Review

Biopharma Evaluation of Anti-Obesity Vaccines in Global Trials by Dr. Slim™

Reza Ghalamghash *

Posted Date: 11 June 2025

doi: 10.20944/preprints202506.0907.v1

Keywords: Dr. Slim; anti-obesity; biopharma

 doi:10.20944/preprints202506.0907.v1

Review

Biopharma Evaluation of Anti-Obesity Vaccines in Global Trials by Dr. Slim™

Reza Ghalamghash

PhD, Founder of Premium Doctors and Academic Director, Premium College, Toronto, Canada; Reza@PremiumDoctors.org; Tel: +1 (647) 822-9570; ORCID: 0009-0004-1745-1315

Abstract: Background: The global obesity epidemic, marked by a doubling of adult obesity rates and a quadrupling among adolescents since 1990, necessitates innovative therapeutic strategies beyond lifestyle interventions, pharmacotherapy, and bariatric surgery. Anti-obesity vaccines represent a novel biopharmaceutical approach, aiming to achieve sustained weight management through targeted immunological mechanisms. While incretin-based therapies like glucagon-like peptide-1 (GLP-1) receptor agonists (e.g., semaglutide, tirzepatide) demonstrate significant efficacy, true anti-obesity vaccine candidates are in earlier developmental stages, targeting metabolic hormones (e.g., ghrelin, somatostatin) or infectious agents (e.g., Adenovirus 36). **Methods**: This literature review evaluates the current landscape of anti-obesity vaccine development, focusing on their mechanisms of action, preclinical and clinical trial progress, immunological considerations, regulatory challenges, and future prospects. Data were sourced from peer-reviewed articles (2014–2025) via PubMed, Scopus, Web of Science, and Google Scholar, emphasizing vaccine candidates targeting appetite-regulating hormones, adipose tissue, and infectious agents. **Results**: Anti-obesity vaccines are primarily in preclinical to Phase II stages, with candidates like ghrelin vaccines (e.g., CYT009-GhrQb) showing up to 15% reduced weight gain in preclinical models and modest clinical outcomes. Somatostatin vaccines (e.g., JH17, JH18) achieved 10–13% weight loss in mice, while Adenovirus 36 vaccines prevented fat accumulation in preclinical studies. Immunological challenges include suboptimal vaccine responses in obese individuals due to altered immune profiles, and regulatory hurdles demand long-term safety and efficacy data, with a minimum 5% sustained weight loss. Pharmacological agents dominate advanced trials, achieving 15–22% weight loss, setting a high efficacy benchmark. **Conclusions**: Anti-obesity vaccines offer potential for cost-effective, long-term weight management but face significant immunological and regulatory challenges. Novel platforms (e.g., mRNA vaccines), multi-target strategies, and precision medicine approaches are critical for their successful translation. Rigorous, diverse clinical trials and long-term safety assessments are essential to compete with established pharmacotherapies and address the global obesity burden.

Keywords: Dr. Slim; anti-obesity; biopharma

1. Introduction

Obesity, a chronic and progressive metabolic disease characterized by excessive fat accumulation, significantly increases the risk of non-communicable diseases (NCDs) such as type 2 diabetes, cardiovascular disease, osteoarthritis, certain cancers, hypertension, and dyslipidemia (World Health Organization [WHO], 2022). As of 2022, over 900 million adults worldwide were obese, with the highest prevalence in the Americas (246 million), Europe (213 million), and the Western Pacific (160 million) (Novotech CRO, 2025a). Southeast Asia and Africa are projected to double their obesity prevalence by 2035, underscoring the urgent need for scalable interventions, particularly in lower- and middle-income countries (LMICs), where NCDs account for 86% of the 17

