Small Molecule GLP-1R Agonists Market Landscape

Fast Follow Patent Strategy by Drug Developers

patsnap

CONTENT

Chapter 1

Preface: Pfizer & Eli Lily's GLP Move Implications

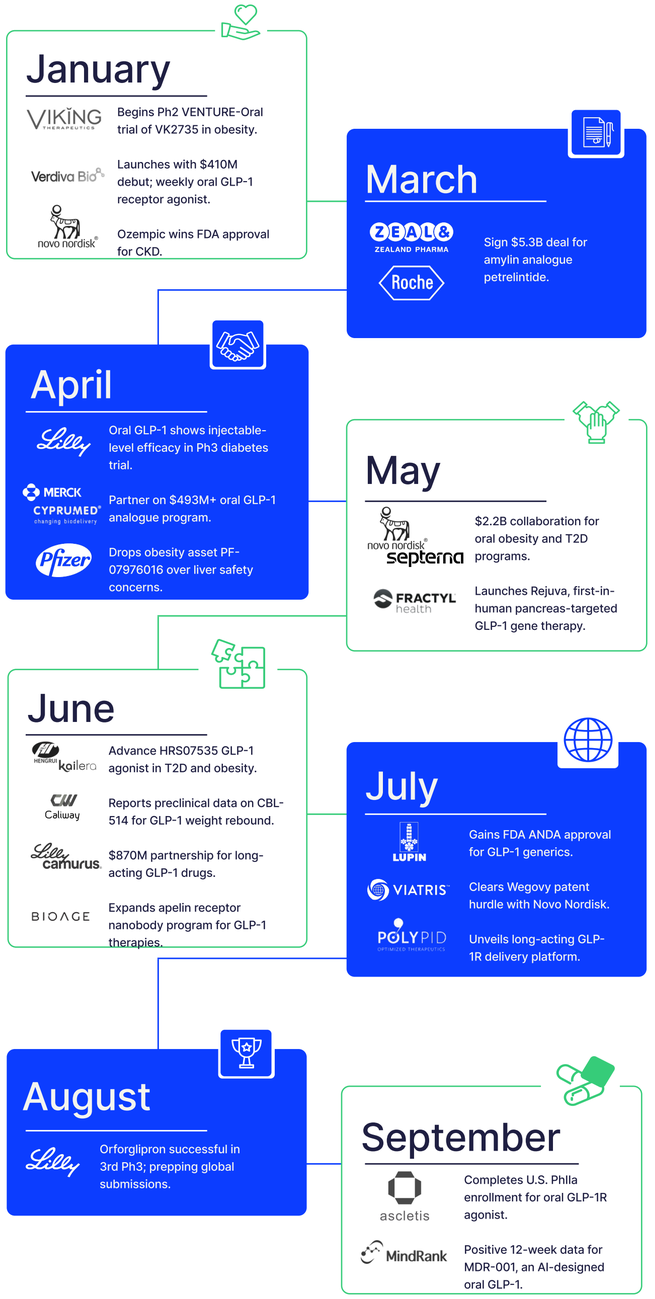
2025 GLP-1 & Obesity Therapeutics

The already overheated GLP-1 market has shown no signs of cooling in 2025. Over the first eight months, the sector experienced a dynamic mix of promising clinical trial results, expanded therapeutic indications beyond weight management, strategic partnerships, as well as emerging safety concerns and intensifying patent disputes with generics entering the fray.

Among the most notable developments were Novo Nordisk's strong commercial performance with Wegovy, which prompted a global restructuring of the company; Pfizer's decision to halt development of its oral GLP-1R agonist PF-06954522 and fully exit the small molecule GLP-1 space; and Eli Lilly's continued momentum, driven by positive Phase 3 data supporting its GLP-1 pipeline.

This report explores the clinical trends and market landscape for GLP-1 receptor agonist, and what is up-and-coming.

As pipelines diversify and new mechanisms enter the race, the next frontier becomes clear: how will GLP-1 innovation expand past obesity in 2026?



This timeline was built using real-time insights from Synapse by Patsnap, where you can track pipeline shifts, deal activity, competitive signals as they happen.

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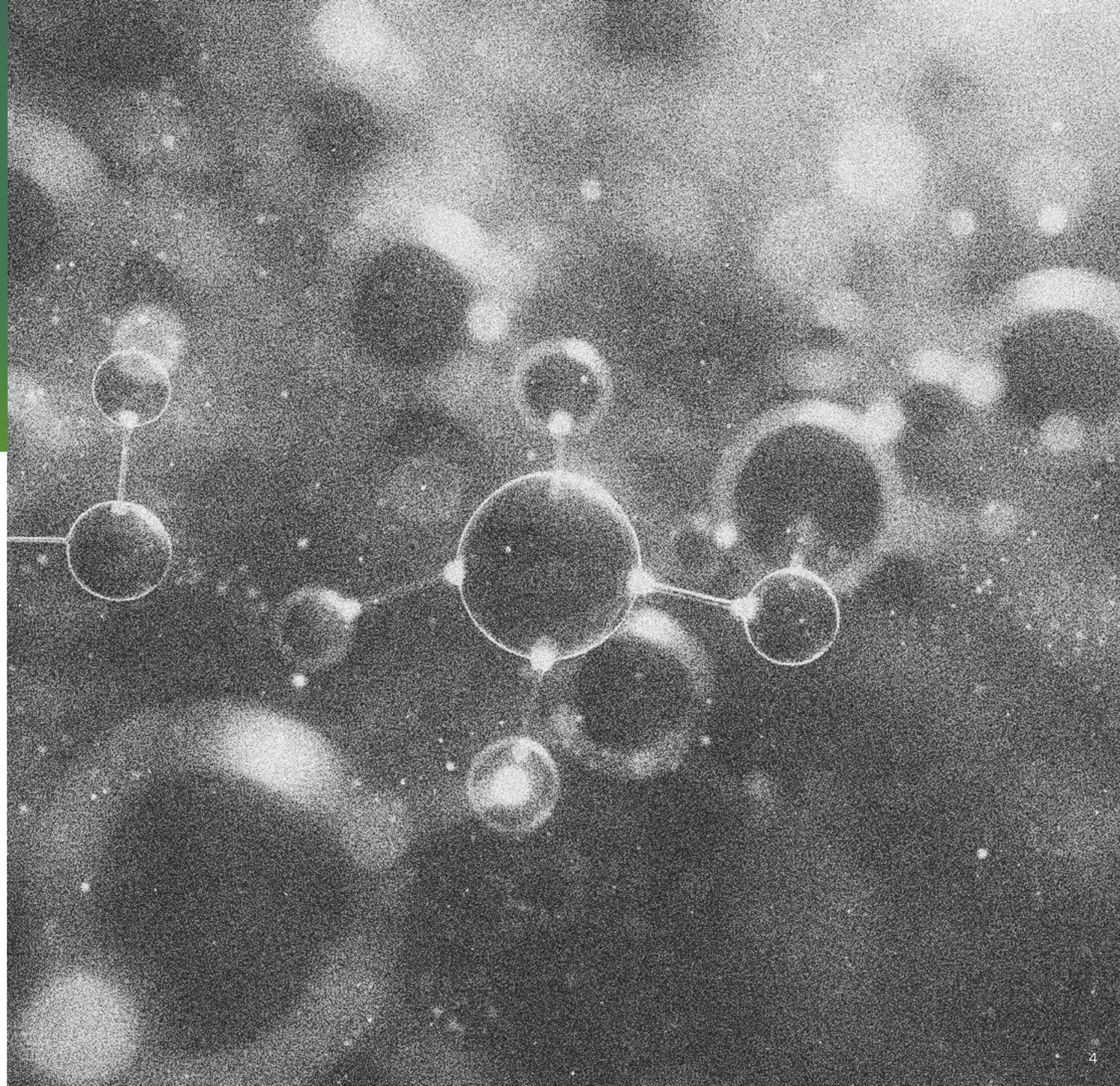
Chapter 2

