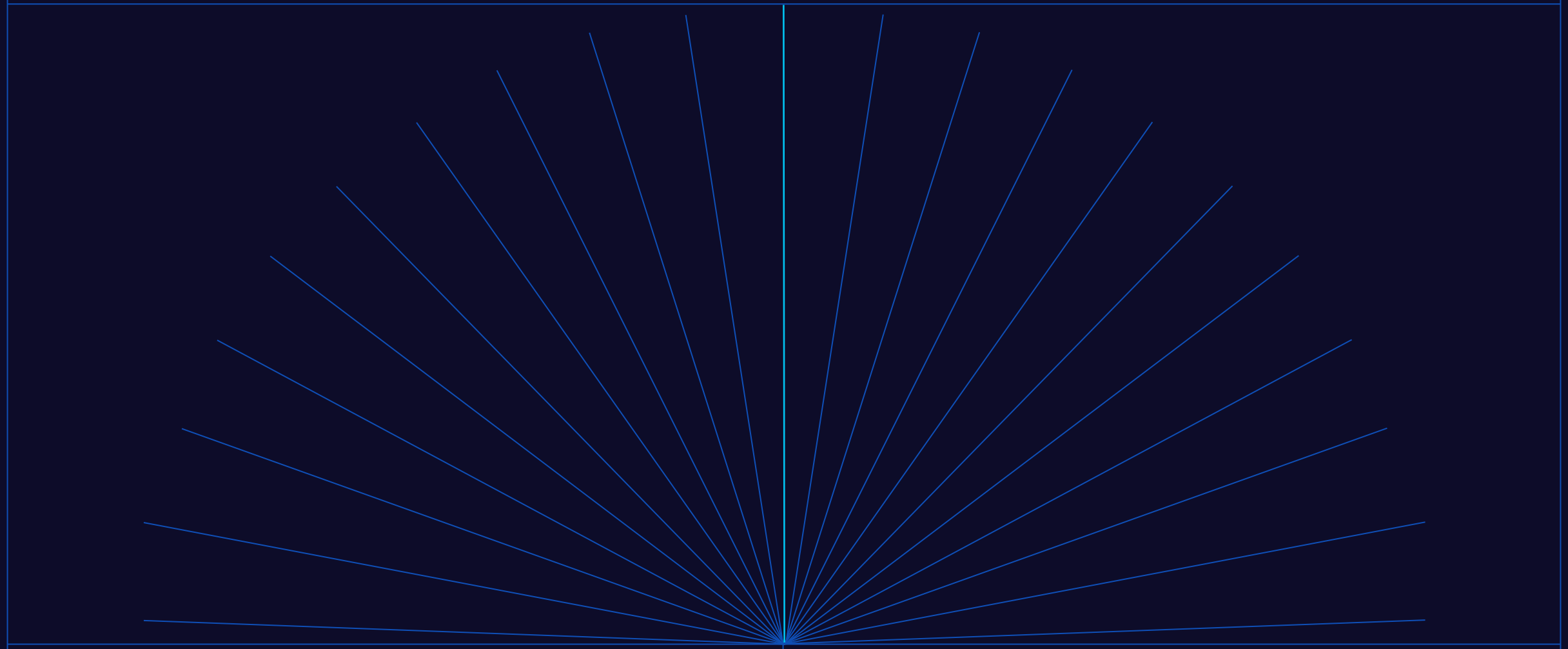

Sleuth

Sleuth Intel Hub
GLP-1 and Metabolic Intelligence Report
Q3 2026

