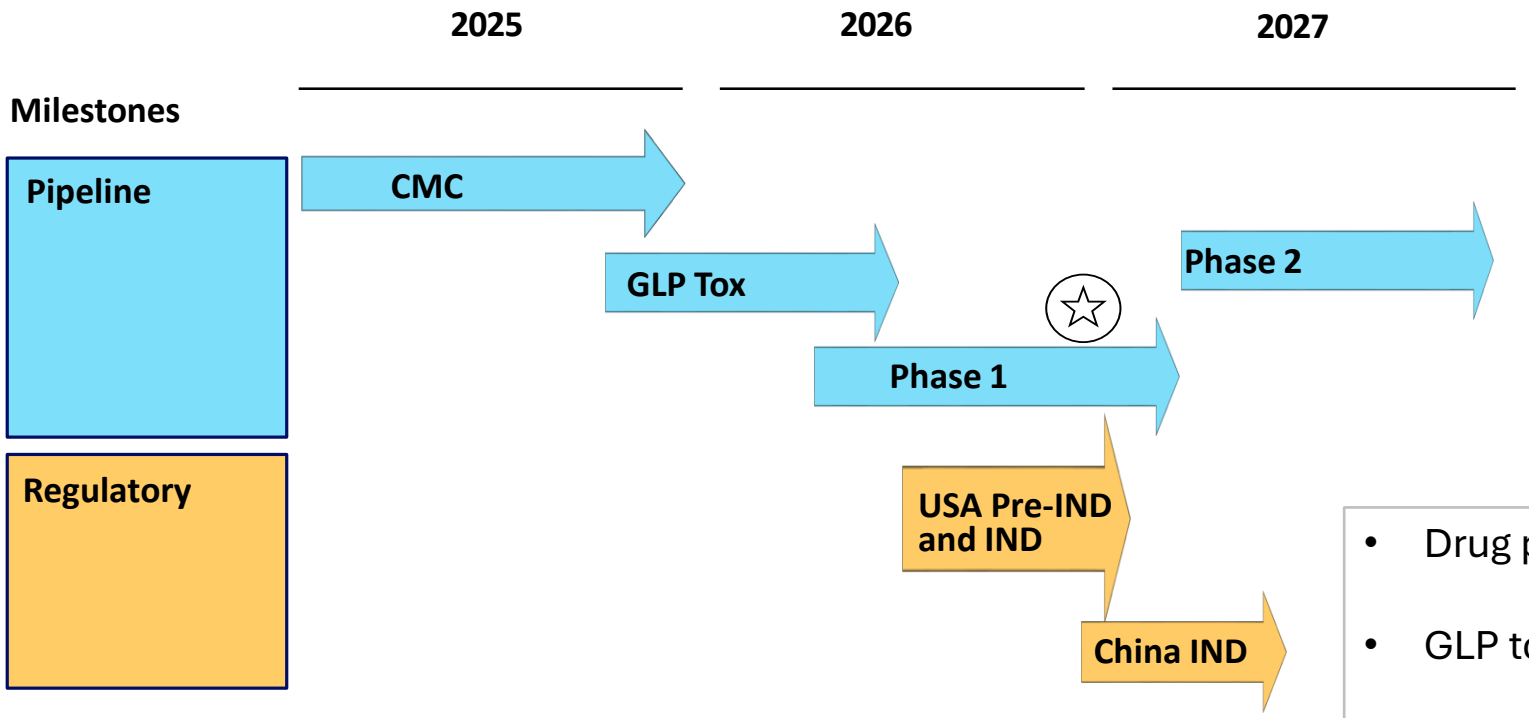
POC clinical weight loss data by the end of 2026



☆ Inflection point: 4-week and 12 week weight loss data

Possible site: CMAX clinical research in Australia

- Drug production (2025 Q1-Q3)
- GLP toxicology studies (2025 Q3-2016 Q2)
- Phase 1 clinical study in Australia (2026 Q2- 2017 Q1)
- USA Pre-IND meeting and IND approval (2026 Q2-Q4)
- China IND approval (2027 Q1)
- Phase 2 study in USA (2027 Q2-2028 Q3)

International recognition

International Federation of Inventors' Associations

IFIA Best Invention Award

International Exhibition of Inventions Geneva 2023

Gold Medal with Congratulations of the Jury

First-in-class Drug for Treatment of Multiple ABCD-related Metabolic Diseases

WE are READY to achieve our MISSION

To the Patients and Their Families

HEALTH

HOPE

HAPPINESS

Abram

Are YOU READY to support US ?