Analysis of Clinical Results and Standard Therapies of GLP-1R Drugs



2.1

2025 GLP-1R Clinical Results & Standard Therapies Evolution

Top 10 Clinical Trials by Country:

US: 1,030
China: 917
Germany: 346
Japan: 278
UK: 258
Canada: 241
Spain: 192
Denmark: 191
Australia: 180
Mexico: 172

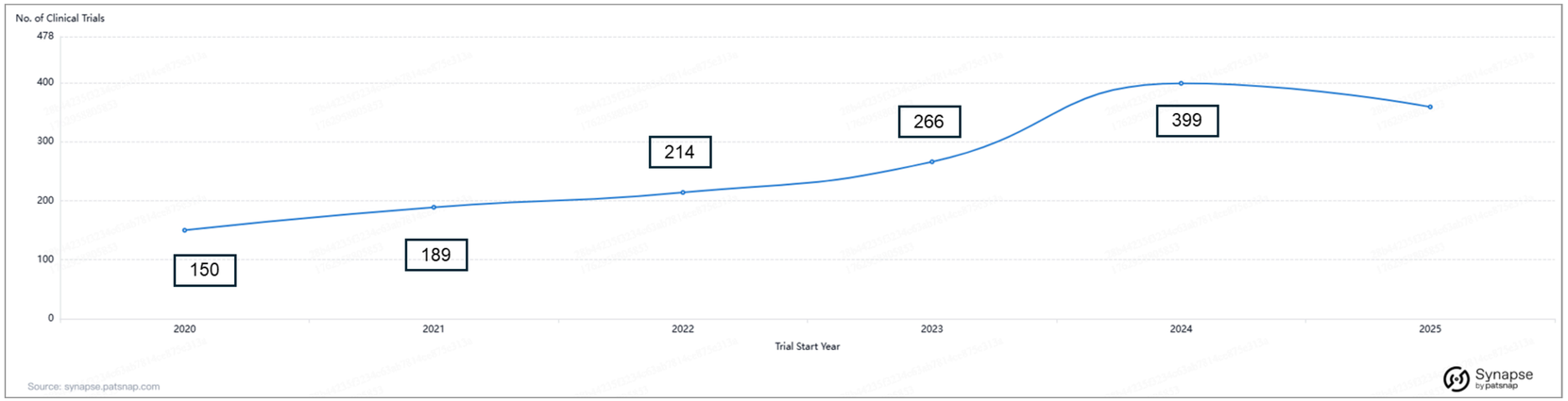


Fig 1. GLP-1R-related clinical trials initiated by year

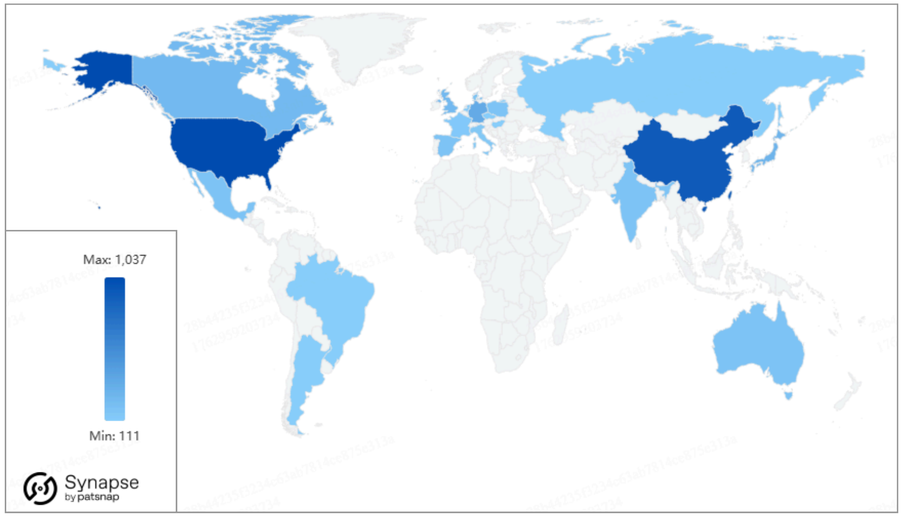


Fig 2. Number of GLP-1 Clinical Trials by Country

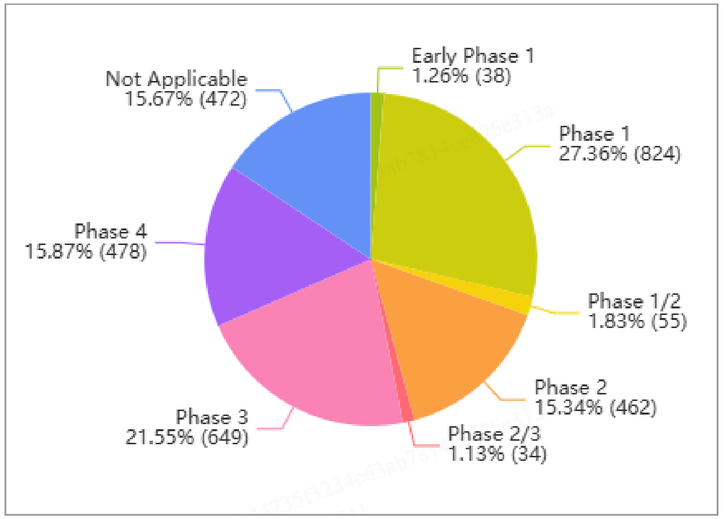


Fig 3. Distribution of phase for clinical trials

Beyond the Top 5: Where GLP-1R Is Heading

The competition between Novo Nordisk and Eli Lilly in the GLP-1 space remains intense in 2025, especially following Pfizer's exit from this increasingly saturated market. Despite consolidation among major players, new entrants continue to emerge, bringing fresh innovation to the field. Long-acting injectables and small molecule delivery methods remain the preferred modalities, although alternative approaches are gaining traction. Notable developments include:

- Insilico's leveraging its generative biologics engine to design GLP-1R peptides within a 72-hour cycle for cardiometabolic diseases.
- Kailera's KAI-4729 injectable advancing KAI-4729, an injectable tri-agonist targeting GLP-1, GIP, and glucagon receptors, into Phase 1 trials for obesity and type 2 diabetes.
- Fractyl Health reporting strong preclinical data for RJVA-002, a dual GIP-GLP-1 gene therapy candidate aimed at treating obesity.

Beyond delivery mechanisms, drug developers are racing to expand indications and labeling to protect market exclusivity and fend off generic competition. Popular targets include Type 2 and Type 1 Diabetes Mellitus, Polycystic Ovary Syndrome (PCOS), Metabolic Dysfunction-Associated Steatohepatitis (MASH), and Chronic Kidney Disease (CKD).

Between January 1st and November 1st 2025, 174 GLP-1R related clinical trial results were recorded globally, with 127 as 'positive' and 2 as 'superior'.