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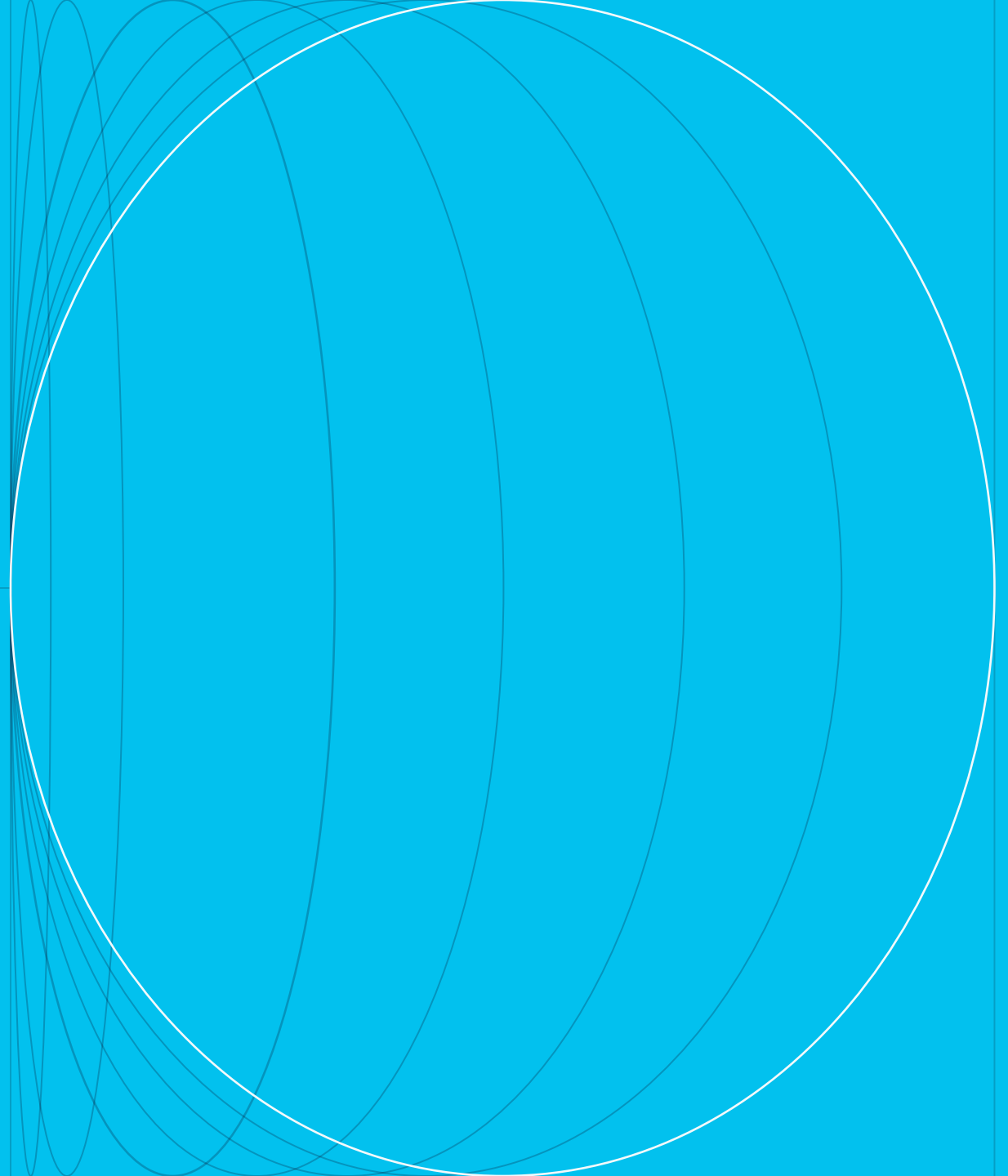
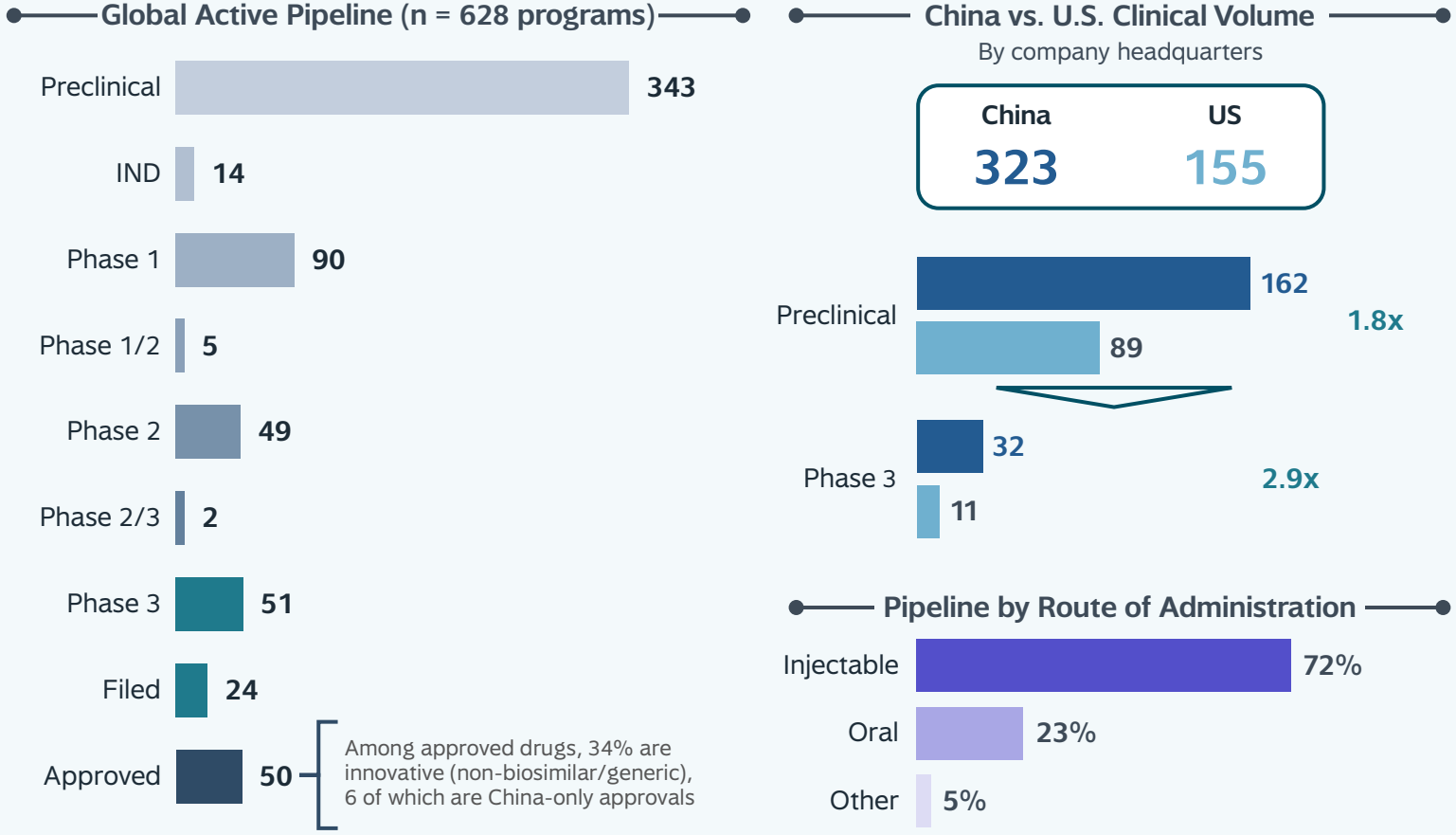