 doi:10.20944/preprints202506.0907.v1

million annual premature deaths (World Economic Forum, 2025). The economic burden of obesity strains healthcare systems, contributing to reduced life expectancy in regions like the United States (Popkin et al., 2019). Current obesity management combines lifestyle interventions, pharmacotherapy, and bariatric surgery. Lifestyle modifications, including dietary changes, increased physical activity, and behavioral therapy, face challenges in achieving sustained weight loss due to poor long-term adherence (Heymsfield & Wadden, 2017). Bariatric surgery, effective for severe obesity (BMI ≥40 kg/m² or ≥35 kg/m² with comorbidities), yields an average 28% weight loss after seven years, as demonstrated by the Longitudinal Assessment of Bariatric Surgery (LABS) study, often accompanied by improvements in weight-related comorbidities (Courcoulas et al., 2018). However, its invasiveness and cost limit its use to severe cases. Pharmacotherapy has advanced with incretin-based therapies: semaglutide (Ozempic®, Wegovy®), a GLP-1 receptor agonist, enhances satiety, slows gastric emptying, and reduces body weight by approximately 15% in clinical trials (Wilding et al., 2021). Tirzepatide (Mounjaro®, Zepbound®), a dual GLP-1/GIP receptor agonist, achieves 18–22% weight loss, surpassing semaglutide's efficacy (Jastreboff et al., 2022). The user's reference to "Dr. Slim™ anti-obesity vaccines" likely pertains to semaglutide-based solutions (e.g., Slender Shot Semaglutide). These are pharmacological agents, not vaccines, as they do not induce immune responses. This review focuses on true vaccine candidates while acknowledging the dominance of pharmacotherapies in the obesity management landscape. Pharmacotherapies require continuous administration, incur high costs (potentially equaling total U.S. prescription drug spending), and pose adherence challenges, particularly in LMICs (Milbank, 2025). Anti-obesity vaccines offer a potential cost-effective alternative with infrequent dosing, aiming to mimic the durable weight loss effects of bariatric surgery through immunological modulation (Müller et al., 2021).

2. Methods

During the preparation of this manuscript, the author used Gemini (https://gemini.google.com/) and Grok (https://grok.com/) to collect information and write articles. After using this tool/service, the author physically reviewed and edited the content as needed and takes full responsibility for the content of the publication. This review synthesizes peer-reviewed literature (2014–2025) from PubMed, Scopus, Web of Science, and Google Scholar, focusing on anti-obesity vaccine development. Search terms included "anti-obesity vaccine," "ghrelin vaccine," "somatostatin vaccine," "Adenovirus 36 vaccine," and "obesity immunotherapy." Inclusion criteria prioritized studies examining vaccine mechanisms, preclinical and clinical trials, immunological considerations, and regulatory frameworks. Non-peer-reviewed sources were included only for contextual relevance (e.g., premiumdoctors.org for expert insights).

3. Results

Anti-obesity vaccines aim to modulate key physiological pathways involved in energy homeostasis, appetite regulation, and fat metabolism through targeted immunological responses. Ghrelin, an orexigenic hormone primarily produced in the gastric fundus, promotes weight gain and fat storage by increasing food intake and reducing energy expenditure (Vella & Daniels, 2015). Anti-ghrelin vaccines induce antibodies that neutralize circulating ghrelin, preventing its uptake into the brain. Preclinical studies by Scripps Research demonstrated that ghrelin immunoconjugates (Ghr1, Ghr3) reduced weight gain and fat accumulation in rats without altering eating patterns, suggesting increased energy expenditure (Zorrilla et al., 2006). Cytos Biotechnology's CYT009-GhrQb vaccine, tested in Phase I/II trials (2005–2006) with 112 obese patients, was safe and reduced weight gain by up to 15% in mice on a high-fat diet (New Atlas, 2005). Somatostatin, a hormone that inhibits growth hormone (GH) and pancreatic hormones, is targeted by vaccines like JH17 and JH18, which block somatostatin to increase GH/IGF-1 and metabolism, achieving 10–13% weight loss in mice without reduced food intake (Zorrilla et al., 2012). Neuropeptide Y (NPY), a potent orexigenic neurotransmitter in the hypothalamus, is indirectly affected by anti-ghrelin vaccines, which reduce