Drug Name	Drug Type	Original Drug Developer	Drug Highest Phase
Semaglutide	Recombinant polypeptide	Novo Nordisk	Approved
Tirzepatide	Synthetic Peptide	Eli Lilly	Approved
Dulaglutide	Fc Fusion Protein	Eli Lilly	Approved
Liraglutide	Recombinant polypeptide	Novo Nordisk	Approved
Exenatide	Synthetic peptide	Ei Lilly, Amylin Pharmaceuticals	Approved

Top 5 GLP-1R Drugs

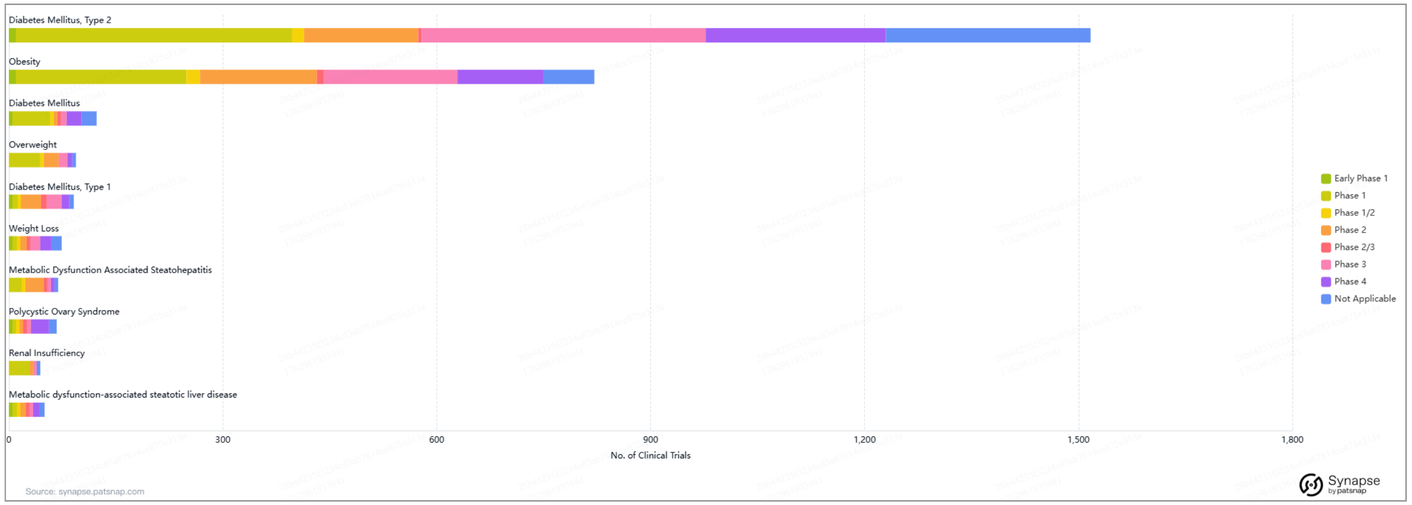
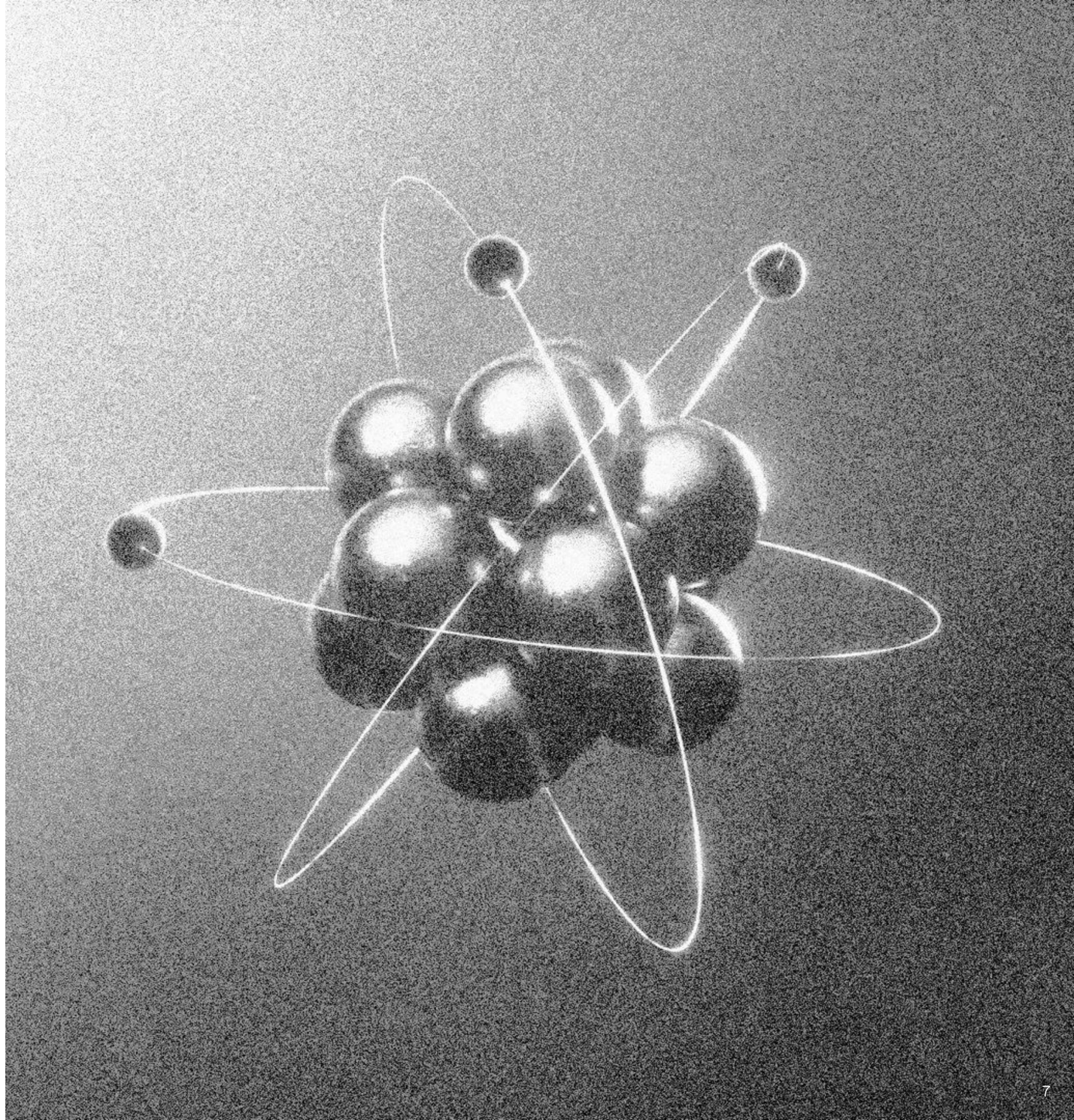


Fig 4. Top 10/20 indications and its clinical trial phase distribution

2.2

GLP-1R Clinical Results, Outcomes & Future Implications



Comparison of emerging GLP-1R targeted therapies

Source: synapse.patsnap.com

Drug Name	Drug Developer	MoA	Summary	Prediction of Next Milestones	Patent Expiry
Tirzepatide	Eli Lilly	Dual-target agonist for GIP/GLP-1	To replace the existing pure GLP-1 agonists in the fields of type 2 diabetes and obesity, and become the first-line or second-line preferred treatment option. The SURPASS and SURMOUNT trials demonstrated superior blood sugar and weight reduction effects compared to semaglutide, while SURPASS-4 and SUMMIT provided further evidence of cardiovascular and heart failure benefits.	Already on the market, with indications expected to continue expanding.	January 2036 in the U.S. This refers to the primary molecule or compound patent, which is distinct from follow-on patents covering formulations or delivery devices that may extend the overall exclusivity period.
Orforglipron (LY3502970)	Eli Lilly, co-developed with Chugai Pharmaceutical	Oral small molecule GLP-1 agonist	Offer a key alternative to injectable GLP-1 agonists, particularly for newly diagnosed obesity and type 2 diabetic patients who prefer oral therapy. Phase III trial results showed that after 72 weeks of treatment, the GLP-1 oral drug achieved 11.2% of weight loss amongst patients, while the observed weight loss was below the 15% benchmark anticipated by analysts and what Novo Nordisk's oral drug achieved, it was still comparable to the earlier injectable formulation, with oral administration offering a key convenience advantage.	Anticipated market launch in 2026 – 2027 with strong potential to rapidly gain market share.	September 2036 in the U.S. While this represents the primary patent covering the molecule itself, additional secondary or follow-on patents may extend market exclusivity beyond this date.
Semaglutide	Novo Nordisk	High Dose/Novel Indication	Expanding to new indications such as cardiovascular protection (SELECT study), HFpEF and NASH, will strengthen and broaden its role as a cornerstone therapy. SELECT study demonstrated cardiovascular benefits in nondiabetic Populations to maintain its competitive advantage.	Expecting new indication approvals between 2026 – 2028	The core composition patent of semaglutide is scheduled to expire in March 2026.
CagriSema	Novo Nordisk	AMYR agonists CALCR agonists GLP-1R agonists	Among patients seeking the most significant weight loss results, it may serve as a strong competitor or a subsequent treatment option for Tirzepatide. The data from Phase II trials indicate that its weight loss effect may surpass that of Tirzepatide	Currently in Phase III development, with key data expected to be released between 2028 – 2030.	The core patent for CagriSema—which covers the active ingredient component (cagrilintide 2.4 mg in combination with semaglutide 2.4 mg)—is anticipated to expire between 2031 and 2034.
Retatrutide	Eli Lilly	GLP-1/GIP/Insulinotropic hormone triple-target agonist	As a leader in next-generation therapies, it is poised to establish a new benchmark in weight reduction and metabolic improvement. The Phase II study demonstrated an unprecedented weight loss effect (with an average weight reduction of over 24%).	Phase III is currently underway. This is the most anticipated breakthrough between 2028 – 2030 and may enter the market at the end of the trial period.	Expected expiry in 2038.