Late-stage entrants are gearing up to capture the market Novo and Lilly own

628 active programs now crowd an increasingly saturated GLP-1 landscape, most still injectable

Active GLP-1 Pipeline by Phase and Origin



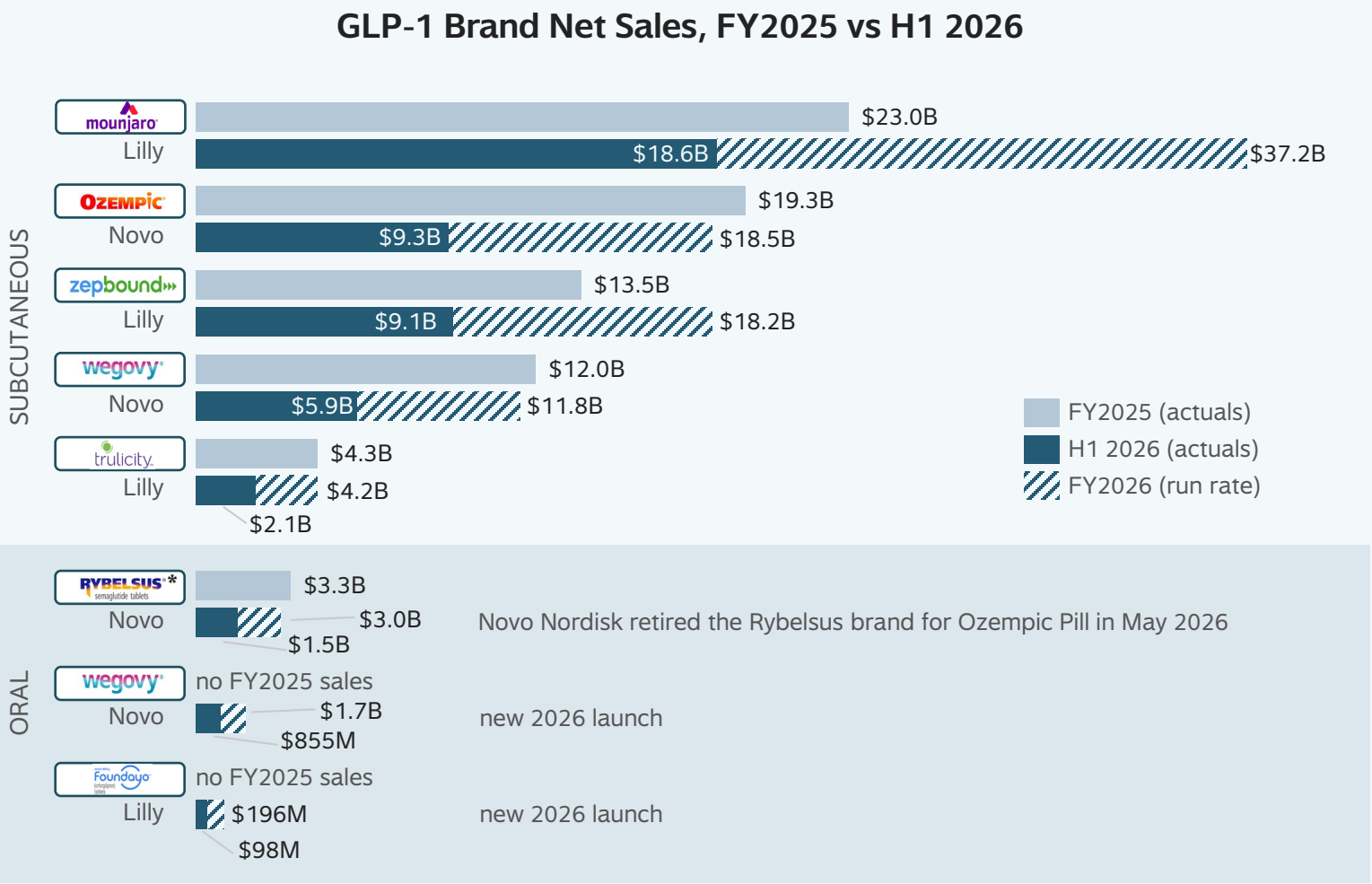
- Despite a growing long tail of competitors, the branded U.S. market remains a Novo Nordisk–Eli Lilly duopoly
- Liraglutide and semaglutide biosimilars saturate the approved and filed counts respectively, with Ex-US semaglutide LOE driving the surge
- By company headquarters, Chinese firms field nearly twice the US pipeline (323 vs 155 active programs), widening to ~2.9x at Phase 3

Competitive intelligence analysis of the global GLP-1 and metabolic pipeline as of August 2026. US-approved means a program carrying a US regulatory approval.

Lilly leads the SC category while Novo still holds the smaller oral lane

Injectables hold 95% of H1 2026 disclosed sales, though new oral launches are starting to broaden the field

- Lilly's tirzepatide franchise reached 58% of disclosed 2026 sales, up from 48%, as Mounjaro grew 106% while Ozempic slipped 6%.
- Oral launches from Novo and Lilly are still a minority of sales but signal the differentiation battle moving from efficacy toward format
- US sales dominate the flagships at 59-70% for Mounjaro, Ozempic, and Wegovy, and the newest launches are effectively US-only