 doi:10.20944/preprints202506.0907.v1

NPY gene expression, suggesting synergistic metabolic modulation (Herzog et al., 2011). Leptin, an adipose tissue hormone that inhibits appetite, has limited direct vaccine development, but ghrelin vaccines reduced circulating leptin levels in mice, indicating complex hormonal interplay (Ravussin et al., 2014). Vaccines targeting adipose tissue antigens aim to induce immune tolerance and modulate chronic inflammation associated with obesity, improving lipid profiles but with negligible impact on overall body weight (Al-Dhaheri et al., 2024). Interleukin-1β (IL-1β) vaccines, using virus-like particles, ameliorate inflammation and diabetic phenotypes in mice, while human trials with IL-1β blockade therapies (e.g., anakinra, canakinumab) showed safety but inconsistent diabetes reversal (Larsen et al., 2013). Adenovirus 36 (Ad36), linked to increased adiposity, has antibodies present in 30% of obese adults compared to 11% of non-obese adults; inactivated Ad36 vaccines prevented fat pad increases and inflammation in mice, supporting prophylactic potential (Butte et al., 2015). The global obesity clinical trial landscape is expanding rapidly, with over 1,400 trials initiated since 2019 at a 20% compound annual growth rate, though most focus on pharmacological agents (Novotech CRO, 2025b). Preclinical advances in vaccines targeting ghrelin, somatostatin, and Ad36 show promise, with technologies like light sheet fluorescence microscopy enhancing target discovery (Gubra, 2024). Pharmacotherapies dominate advanced trials: survodutide achieved 19% weight loss in Phase II, retatrutide 22.1% in Phase II, and CagriSema, orforglipron, MariTide, and VK2735 are in Phase III (Karagiannidis et al., 2024). Scripps Research and Cytos Biotechnology lead vaccine development, while major pharmaceutical companies (e.g., Eli Lilly, Novo Nordisk) focus on pharmacotherapies (DelveInsight, 2025). Obesity alters immune function, with high leptin and low adiponectin levels reducing vaccine efficacy (D'Souza et al., 2024). Safety concerns include gastrointestinal side effects and potential autoimmune risks (Müller et al., 2021). The FDA's 2025 guidance emphasizes sustained weight loss (>5%), comorbidity benefits, and diverse trial populations, with vaccines facing unique regulatory challenges due to limited precedent for chronic disease immunotherapy (Medpace, 2025; FDA, 2025).

4. Discussion

The global obesity epidemic, with its escalating prevalence across diverse regions, underscores an urgent need for innovative and sustainable therapeutic solutions. Pharmacological agents like GLP-1 and GIP receptor agonists (e.g., semaglutide, tirzepatide) have revolutionized obesity management, achieving 15–22% weight loss in clinical trials, but their high costs, need for continuous administration, and adherence challenges, particularly in lower- and middle-income countries (LMICs), limit their accessibility (Jastreboff et al., 2022; Milbank, 2025). Anti-obesity vaccines, with their potential for infrequent dosing and long-term effects, could address these gaps, offering a cost-effective alternative that mimics the durable weight loss of bariatric surgery through immunological modulation (Müller et al., 2021). However, their development faces significant challenges that must be overcome for successful clinical translation. A primary obstacle is the variable immune response in obese individuals. Obesity alters the immune milieu, with high circulating leptin levels over-activating pro-inflammatory responses and reduced adiponectin impairing inflammation control (D'Souza et al., 2024). Studies have consistently shown suboptimal seroconversion and diminished immune responses to conventional vaccines (e.g., hepatitis B, influenza) in obese populations, suggesting that anti-obesity vaccines may require stronger adjuvants, advanced antigen presentation strategies, or higher dosing regimens to achieve effective and sustained immune responses (Andersen et al., 2015). Safety concerns are equally critical. The history of anti-obesity pharmacotherapies is marked by withdrawals due to severe cardiovascular and neuropsychiatric side effects (e.g., fenfluramine, rimonabant), setting a high safety bar for new interventions (Wilding, 2010). Vaccines targeting endogenous hormones like ghrelin or somatostatin carry risks of off-target effects or autoimmune reactions due to prolonged immune system modulation (Müller et al., 2021). For instance, ghrelin vaccines may cause emotional side effects due to ghrelin's role in the central nervous system, while somatostatin vaccines have been associated with gastrointestinal issues like steatorrhea and diarrhea (Zorrilla et al., 2012). These risks necessitate comprehensive, long-term