Patent Status of GLP-1R Targeted Drugs

Since 2005, there have been 9,686 patent applications of GLP-1R drugs, but saw a continuing decrease in applications and number of patents granted.

Between 2023 to 2045, we expect several key patents expiring, not only opening doors to generics but also sparking original drug developers to initiate patent protection and portfolio strategy to mitigate commercial risks, such as

1) Alternative formulation and delivery mechanism to improve patient adherence (e.g. Eli Lilly and Chugai's oral non-peptide GLP-1R agonist orforglipron LY3502970)
2) Lower-frequency and lower-dosage with increased bioavailability to be the best-in-class treatment option (e.g. AstraZeneca ECC5004)
3) More targeted patient population with BBB penetration, e.g. Gilead's GS-4571, an oral non-peptide SM
4) Novel modality beyond small molecules, e.g. Amgen's AMG 133 MariTide, an ADC, entering China market for clinical trials to be first-in-class treatment option with subcutaneous injection as route of administration but at a monthly frequency

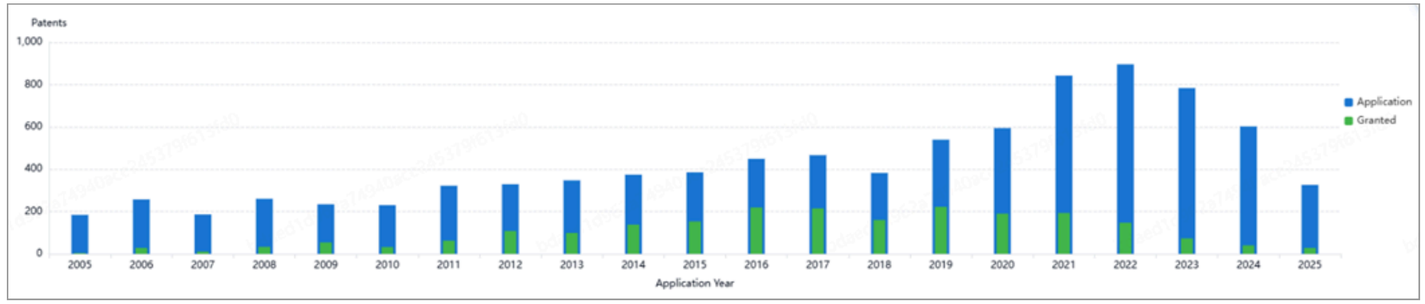


Fig 5. Patent applications # of GLP-1R drugs by application year

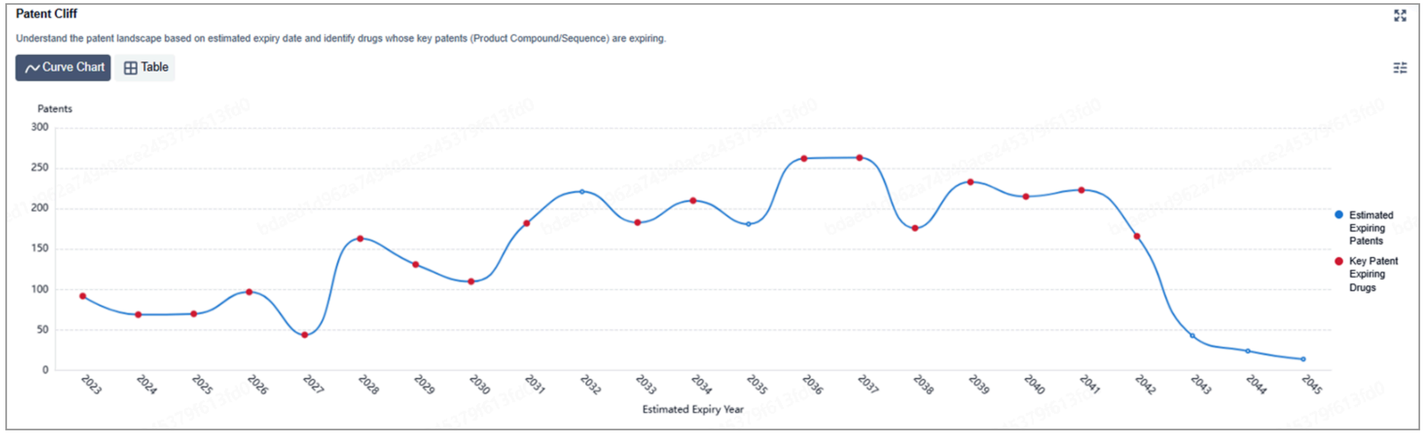
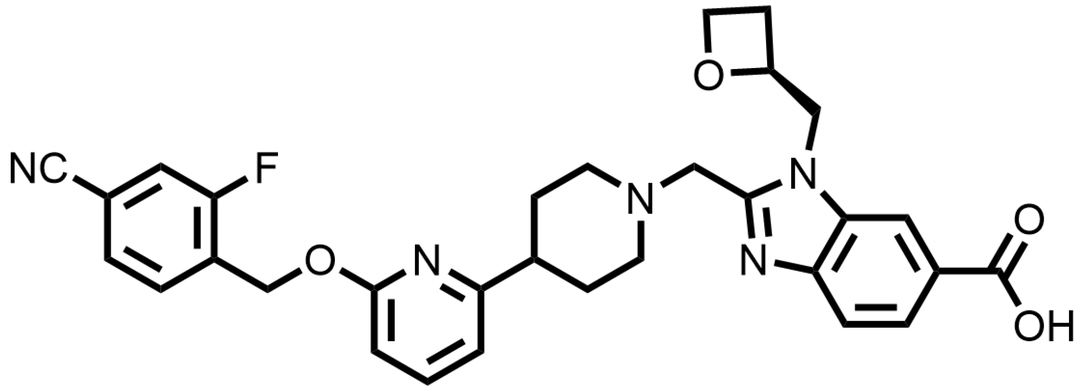


Fig 6. Patent expiry of GLP-1R drugs by year

Example 1

Pfizer

Danuglipron (PF-06882961) is Pfizer’s first-generation small-molecule GLP-1 receptor agonist (GLP-1RA), discovered through high-throughput screening of 2.8 million compounds. It acts as a positive allosteric modulator, binding to an allosteric site on the receptor to enhance its sensitivity. This mechanism allows optimization of molecules with relatively weak binding, and its comparatively simple scaffold has been widely adopted by other companies.



