Whitepaper:

THE EVOLVING GLP-1 LANDSCAPE: GLOBAL TRENDS IN METABOLIC DISEASE AND CLINICAL TRIALS

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INTRODUCTION

The global prevalence of metabolic diseases has reached an unprecedented scale, presenting a compounding challenge to healthcare systems, economies, and clinical research infrastructure worldwide. Type 2 diabetes mellitus (T2DM), obesity, and metabolic dysfunction-associated steatotic liver disease (MASLD) are increasing at accelerating rates, with aggregate direct healthcare expenditures already exceeding several trillion USD annually and projected to rise substantially through 2050. Within this context, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have emerged as a therapeutically and commercially transformative drug class — one whose rapid evolution has had broad implications for clinical treatment, pharmaceutical development strategy, and the conduct of clinical trials globally. This whitepaper provides a comprehensive analysis of the GLP-1 RA landscape across four domains: the epidemiological and economic burden of the most common metabolic diseases; the development, approval, prescribing and regulatory trajectory of GLP-1 RAs across major global markets; the emergence of alternative patient access channels, including telehealth platforms and compounding pharmacies, and their implications for clinical trial design; and the evolving competitive landscape of GLP-1 RA trials across T2DM, obesity, and MASH/MASLD. Lastly, these domains will be examined to provide an expert analysis of how trends may impact clinical trial design and management. Collectively, these analyses are intended to provide a rigorous, evidence-based foundation for informing clinical development strategy in one of the most rapidly advancing areas of contemporary medicine.

CURRENT LANDSCAPE OF APPROVED GLP-1s

Impact and Prevalence of Metabolic Diseases

In 2021, the five most common metabolic related diseases were T2DM, hypertension, obesity, hypercholesterolemia, and MASLD. While the burden of hypercholesterolemia and hypertension have slowed since 1990, obesity and T2DM have seen an accelerated rate of burden on populations globally.[1] In 2024, an estimated 589 million adults aged 20-79 have diabetes, roughly 11% of the global population. Current projections show this number climbing to about 12% of the global population by 2050, impacting 853 million people.[2] According to the World Health Organization, roughly 2.5 billion adults 18 years of age and older are overweight or obese, with a subset of 890 million living with obesity. This represents an increase from 25% to 43% of overweight adults from 1990 to 2022.[3] Supporting this trend, in 2024, the estimated number of overweight children under the age of 5 was noted at 35 million, contributing to earlier onset of obesity.[3] According to the World Obesity Federation, by 2035 the projected number of overweight and obese adults is expected to reach 1.77 billion and 1.53 billion respectively.[4] Along with increased rates of obesity and T2DM, MASLD and metabolic dysfunction-associated steatohepatitis (MASH) rates have also climbed. As noted in Clinical and Molecular Hepatology, 28% of adults were estimated to have MASLD in 2024, with projections estimating an increase to over 55% by 2040.[5]

The economic burden on countries and individuals is expected to rise with the acceleration of T2DM, obesity, and MASLD global prevalence. In T2DM alone, global economic burden has increased from 0.232 trillion USD in 2007 to 1.005 trillion USD in 2024 for adults aged 20-79. Global expenditure is expected to rise to 1.043 trillion USD by 2050.[6] In 2022, the economic impact of obesity globally was estimated to be 1.96 trillion USD with that projected to balloon to 4.32 trillion USD by 2035.[7] These costs are not independent of each other, especially when considering the comorbidity rate across MASLD, T2DM, and obesity. According to Allen et al., 55-70% of people with T2DM have MASLD and 30-60% have MASH. They noted the projected cumulative estimated direct healthcare costs were 1.208 trillion for those patients who were obese and had MASH.[8] Given growing prevalence globally and the economic impact of these common metabolic related diseases, developing safe and effective treatments is critical to long-term global health and economic outcomes.

GLP-1 Receptor Agonist Development

GLP-1 RAs have exploded into mainstream media and brands have become household names globally since Wegovy's approval for obesity in 2021. The foundations for GLP-1 RA development began in 1902 with the discovery of the first hormone secretin by William Bayliss and Ernest Starling. In 1964, Murray Perley and David Kipnis discovered the incretin effect by demonstrating that insulin response was markedly higher in oral glucose administration over intravenous administration.[9]

In 1987, Stephen Bloom and his team confirmed GLP-1 was an intestinal hormone that stimulated insulin production in the pancreas and lowered blood sugar. Then in 1992, John Eng identified exendin-4, a peptide from Gila monster venom that exhibited GLP-1-like properties and was resistant to enzymatic degradation. John Eng secured a patent and partnered with Amylin Pharmaceuticals, who initiated development of synthetic exendin-4, named exenatide, which became the first GLP-1 RA approved in 2005.[10]