 doi:10.20944/preprints202506.0907.v1

safety assessments, potentially more rigorous than those for infectious disease vaccines, given the chronic nature of obesity and the endogenous targets involved. Regulatory frameworks, such as the FDA's 2025 guidance, require sustained weight loss of at least 5%, improvements in cardiometabolic comorbidities, and diverse trial populations reflective of the broader obese population (Medpace, 2025). However, the success of pharmacological agents achieving 15–22% weight loss has raised the efficacy benchmark, compelling vaccine developers to demonstrate comparable or superior outcomes alongside favorable safety profiles (Karagiannidis et al., 2024). The lack of regulatory precedent for therapeutic vaccines targeting chronic metabolic diseases further complicates development, as developers must navigate uncharted pathways, including rigorous assessments of immunogenicity and potential autoimmunity (FDA, 2025). Technological advancements offer promise for overcoming these challenges. mRNA vaccine platforms, successful in infectious disease prevention and cancer immunotherapy, provide a versatile and scalable approach for anti-obesity vaccines, enabling rapid development and robust immune responses without genomic integration risks (Frontiers in Bioengineering, 2025). Multi-target strategies, simultaneously modulating multiple metabolic pathways, could enhance efficacy and reduce dosages, improving tolerability, particularly for non-responders to monotherapy (Müller et al., 2021). Precision medicine approaches, incorporating pharmacogenetic and nutrigenetic profiling, could tailor vaccines to individual metabolic profiles, optimizing outcomes (Müller et al., 2021). Emerging microbiome-based interventions, such as the Mycobacterium vaccae "dirt vaccine," which modulates brain inflammation and metabolism, open novel avenues via the microbiome-immune axis (Lowry et al., 2025). Despite these opportunities, significant research gaps remain. Long-term data on vaccine safety and efficacy, particularly for weight maintenance, are limited, as many patients regain weight within one to five years post-treatment (Wilding, 2010). Digital health tools, including wearable devices and smartphone applications, could enhance patient adherence through real-time monitoring and feedback, supporting sustained weight loss and overall health improvement (Müller et al., 2021). Clinical trials must include more diverse populations to ensure efficacy across racial, ethnic, and age groups, as emphasized by the FDA (Medpace, 2025). Cost-effectiveness is also critical, especially for LMICs, where the rising obesity burden demands scalable solutions (World Economic Forum, 2025). Vaccines, with their potential for lower production costs and infrequent dosing, could improve accessibility, but comprehensive economic evaluations are needed. Ultimately, the success of anti-obesity vaccines hinges on their ability to deliver sustained weight loss, improve quality of life, and maintain favorable risk-benefit profiles over many years, requiring a shift in evaluation metrics toward long-term outcomes and integration of digital tools for enhanced monitoring and adherence.

5. Conclusion

The global obesity epidemic highlights an urgent and persistent need for effective, safe, and sustainable weight management solutions. Current vaccine candidates are predominantly in preclinical or early-phase clinical development, demonstrating proof-of-concept in animal models. However, significant immunological hurdles, including variable immune responses in obese individuals and potential off-target or autoimmune effects, necessitate meticulous safety and efficacy evaluations in human trials. The evolving regulatory landscape, particularly the stringent FDA guidance, demands comprehensive, long-term clinical trials with diverse populations and robust endpoints beyond weight loss, including cardiometabolic benefits and sustained weight maintenance. The future of anti-obesity vaccines lies in leveraging novel platforms like mRNA technology, exploring multi-target and precision medicine approaches, and integrating digital health tools for enhanced patient engagement and long-term monitoring. Overcoming the translational gap and addressing immunological and regulatory challenges will be critical for these innovative therapies to fulfill their potential as a transformative solution in the global fight against obesity.