Danuglipron, (PF-06882961)

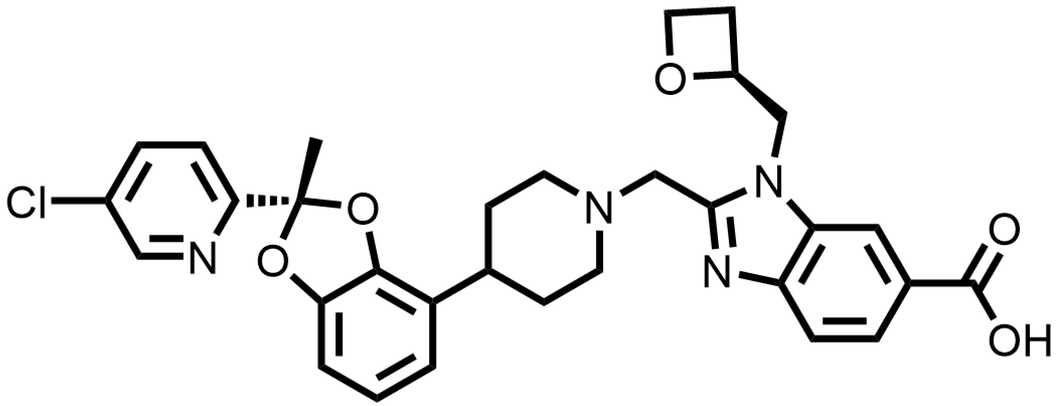
Fig 7. Structure of Pfizer's small molecule GLP-1 receptor agonist

In the Phase I/II clinical trials, this drug demonstrated hypoglycemic efficacy and weight reduction effects in patients. Common side effects include nausea, diarrhea, and vomiting. Its short half-life and low oral bioavailability required twice-daily dosing, and a strong inhibitory effect on hERG potassium ion channel raised potential cardiac safety issues.

Although it showed consistent safety with other GLP-1RAs in over 1,400 patients (only dose-dependent gastrointestinal reactions), and no significant elevation in liver enzymes (in contrast to the lotiglipron that was terminated in 2023 due to asymptomatic persistent liver enzyme elevation), a confirmed case of drug-induced liver injury (DILI) reported in April 2025 prompted Pfizer to terminate all clinical projects.

Although the liver toxicity was reversible and isolated, development was discontinued after a comprehensive assessment. This not only challenged prior assumptions about the drug’s hepatic safety but also underscored the unpredictability of liver toxicity in such compounds.

Pfizer’s second-generation small-molecule GLP-1RA, Lotiglipron, was developed to improve on Danuglipron’s short half-life and metabolic instability, enabling once-daily dosing. However, clinical trials revealed elevated liver enzymes (mainly ALT/AST) in some patients, prompting Pfizer to terminate development in June 2023.



Lotiglipron, (PF-07081532)

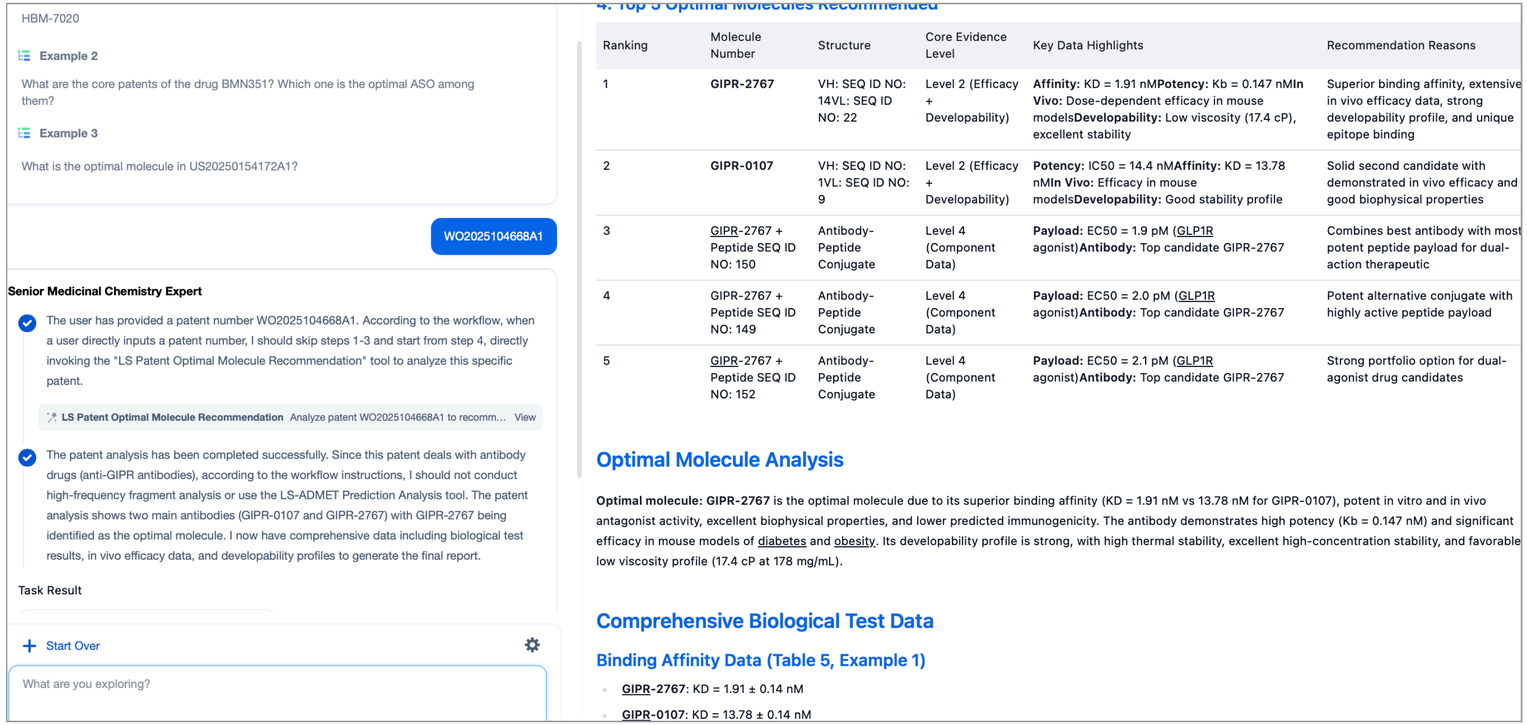
Fig 8. Structure of Pfizer’s small molecule GLP-1 receptor agonist

Although the two drugs share the advantages of Gs bias signaling, oral bioavailability and preclinical tolerability, their failure in the end is of the same nature, challenging the core assumption of safety prediction for small molecule GLP-1RAs: that biased agonism can improve receptor desensitization and gastrointestinal symptoms, but cannot avoid off-target hepatotoxicity.

PF-06954522, an oral small-molecule GLP-1RA developed by Pfizer, was also discontinued. Unlike previous candidates, it showed no toxicity; termination was driven by anticipated competitive pressure from single-target GLP-1 therapies, prompting a strategic reorientation. This decision marked a major setback for oral incretin-based treatments.

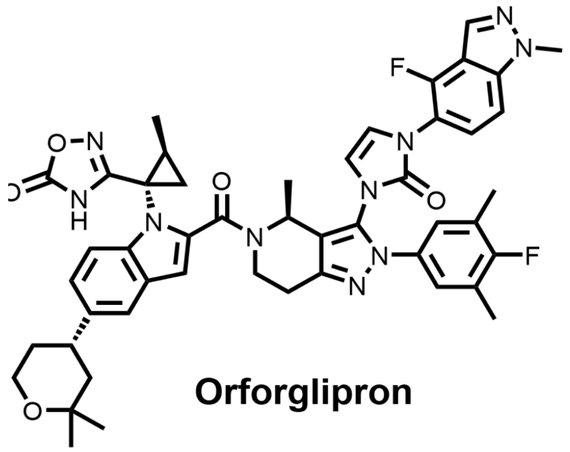
Pfizer is also active in the GLP-1 ADC patent space, developing a drug that couples a GLP-1 receptor agonist with an anti-GIPR antibody (patent WO2025104668A1). This coupled drug aims to enhance the effects of lowering blood sugar and weight loss by simultaneously activating the GLP-1 receptor and inhibiting the GIP receptor. From the analysis of the Lead Compound by the agent, it can be seen that GIPR-2767 and GIPR-0107 are the speculated optimal molecules.