From 2005 until late 2014, drugs such as Trulicity, Byetta, and Victoza were marketed targeting T2DM. The first weight management approval was received for liraglutide (brand name Saxenda) in late 2014. The global development of GLP-1 RAs for weight management and other indications did not gain steam until the approval of semaglutide (brand name Wegovy) for weight management in 2021. Since then, oral GLP-1 RAs (semaglutide, orfoglipron), and dual GLP-1/GIP coagnist (tirzepatide) have been approved by the FDA as weight management/weight loss products. Triple GLP-1-GIP-Glucagon agonists (retatrutide) are currently in phase 3 clinical development for T2DM and obesity. In China, mazdutide and ecnoglutide have been approved for use in weight management/weight loss. Additionally, semaglutide received approval in treating MASH from the Food and Drug Administration (FDA) in August of 2025, Health Canada in December of 2025, and Therapeutic Goods Administration (TGA) in April of 2026. Other label expansions include the reduction of cardiovascular risk (CV Risk) in patients with T2DM, obstructive sleep apnea (OSA), and chronic kidney disease (CKD). The timeline in **Figure 1** depicts key GLP-1 RA approval dates by the FDA (United States), Health Canada (Canada), European Medicines Agency (EMA), TGA (Australia), National Medical Products Administration of China (NMPA; China), and Pharmaceuticals and Medical Devices Agency (PMDA; Japan) to capture trends in select major markets globally for GLP1s.

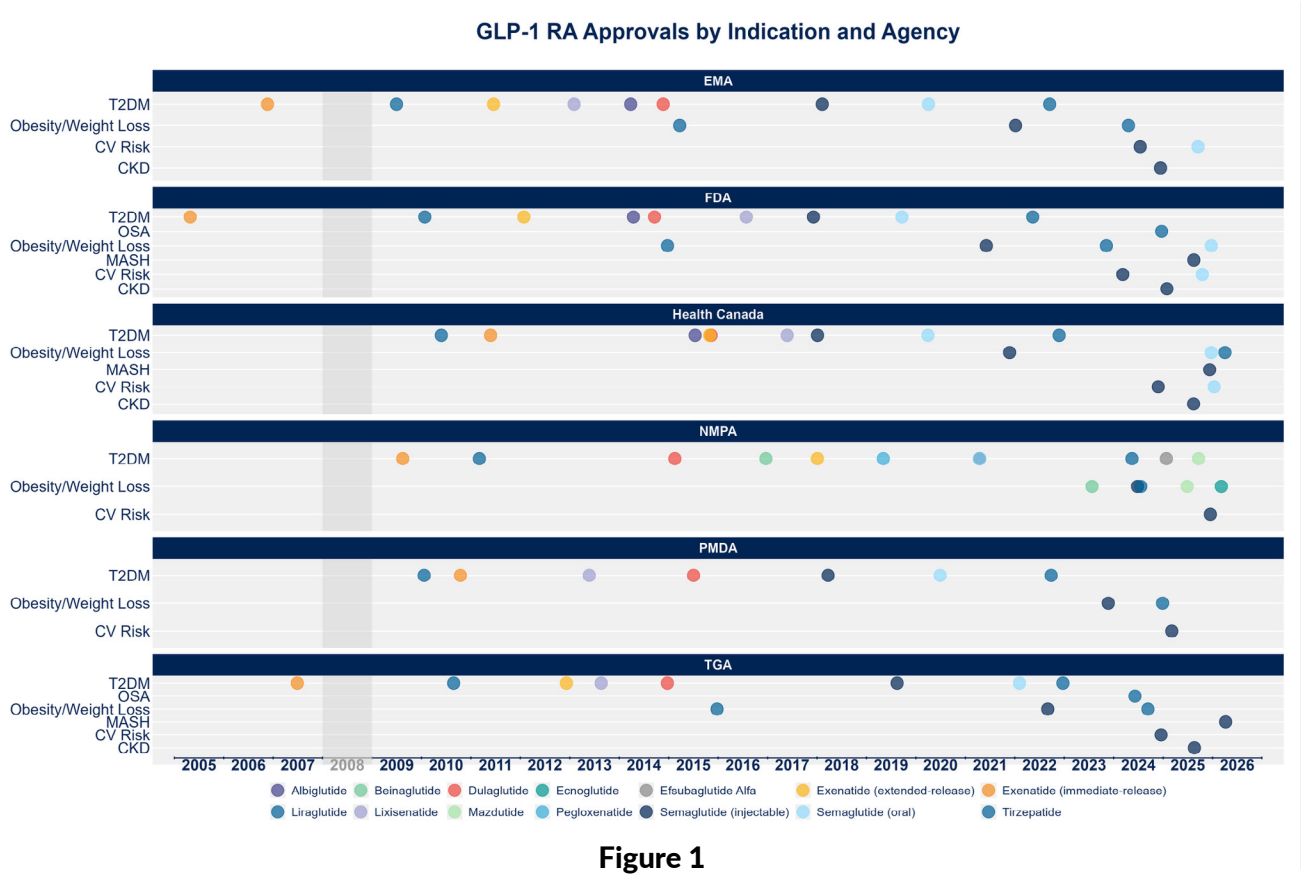

Figure 1

Utilizing real world patient-level data Medpace analyzed the number of newly prescribed GLP-1 RAs globally from 2020 to 2025 within this dataset. The data used in this study was collected on April 17th, 2026 from the TriNetX Global with Japan Growth Network, which provided access to electronic medical records (diagnoses, procedures, medications, laboratory values, genomic information) from approximately 281 million patients from 236 healthcare organizations. Learn more about TriNetX at trinetx.com. The following graph was created from this dataset (**Figure 2**):