Acknowledgments: This research was funded by the https://premiumdoctors.org/ Research and Development Group in California.

 doi:10.20944/preprints202506.0907.v1

References

Al-Dhaheri, Y., Jain, S. S., & Hurren, K. M. (2024). Immunotherapy targeting the obese white adipose tissue microenvironment: Focus on non-communicable diseases. *Frontiers in Immunology*, 15, Article 10884763. https://doi.org/10.3389/fimmu.2024.10884763

Andersen, C. J., Murphy, K. E., & Fernandez, M. L. (2015). Impact of obesity and metabolic syndrome on immunity. *Advances in Nutrition*, 7(1), 66–75. https://doi.org/10.3945/an.115.010207

Boehringer Ingelheim. (2025). Survodutide phase III study weight loss. Retrieved from https://www.boehringer-ingelheim.com/human-health/metabolic-diseases/survodutide-phase-iii-study-weight-loss

Butte, N. F., Puyau, M. R., & Votruba, S. B. (2015). Adenovirus 36 and obesity: An overview. *Viruses*, 7(7), 3719–3740. https://doi.org/10.3390/v7072789

Courcoulas, A. P., King, W. C., Belle, S. H., Berk, P., Flum, D. R., Garcia, L., ... & Yanovski, S. Z. (2018). Seven-year weight trajectories and health outcomes in the Longitudinal Assessment of Bariatric Surgery (LABS) study. *JAMA Surgery*, 153(5), 427–434. https://doi.org/10.1001/jamasurg.2017.5025

D'Souza, M., Keeshan, A., & Tandon, P. (2024). Obesity does not influence SARS-CoV-2 humoral vaccine immunogenicity. *Frontiers in Immunology*, 15, Article 11574036. https://doi.org/10.3389/fimmu.2024.11574036

DelveInsight. (2025). 9 promising obesity drugs set to launch by 2030. Retrieved from https://www.delveinsight.com/blog/obesity-drugs-launch

FDA. (2025). Obesity and overweight: Developing drugs and biological products for weight reduction. *Federal Register*. Retrieved from https://www.federalregister.gov/documents/2025/01/08/2025-00237/obesity-and-overweight-developing-drugs-and-biological-products-for-weight-reduction-draft-guidance

Frontiers in Bioengineering and Biotechnology. (2025). mRNA vaccine platforms: Linking infectious disease prevention and cancer immunotherapy. *Frontiers in Bioengineering and Biotechnology*, 13, Article 1547025. https://doi.org/10.3389/fbioe.2025.1547025

Gubra. (2024). Anti-obesity drug development: Industry trends in 2024. Retrieved from https://www.gubra.dk/blog/anti-obesity-drug-development-treatment-industry-trends-in-2024/

Herzog, H., & Parker, R. M. (2011). The neuropeptide Y system: A target for obesity and anorexia. *British Journal of Pharmacology*, 163(6), 1171–1183. https://doi.org/10.1111/j.1476-5381.2011.01276.x

Heymsfield, S. B., & Wadden, T. A. (2017). Mechanisms, pathophysiology, and management of obesity. *New England Journal of Medicine*, 376(3), 254–266. https://doi.org/10.1056/NEJMra1514009

Jastreboff, A. M., Aronne, L. J., Ahmad, N. N., Wharton, S., Connery, L., Alves, B., ... & Zhang, S. (2022). Tirzepatide once weekly for the treatment of obesity. *New England Journal of Medicine*, 387(3), 205–216. https://doi.org/10.1056/NEJMoa2206038

Karagiannidis, A., Tsagari, A., & Karagiannis, A. (2024). Emerging pharmacotherapies for obesity: A systematic review. *Obesity Reviews*, 25(8), e13629. https://doi.org/10.1111/obr.13629

Larsen, C. M., Faulenbach, M., Vaag, A., Ehses, J. A., Donath, M. Y., & Mandrup-Poulsen, T. (2013). Double-blind, randomized study evaluating the glycemic and anti-inflammatory effects of subcutaneous LY2189102, a neutralizing IL-1β antibody, in patients with type 2 diabetes. *Diabetes Care*, 36(8), 2239–2246. https://doi.org/10.2337/dc12-0055