Fig 9. Lead Compound Analysis agent - Interpretation of patent WO2025104668A1

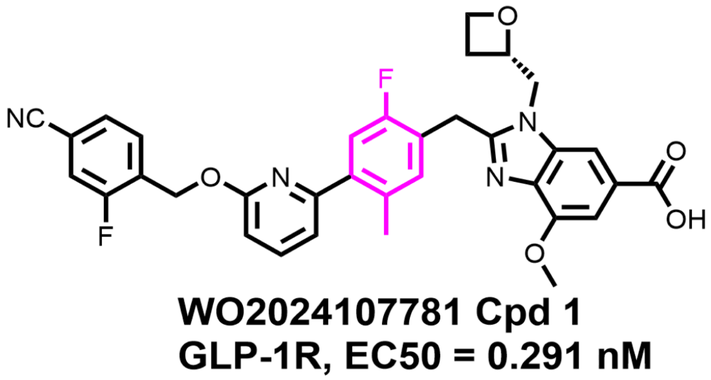


Example 2

Eli Lilly



Structure of Lilly's small molecule GLP-1 receptor agonist



The potential molecular structure of the compound associated with Eli Lilly's acquisition of Qilu Rui Ge

The oral non-peptide GLP-1 receptor agonist orforglipron (LY3502970) developed by Eli Lilly is one of the fastest-clinical-progressing small molecule drugs in this emerging therapeutic field. It was jointly developed by Eli Lilly and Chugai pharmaceutical.

The clinical phase III results show that after 72 weeks of treatment, the GLP-1 oral drug helped obese patients lose up to 11.2% of their weight. The observed weight loss is below the 15% benchmark expected by analysts and less than that achieved by Novo Nordisk’s oral drug. Eli Lilly is prioritizing submission of Orforglipron for obesity and expects to complete the approval process this year.

In addition to Orforglipron, Eli Lilly developed the small molecule GLP-1 receptor agonist called LY-3549492, undergoing clinical trials in the United States and Japan. Likely similar in structure to Pfizer’s scaffold (acquired by Qilu Rui Ge Molecular), its 2024 patent (WO 2024107781) showed promising activity for compound 1. However, Eli Lilly recently discontinued further development.

Example 3

AstraZeneca

ECC5004 is an oral small molecule GLP-1 receptor agonist originally developed by Eccogene Inc. (Shanghai) and later licensed to AstraZeneca. It belongs to a new generation of G protein biased agonists. On November 9, 2023, AstraZeneca acquired exclusive rights to develop and commercialize ECC5004 outside China, with a $185 million upfront payment, up to a $182.5 million in milestone payments for clinical, registration, and commercialization, and tiered royalties on net sales.

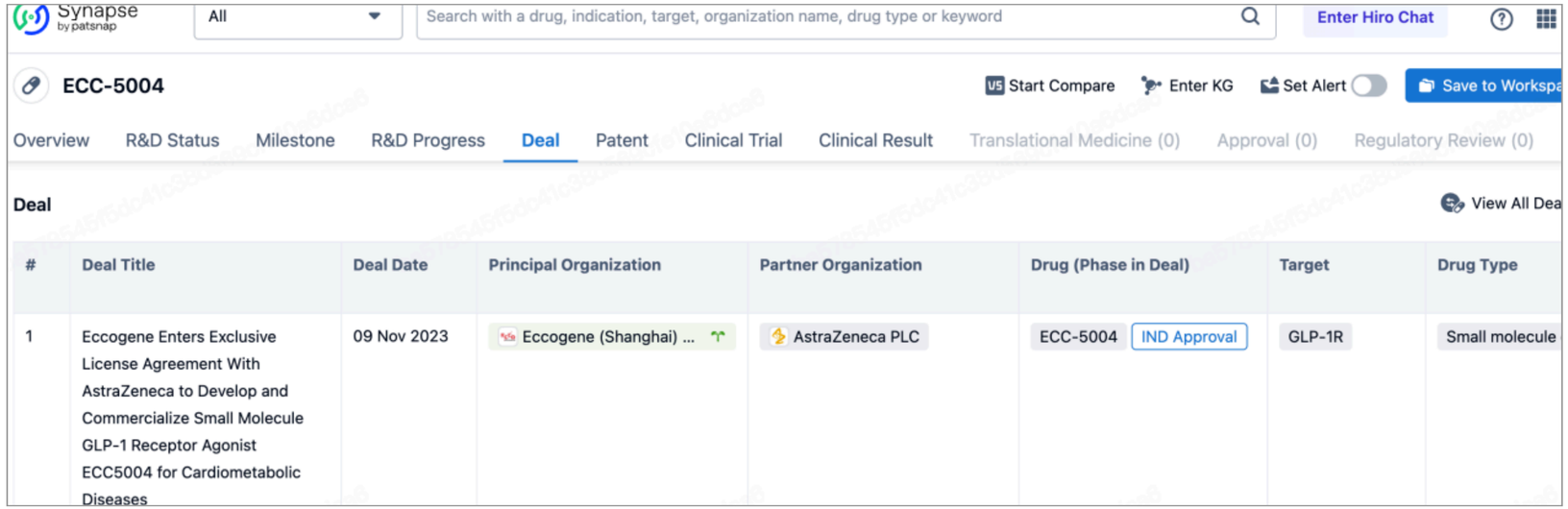


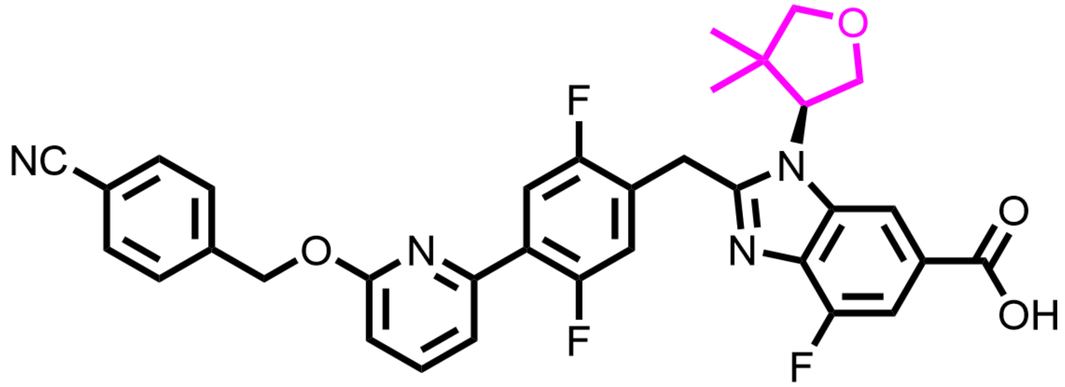
Fig 10. The acquisition of ECC5004 by AstraZeneca

ECC5004 is a once-daily, low-dose, oral small molecule GLP-1 receptor agonist. Its pharmacokinetic profile has been significantly improved compared to Eli Lilly's Orforglipron (bioavailability: 10% vs. 90%). After 4 weeks of treatment, the average weight loss was 5.8%. The main adverse reactions were mild nausea (≤15%) and loss of appetite (≤12%). There have been no reports of treatment discontinuation or serious adverse events, and no elevation of liver enzymes (unlike similar drugs that were discontinued due to hepatotoxicity). In October 2024, AstraZeneca announced that a global 2b phase trial is underway (for obesity and T2DM indications).

Example 4

GS-4571

GS-4571 is an oral non-peptide small molecule GLP-1 receptor agonist developed by Gilead. It is currently undergoing phase 1a clinical trials (NCT06562907). The main purposes are to verify the safety in healthy individuals, evaluate the pharmacokinetics in obese/T2DM patients, and conduct exploratory biomarker response analysis. Preclinical data indicate that a daily dose of 6.5% weight loss was observed over 36 days in rhesus monkeys, and it can penetrate the blood-brain barrier.