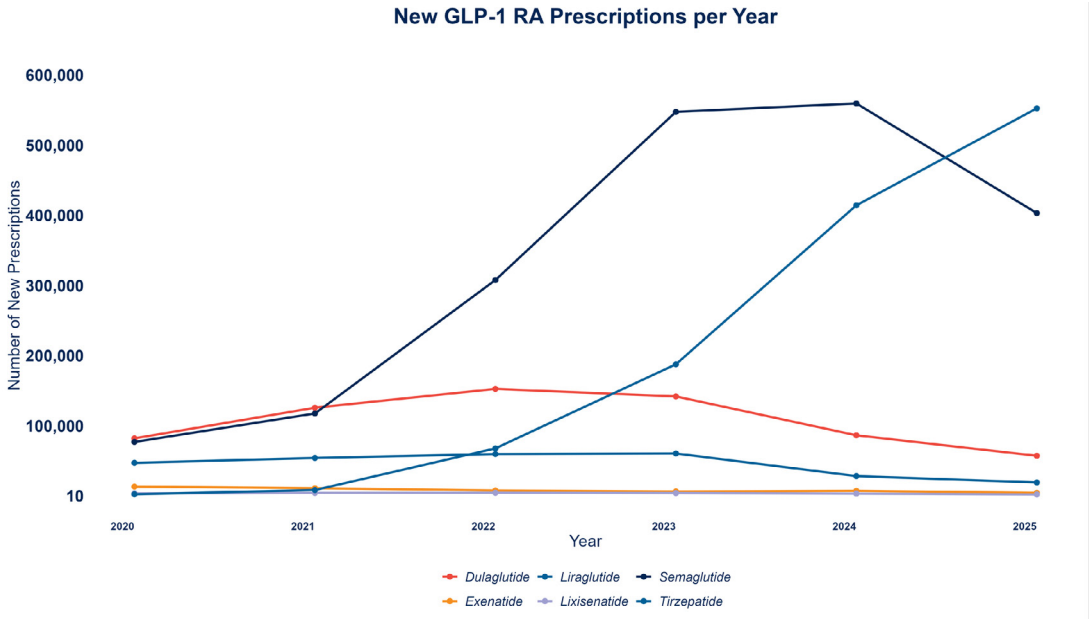

Figure 2

Albiglutide was pulled from the market in the US and EU in 2017 and therefore is not displayed. While dulaglutide, exenatide, liraglutide, and lixisenatide have seen a decrease in new prescriptions in recent years, semaglutide and trizepatide have seen sharp increases starting in 2021. This is likely due to the explosion in popularity of GLP-1 RAs, approval of these drugs in obesity, development of oral formulations, and overall efficacy. Semaglutide boasts superior efficacy in both weight loss and glycemic control and once-weekly dosing schedule for the subcutaneous drug and the approval of the oral formulation contribute to its popularity.[11] Trizepatide offers similar improved efficacy compared to other GLP-1 RAs and convenient once weekly dosing for injections, but as the drug targets both GIP and GLP-1 receptors, it continues to be an attractive option for patients and physicians.[12] The recently approved orfoglipron, an oral, non-peptide GLP-1 agonist, will likely be very competitive for new GLP-1 prescriptions. Based on phase 3 data, orforglipron (12 mg/36 mg) was more effective than oral semaglutide (7 mg/14 mg) for lowering HbA1c and weight reduction in T2D, though the rate of GI side effects was higher.

One limitation to this data is that it does not show how many patients are newly introduced to GLP-1 RAs or switched GLP-1 RAs. Xie et al., investigated GLP-1 RA switching in adults with diabetes using claims data and found that overall GLP-1 RA persistence was low.[13] Patient switching treatments should be considered during study planning, especially as new GLP-1 RAs continue to be approved and generics come to market in the future.