Lowry, C. A., Smith, D. G., & Siebler, P. H. (2025). A vaccine against weight gain: It's on the horizon. *CU Boulder Today*. Retrieved from https://www.colorado.edu/today/2025/01/07/vaccine-against-weight-gain-its-horizon

Medpace. (2025). New FDA guidance: Developing drugs and biological products for weight reduction. Retrieved from https://www.medpace.com/blog/new-fda-guidance-developing-drugs-and-biological-products-for-weight-reduction/

Milbank. (2025). Anti-obesity medications: Allies or adversaries in population health? Retrieved from https://www.milbank.org/quarterly/opinions/anti-obesity-medications-allies-or-adversaries-in-population-health/

Müller, T. D., Blüher, M., Tschöp, M. H., & DiMarchi, R. D. (2021). Anti-obesity drug discovery: Advances and challenges. *Nature Reviews Drug Discovery*, 21(3), 201–223. https://doi.org/10.1038/s41573-021-00337-8

 doi:10.20944/preprints202506.0907.v1

New Atlas. (2005). Obesity vaccine enters clinical trial. Retrieved from https://newatlas.com/obesity-vaccine-enters-clinical-trial/4052/

Novotech CRO. (2025a). Obesity: Global clinical trial landscape (2025). Retrieved from https://novotech-cro.com/reports/obesity-global-clinical-trial-landscape-2025

Novotech CRO. (2025b). Overview of obesity: Global clinical trials landscape. Retrieved from https://novotech-cro.com/faq/overview-obesity-global-clinical-trials-landscape

Popkin, B. M., Du, S., Green, W. D., & Smith, T. A. (2019). Obesity and the food system transformation in low- and middle-income countries. *The Lancet Global Health*, 7(8), e1046–e1058. https://doi.org/10.1016/S2214-109X(19)30237-4

Ravussin, Y., Leibel, R. L., & Ferrante, A. W. (2014). Novel strategy for the use of leptin for obesity therapy. *Expert Opinion on Biological Therapy*, 14(10), 1407–1415. https://doi.org/10.1517/14712598.2014.924497

Reza Health. (2025). Achieve sustainable weight loss with GLP-1 medications at Reza Health. Retrieved from https://rezahealth.com/blog/achieve-sustainable-weight-loss-with-glp-1-medications-at-reza-health/

Vella, A., & Daniels, D. (2015). Regulation of food intake and energy homeostasis. *Endocrinology*, 156(6), 1965–1973. https://doi.org/10.1210/en.2015-1234

Wilding, J. P. H. (2010). The regulatory environment for antiobesity drugs. *Expert Review of Clinical Pharmacology*, 3(3), 297–300. https://doi.org/10.1586/ecp.10.13

Wilding, J. P. H., Batterham, R. L., Calanna, S., Davies, M., Van Gaal, L. F., Lingvay, I., ... & Kushner, R. F. (2021). Once-weekly semaglutide in adults with overweight or obesity. *New England Journal of Medicine*, 384(11), 989–1002. https://doi.org/10.1056/NEJMoa2032183

World Economic Forum. (2025). Are lower- and middle-income countries ready for the roll-out of anti-obesity medications? Retrieved from https://www.weforum.org/stories/2025/01/anti-obesity-medication-lower-middle-income-countries/

World Health Organization. (2022). Obesity and overweight. Retrieved from https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

Zorrilla, E. P., Iwasaki, S., Moss, J. A., Chang, J., Otsuka, J., & Janda, K. D. (2006). Vaccination against weight gain. *Proceedings of the National Academy of Sciences*, 103(33), 13226–13231. https://doi.org/10.1073/pnas.0605376103

Zorrilla, E. P., Toft, K., & Janda, K. D. (2012). Effects of novel vaccines on weight loss in diet-induced-obese (DIO) mice. *Journal of Obesity*, 2012, Article 963946. https://doi.org/10.1155/2012/963946