GS-4571

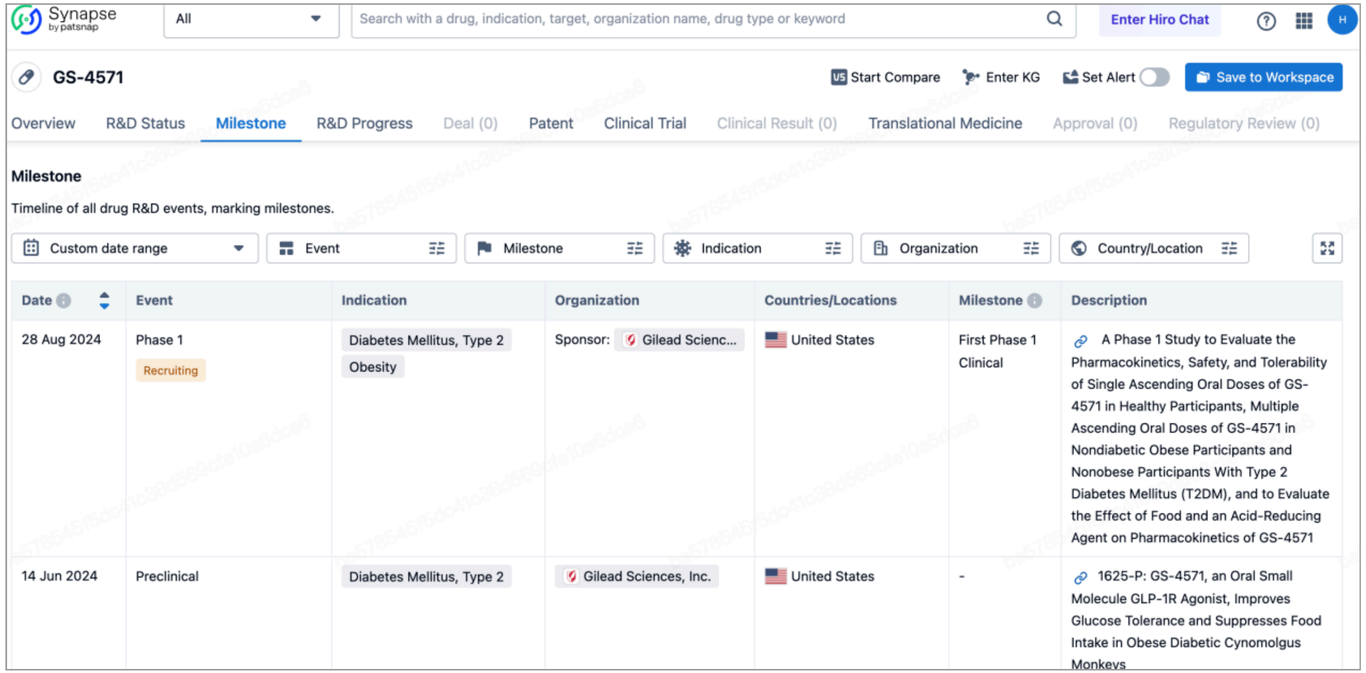
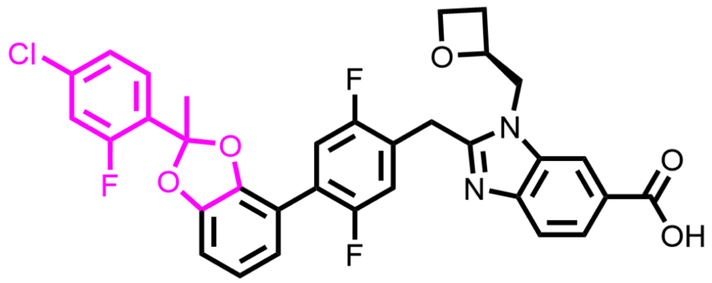
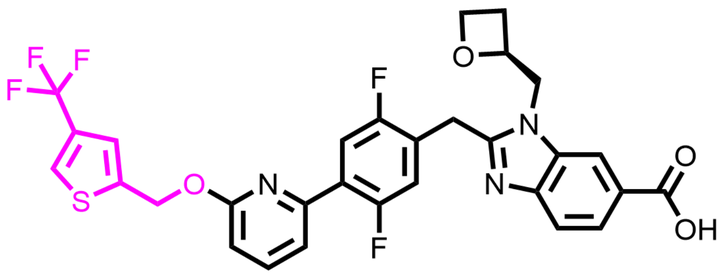


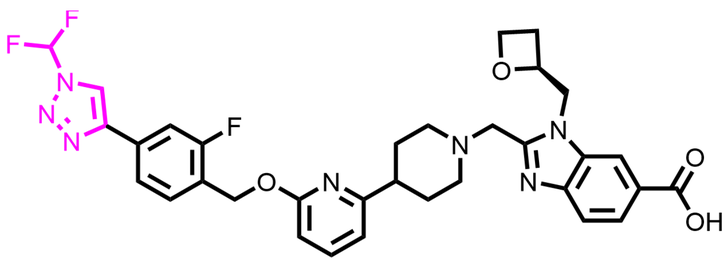
Fig 11. The milestone events of GS-4571



WO 2021154796 Cpd 44
GLP-1R, EC50: 0.033 nM



WO 2022192428 Cpd 10
GLP-1R, EC50: 0.4 nM



US012180197 B2 Cpd 19
GLP-1R, EC50: 0.2 nM

Structure of Gilead's small molecule GLP-1 receptor agonist

Other patents of Gilead, such as WO2022109182, US01280197B2, WO2022192428, WO 2021154796, WO2022225941, etc.,are all based on the structural modification of Pfizer's Danuglipron.

Example 5

Amgen’s antibody-peptide conjugation technology

The new drug AMG 133 (MariTide), an antibody-peptide conjugate based on the GIPR/GLP-1R antibody, has been approved for clinical trials in China. It is a potential "first-in-class" investigational antibody-peptide conjugate. Two GLP-1 analogues are conjugated at the specific site targeting the gastric inhibitory peptide receptor (GIPR), thereby activating the GLP-1 receptor while inhibiting GIPR. It can be administered by subcutaneous injection at a monthly or lower frequency.

In a Phase 2 study, MariTide achieved roughly 20% average weight loss in obese participants without type 2 diabetes (vs. 2.6% with placebo) and approximately 17% in those with diabetes (vs. 1.4% with placebo). Weight loss showed no plateau at week 52, suggesting continued potential for reduction.

In addition to the significant weight loss effect, MariTide also achieved a sustained and significant decrease of up to 2.2 percentage points in glycated hemoglobin (HbA1c) in those obese with diabetes. Weight loss was accompanied by improvements in a series of cardiovascular metabolic indicators, including waist circumference, blood pressure, high-sensitivity C-reactive protein (hs-CRP), and some lipid parameters.