An additional trend that needs to be monitored for both clinical research and clinical care is upcoming patent expirations for GLP-1 RAs. As patents expire, it is expected that the pharmaceutical industry will react swiftly with submissions for generic formulations, making GLP-1 RAs more accessible and less expensive. This is evidenced by the approval of generic subcutaneous semaglutide in Canada on April 28, 2026. In a news release by Health Canada, it was also announced that eight other submissions for generic semaglutide are currently under review as of the writing of this article.[14] Assuming this trend continues across other countries upon patent expiry, these markets may become saturated by generics quickly, making clinical trials more challenging to enroll. Along with Canada, semaglutide patent exclusivity has expired in China, India, and Brazil. Strategic country selection in consideration of expiry dates will be needed in order to ensure trials are best placed. Since patent expiry of semaglutide in key markets will greatly affect the clinical trial landscape, Medpace has compiled key patient expiry date estimates in the table below across key markets (**Figure 3**).

COUNTRY/REGION	SEMAGLUTIDE EXCLUSIVITY STATUS	EFFECTIVE LOSS-OF-EXCLUSIVITY (LOE) ESTIMATE
Canada (Health Canada)	Expired	Jan-26
China (NMPA)	Expired	Mar-26
India (CDSCO)	Expired	Mar-26
Brazil (ANVISA)	Expired	Mar-26
Australia (TGA)	Active	~2029–2031
European Union	Active	~2031
Japan (PMDA)	Active	~2031
United States (FDA)	Active	~2031–2032

Figure 3

Based on a Gallup poll conducted in February of 2024, about 1 in 8 Americans have taken a GLP-1 RA treatment.[15] As J.P. Morgan has projected, the global incretin will be valued at 200 billion USD by 2030 with approximately 25 million Americans expected to be on GLP-1 treatment.[16] Trends are very likely to continue in this direction as oral and subcutaneous formulations are developed, patents expire and generics are produced, GLP-1s continue to be approved globally, and labels expanded for additional indications.

ALTERNATIVE ACCESS PATHWAYS

As a result in the boom in GLP-1 RA demand, a shortage of semaglutide (Ozempic, Wegovy) and tirzepatide (Mounnjaro, Zepbound) was declared by the FDA in 2022.[17] This resulted in exemptions being put in place for compounding pharmacies to help meet patient demand. Per FDA Guidelines, the intent of compounding is to provide medications for patients whose needs cannot be met by FDA approved drugs. For example, "a patient who has an allergy and needs a medication to be made without a certain dye." Compounded drugs cannot be medications that are "essentially copies" of FDA approved drugs or drugs that are compounded regularly or in inordinate amounts.[18] The FDA declaring a shortage of semaglutide and trizepatide enabled compounding pharmacies to replicate the brand-name drugs for dispensing to consumers by purchasing active pharmaceutical ingredients.[17] This led to an increase in compounding pharmacies, online pharmacies, medical spas, and telehealth platforms to start offering compounded GLP-1 RA treatments. As of February 2025, the shortage was declared to be at an end, and the FDA has reaffirmed its policy on compounding numerous times.[19]

While there is no ongoing shortage in the US and a tightening regulatory landscape for compounding pharmacies, accessibility online and via telehealth appears to have stuck. A non-exhaustive dataset of online GLP-1 providers was assembled in April of 2026 to assess the GLP-1 online/telehealth market. This process began with identifying providers through Google paid search results. For each provider, the primary evidence source was the official company website. Thirty-eight providers were identified offering a range of services, such as an initial health/weight loss quiz, virtual consultation, coaching, same-day shipping, weight-loss guarantees, and nutrition support. Brands included were Hims & Hers, WeightWatchers, Noom, Walgreens Weight Loss, Mochi Health, and Ro. Eighteen providers offer compounded GLP-1s, eight offered brand name GLP-1s only, and the remaining ten offer both compounded and brand name options. All providers primarily rely on cash-pay options, but ten do allow the use of insurance to cover GLP-1 RAs. Cash payment options include memberships/subscriptions and financing support from buy-now-pay-later apps such as Klarna and Affirm. In addition to online options, brick and mortar weight loss clinics and medical spas also offer GLP-1 access through branded and compounded options. In a brief search of major chains, thousands of locations across all 50 states were identified.

This trend is not without some legal push pack. According to Sood and Garg, as of 2024 the FDA received "392 reports of adverse events for compounded semaglutide and 215 reports with tirzepitide." Concerns with compounded GLP-1s include but are not limited to: lack of data on bioequivalence, different forms of the active ingredients resulting in differing absorption and plasma concentration, and a lack of standardized dosing instructions and contraindications.[16] The FDA has issued warning letters to compounding pharmacies and a recent lawsuit between Novo Nordisk and Hims & Hers has resulted in a settlement that Novo Nordisk's branded products will be marketed on Him & Hers websites and Hims & Hers will remove marketing for compounded products.[20]

In summary, while regulatory restrictions are tightening on compounded products, a wide market for alterative access to GLP-1s still remains and will likely continue to provide a significant amount of access to consumers. Eli Lilly is now also offering direct-to-consumer cash-pay options for their newly approved GLP-1 orforglipron. Decisions on how to manage compounded GLP-1s and GLP-1 stability for participants in clinical trials will need to be carefully considered when designing protocols.

GLP-1 RA CLINICAL TRIAL COMPETITIVE ANALYSIS

In addition to drug approvals and prescribing trends, Medpace continually tracks pharmaceutical market and research trends to inform study strategy. As part of the effort to track trends in metabolic research and GLP-1 RA development, a database of global GLP-1 trials has been created. This database includes both industry and Investigator-initiated trials across all countries going back to the early 2000s. Data was sourced from Citeline®, ClinicalTrials.Gov, and TrialHub. The search terms GLP-1, GLP-1 RA, glucagon-like peptide, and GLP-1 receptor agonists, were used to pull data. All data was collated into one master listing and was deduplicated. All discrepancies were flagged, documented, and resolved. Lastly, the database was reviewed for any studies not including a GLP-1 RA and those were subsequently removed from the dataset.

An analysis was performed to identify trends in GLP-1 RA development from 2021 through April of 2026. The maps below show the number of GLP-1 RA related trials by country globally across 2021 and 2025 for Phase 1 through Phase 3 trials across all indications (**Figure 4**).

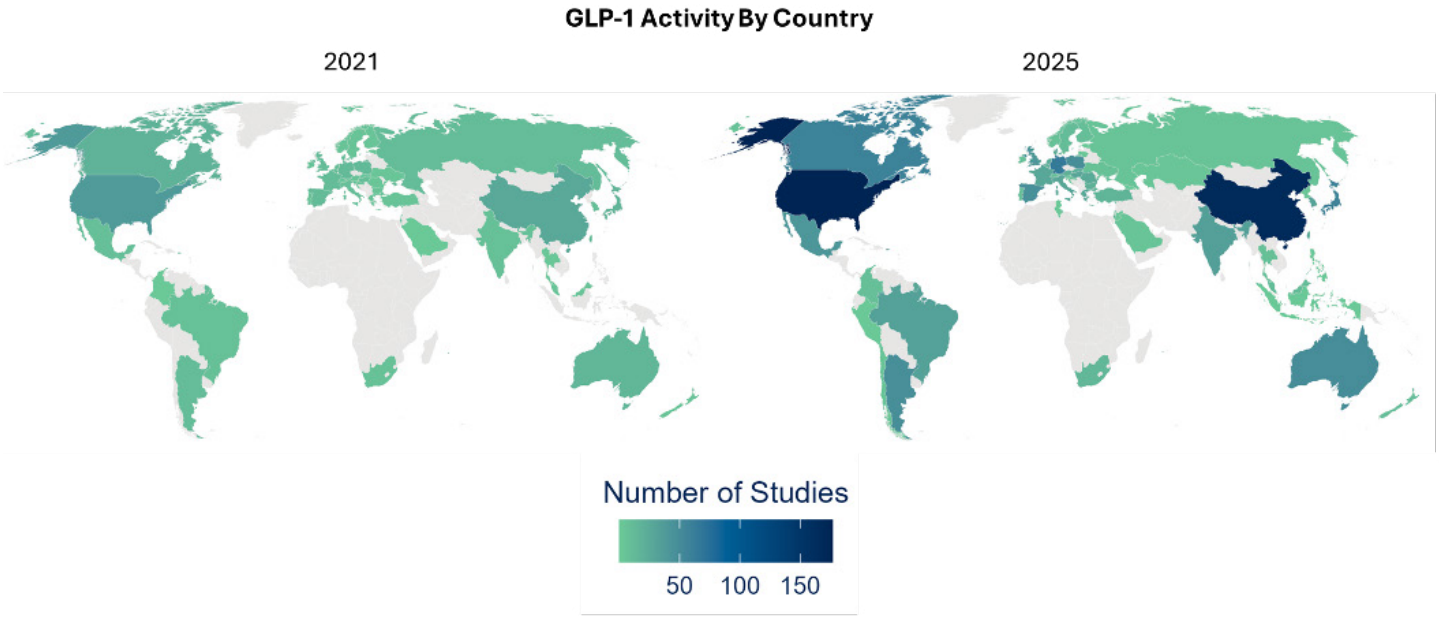

Figure 4

The United States and China saw the most dramatic increase in the number in active GLP-1 RA trials between 2021 and 2025. China saw an increase of about 640% and the United States saw an increase of about 470%. In Europe, Poland, Germany, and Spain saw the largest increase in studies being conducted, while the region experienced a larger study load. Following China in Asia-Pacific (APAC), Japan, Australia, and India had the largest increases in the number of studies. Finally, in South America, Argentina saw a large increase in studies with Brazil following. Countries like Chile and Peru conducted their first GLP-1 trials. **Figure 5** shows the top 10 countries by increase in GLP-1 RA studies between 2021 and 2025. This data also mirrors the top 10 countries by number of total GLP-1 RA studies in 2025. China and the US have approximately the same rate of increase within this period while the remaining eight countries follow a slower, but similar rate of increase.