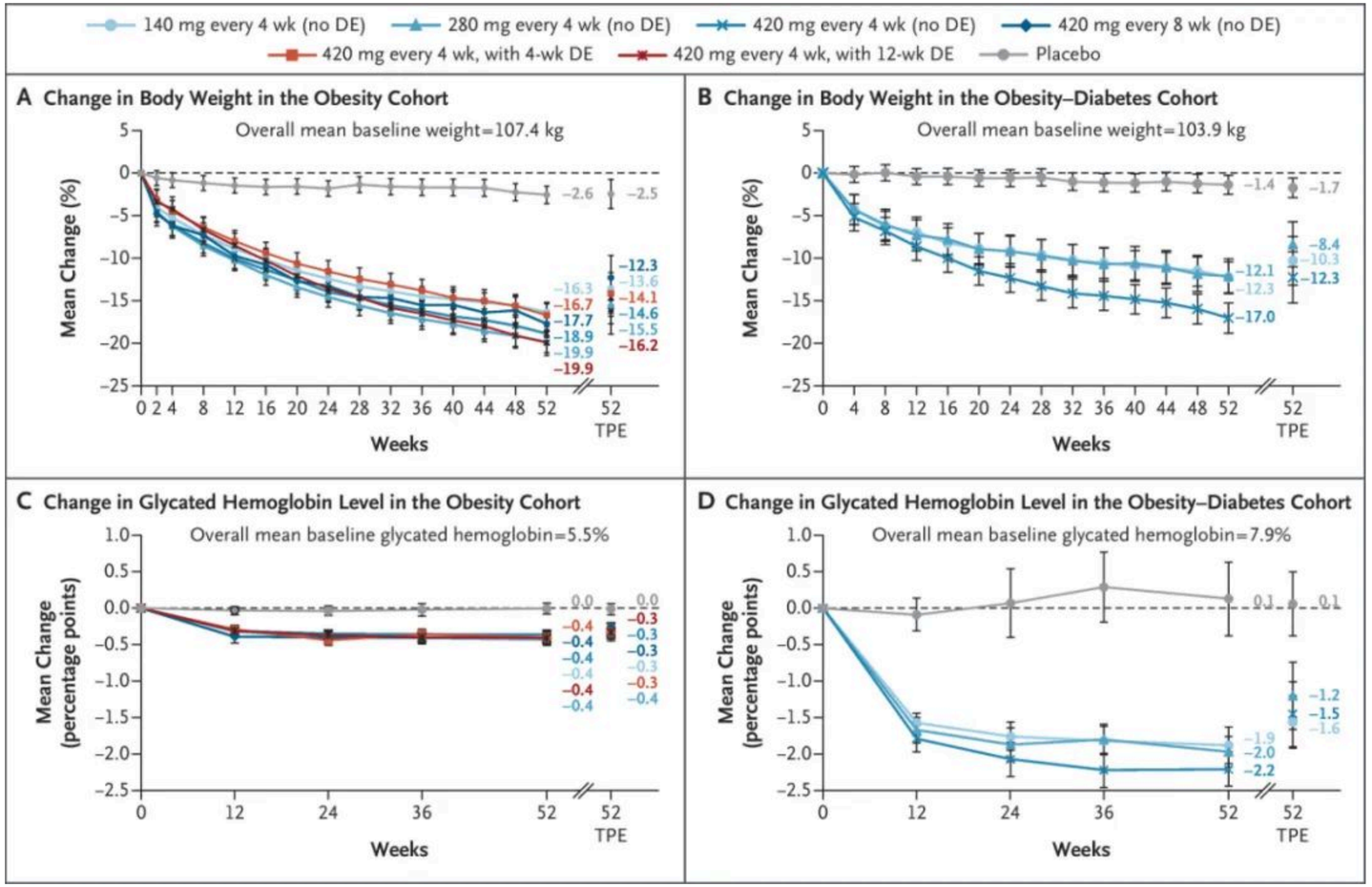


Fig 12. The clinical trial results of MariTide

In conclusion, small molecule GLP-1 receptor agonists will reshape the treatment landscape for metabolic diseases - their value is not to replace peptide drugs, but to serve as complementary treatment options to enhance treatment accessibility and individualization. Therefore, the commercial success of small molecule GLP-1RA depends on "three validations" namely large sample validation of liver safety, validation of cardiovascular hard endpoints, and head-to-head validation of injection formulations.

Chapter 3
Summary

GLP-1R market competition is not slowing down – to survive, R&D efforts and IP strategy are crucial. Going beyond small molecules, drug developers are actively exploring biologics like fusion proteins, ADCs, and even gene therapy for a combination therapies approach and expanding disease indication beyond obesity.

Hence, patent monitoring and strategy become mission-critical. Companies need always-on patent surveillance for GLP-1/adjacent modalities, run routine FTO checks, and refine filing strategy (composition, combo, RoA, dose/formulation) to protect differentiation.

Winning on safety will be as important as winning on efficacy. With growing concern around adverse events, demonstrating superior safety and PK/PD during clinical trials are crucial to be recognized as best-in-class, with RoA and dosage strength as the potential niche to drive patient adherence.

Finally, APAC will be central to the next phase of competition. Novo Nordisk and Pfizer's news in the obesity market in 2025 serve as an important lesson and case study, and reset the playing field for others.

Against a backdrop of shifting geopolitical and market dynamics, China remains a critical arena that innovators cannot overlook. Real-time competitive intelligence and ongoing assessment of potential APAC collaborators will be pivotal to future success.

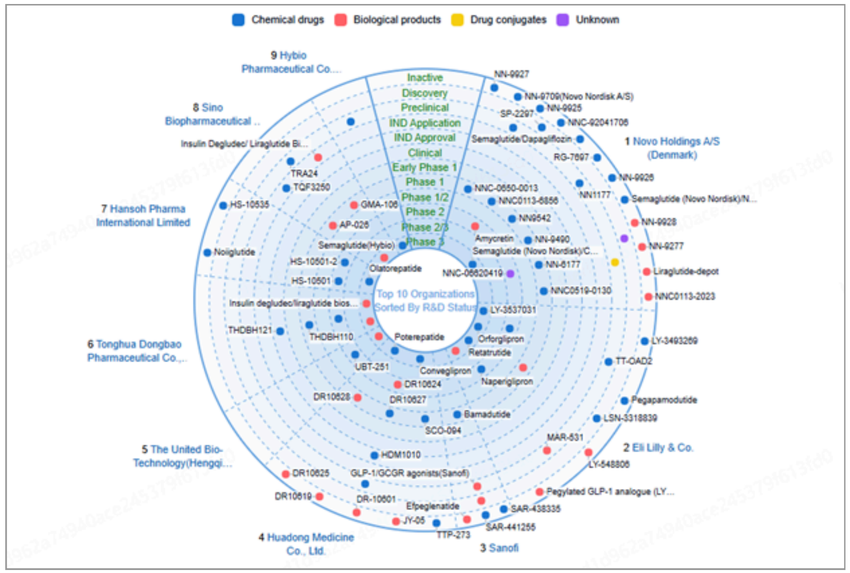


Fig 13. Top 10 GLP-1R targeting drug developers (excluding approval)

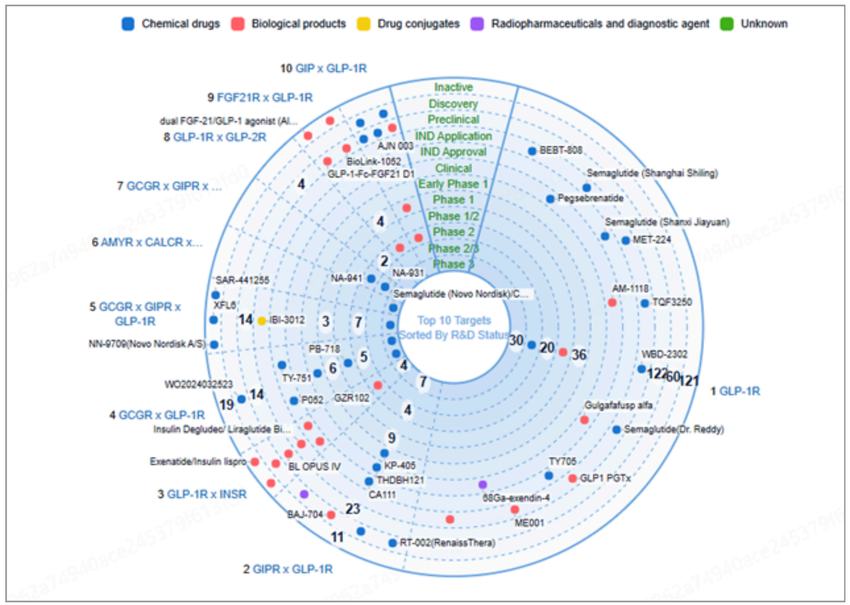


Fig 14. Top 10 GLP-1R related targets (excluding approval)

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4 https://synapse.patsnap.com/drug-list?query_id=4234db38-2697-43e7-9b30-7b531e499242&tab=analysis

5 https://synapse.patsnap.com/literature-detail/8a17b04d-f2c8-3460-8871-1bb24080a4ea

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9 https://synapse.patsnap.com/drug/0a551ce6f1d04e458ce60183148a693f

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