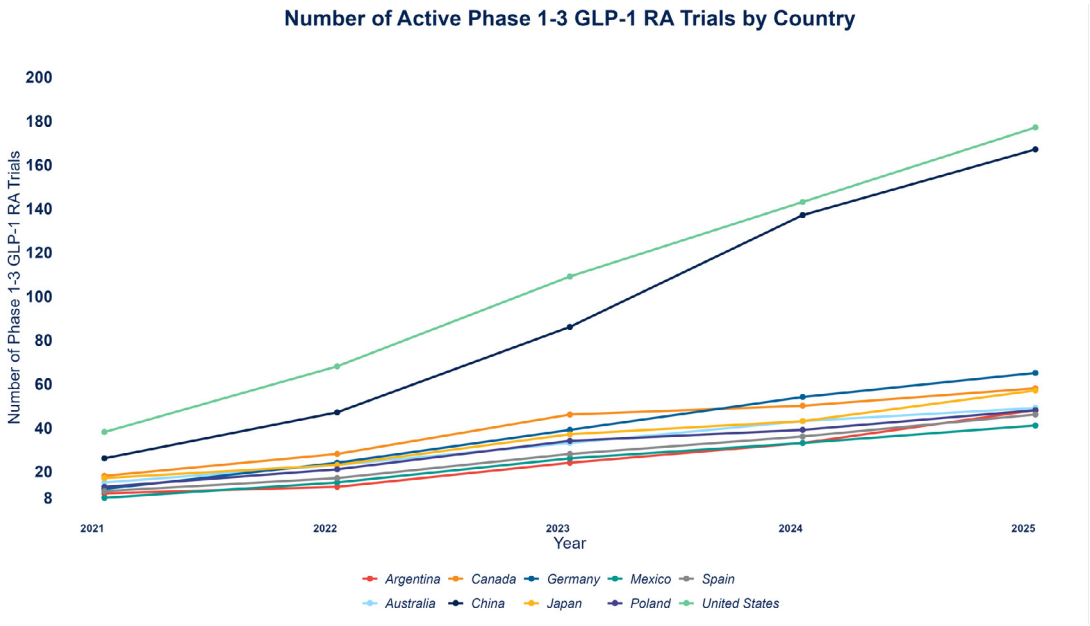

Figure 5

Overall, the global saturation of studies increased from approximately 100 GLP-1 RA trials across obesity, T2DM, and MASH/MASLD in 2021 to 476 in 2025.

An analysis was also conducted to identify trends by indication and phase across obesity, T2DM, and MASH/MAFLD. The charts **Figure 6** depict each indication from 2021 through April of 2026 for Phase 1 through Phase 3 trials.

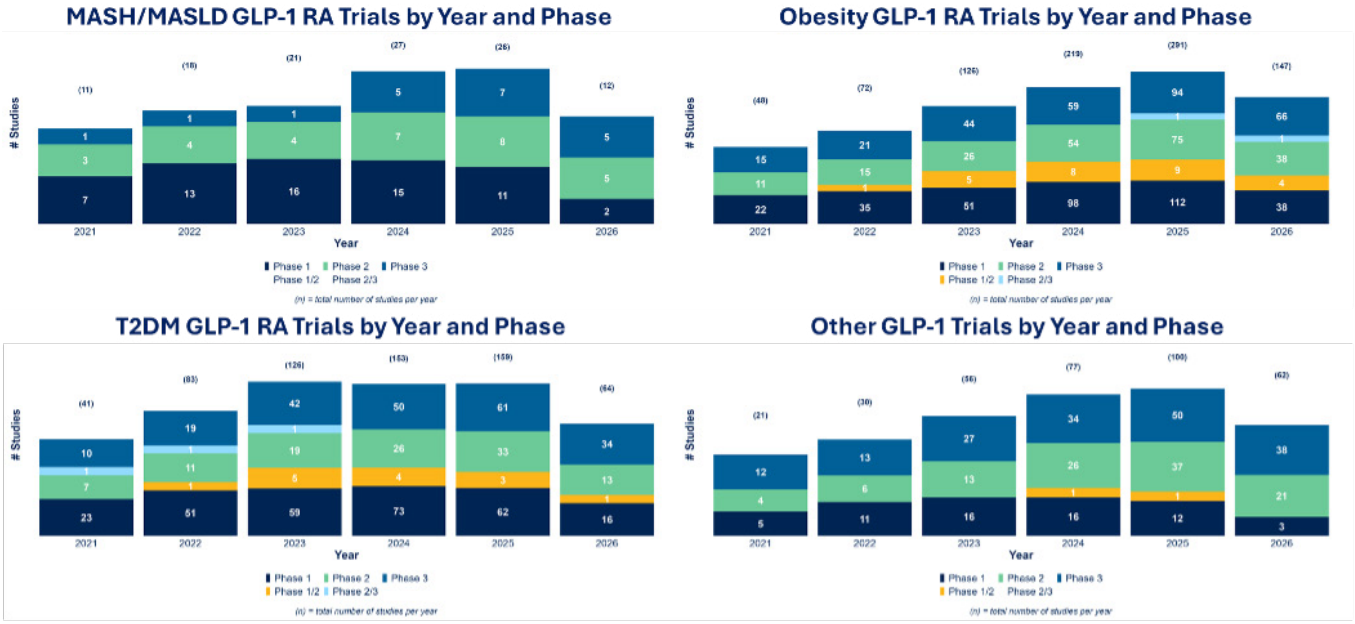

Figure 6

While numbers in 2026 appear lower than 2025, this only accounts for trials through April 13th of 2026. The upwards trend in total number of GLP-1 trials is expected to continue increasing. Notably, the trend of GLP-1 RAs moving to phase 3 trials has also been increasing, meaning a continued upwards trend in approvals is likely to continue.

An analysis was done on the other GLP-1 trials that did not fall into a category of MASH/MASLD, obesity, or T2DM to determine the next largest indication contributors. It is expected that trials within these therapeutic areas will continue to increase and companies with GLP-1 RA compounds may look to expand the use of their product or possibly shift focus.

- **Cardiovascular (CV) Indications:** GLP-1 RAs are being investigated in heart failure, coronary artery disease, dyslipidemia, and peripheral artery disease. Patients with metabolic conditions are more likely to experience cardiovascular complications, therefore, analyzing efficacy of GLP-1 RAs in patients with cardiovascular disease is a natural progression.[21] In addition to studies focused on CV patients, there are examples of MASH/MASLD, T2DM, and obesity studies that require patients to have CV disease or risk factors or include this group as a cohort within a larger study. To receive regulatory approval, it is likely an increase in cardiovascular outcomes trials involving GLP-1 RAs will be seen, which involve large numbers of patients and often occupy sites globally. The approval of semaglutide for CV risk is a promising sign of efficacy and approvals for GLP-1 RAs across the CV therapeutic space. At the time this article was written, there are 13 planned or open phase 3 trials including patients with CV disease or CV risk, and five of these studies are evaluating the efficacy of orforglipron.
- **Central Nervous System (CNS) Indications:** The main indications with trials testing a GLP-1 RA compound include substance abuse/dependency (specifically alcohol and cannabis), Parkinson's disease, and stroke. At the time this article was written, there are open or planned phase 3 programs with GLP-1 RAs in Alcohol Use Disorder, depression, and patients taking antipsychotic medications. Studies show that activating GLP-1 receptors has anti-inflammatory properties, which indicates potential benefit in CNS indications.[22] Notably Novo Nordisk published results from their evoke and evoke+ trials on March 19, 2026 and findings do not support the efficacy of daily oral semaglutide (14 mg/day) in patients with Alzheimer's disease in the MCI or mild dementia stage.[23] Medpace anticipates GLP-1 RA studies within the CNS space will trend away from Alzheimer's disease and focus on other indications with potential benefits.

Lastly, the authors analyzed enrollment rates across T2DM, obesity, and MASH/MASLD using the year the study started as the anchor point for the enrollment rate. The following graph was developed from this data:

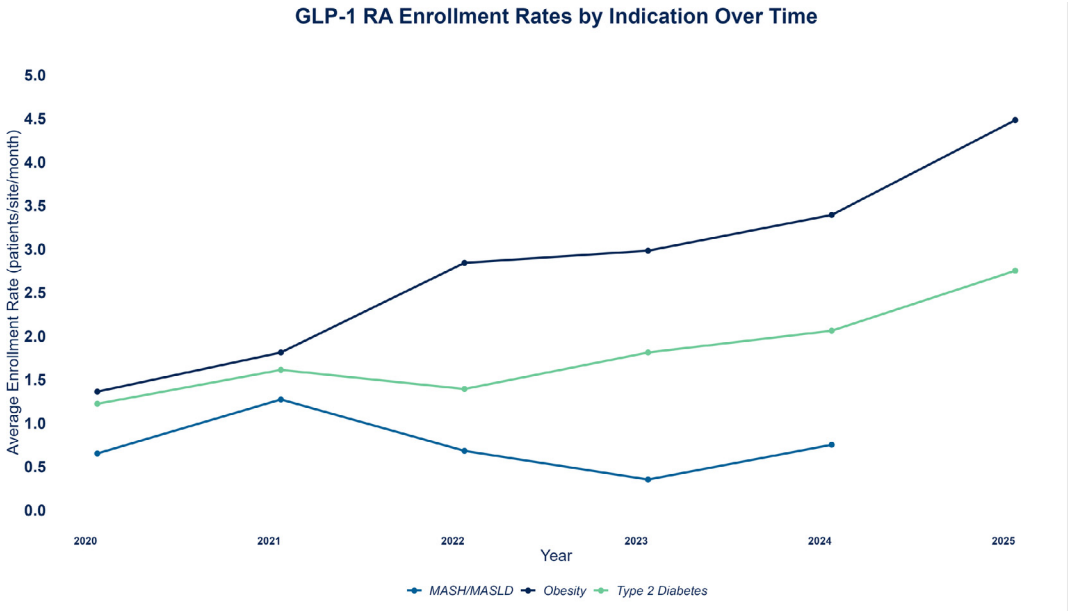

Figure 7

While trial saturation has increased globally, the demand for access to GLP-1 RAs and increasing rates of T2DM, obesity, and MASH/MASLD have appeared to keep enrollment rates for trials high (**Figure 7**). Obesity and T2DM enrollment rates have steadily increased from 2020 through 2025. MASH/MASLD enrollment rates have slightly decreased over the same period. This is likely due to the comorbidity of MASH/MASLD across T2DM and obesity and the more invasive procedures that are typically associated with MASH trials, such as a liver biopsy. Patients are just as likely to receive hepatic benefits through weight loss from a GLP-1 RA on an obesity trial without the hassle of liver biopsies and MRI-PDFFs. For obesity and T2DM, this means that despite the large increase in number of studies, research, and access to GLP-1 RAs, enrollment does not look like it will slow in the immediate future.

DISCUSSION AND CONCLUSIONS

The analyses presented in this whitepaper collectively illustrate the scale and velocity of transformation occurring across the GLP-1 RA landscape. The epidemiological data are across T2DM, obesity, and MASLD/MASH show accelerating rates globally, with economic consequences projected to reach several trillion USD annually by mid-century. These trends establish a sustained and growing patient population for whom effective pharmacological intervention is warranted and economically imperative. GLP-1 RAs, having demonstrated superior efficacy in glycemic control, weight reduction, and increasingly in hepatic outcomes, have positioned themselves as a new cornerstone in the treatment of metabolic disease. The breadth of regulatory approvals across major global markets — and the continued expansion of approved indications including MASH, OSA, and CKD — further underscore the trajectory of this drug class.

While earlier-generation agents such as liraglutide, dulaglutide, and exenatide have experienced declining uptake, semaglutide and tirzepatide have seen sharp increases in new prescriptions since 2021. The recent approval of oral orforglipron which is a non-peptide, small molecule GLP-1 RA, introduces an additional competitive variable that is likely to further reshape prescribing behavior in coming years. Compounding these dynamics are impending patent expirations across key markets. As evidenced by the recent Health Canada announcement, generic approvals are expected to flood the market upon patent expiration, further expanding patient access with downstream implications for both clinical care and research. Combined with alternative access channels via telehealth and through compounding pharmacies, Sponsors and clinical research organizations must develop robust screening and inclusion/exclusion criteria to identify and manage prior or concurrent use of GLP-1 RAs among enrolled participants, while also balancing the likelihood of patients switching GLP-1 RAs.

The global competitive trial landscape reinforces the necessity of rigorous feasibility planning for GLP-1 RA development programs. The approximately 376% increase in active GLP-1 RA trials from 2021 to 2025, concentrated most heavily in the United States and China but extending across Europe, Asia-Pacific, and South America, reflects accelerating competitive trial saturation. Despite this, enrollment rates for obesity and T2DM trials have increased during this period, suggesting that demand for clinical trial participation continues to track with the growing patient population for the time being. However, the observed decline in MASH/MASLD enrollment rates warrants particular attention. Sponsors developing MASH-focused protocols should carefully evaluate the tradeoffs between biopsy-based and non-invasive endpoint strategies and assess the degree to which participants may perceive therapeutic alternatives outside of trial participation. While enrollment rates do not show immediate signs of a downward trend, the number of trials and the availability of new GLP-1 RAs, as discussed above, continues to increase. It is unlikely that the increasing enrollment rates will continue indefinitely.

Looking ahead, several considerations should inform clinical development strategy in this space. First, site and country selection for GLP-1 RA trials will require increasingly dynamic assessment, given the rapid shifts in trial saturation across geographies identified in this analysis. Regions such as South America, where GLP-1 trial activity is relatively nascent, may offer favorable enrollment conditions in the near term. This needs to be balanced with the fact that Brazil will likely have generic semaglutide by the end of 2026. Additionally in APAC, China and India may become harder to recruit in due to trial saturation and semaglutide patent expiration in March-2026, while countries such as Australia and South Korea may warrant a larger focus. Second, the anticipated proliferation of generic GLP-1 RAs following patent expiration will necessitate updated participant eligibility criteria and washout period guidance, as the accessibility and affordability of these agents continues to increase. This will also likely shift target countries for clinical trials in the coming years. Finally, ongoing surveillance of prescribing trends, alternative access channel activity, and competitive landscapes will be essential for sponsors seeking to maintain enrollment competitiveness in what is, by any measure, the most active area of cardiometabolic drug development in decades.

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