Competitive intelligence analysis of approved GLP-1 brand net sales, FY2025 and first-half 2026, from company disclosures, focused on Novo Nordisk and Eli Lilly. Shares are of disclosed dollars. First-half 2026 figures are actuals, not annualized, and compounded semaglutide and tirzepatide supply sits outside these branded figures. *Accounts for Rybelsus / Ozempic Pill net sales given brand transition. Novo Nordisk figures are converted from Danish kroner to US dollars at the period-average rate, about 6.6 DKK per USD for FY2025 and 6.40 for first-half 2026. The 2026 column annualizes reported H1 2026 net sales (H1 doubled) into a full-year run-rate, shown dotted, and reads as a conservative floor.

Approved GLP-1s broaden indications while challengers carve differentiation

Outcome readouts in cardiovascular disease and MASH keep opening new indications

Count of Drugs By Phase (Non-obesity / T2D)

Indication cluster	Preclin.	Phase 1	Phase 2	Late stage: 144 programs			Total
				Phase 3	Filed	Approved	
Cardiovascular	~31	~64	~16	~59	~2	~9	181
Liver and MASH	~74	~26	~32	~13	~1	~1	147
Kidney	~7	~7	~9	~11		~1	35
Sleep apnea, respiratory	~10	~4	~5	~10		~1	30
Metabolic, endocrine	~35	~31	~12	~12			90
Inflammation, immunology	~1	~16	~9	~4			30
Neurology, psychiatry	~15	~9	~14	~15			53
Addiction, substance use	~1	~5	~22	~5			33

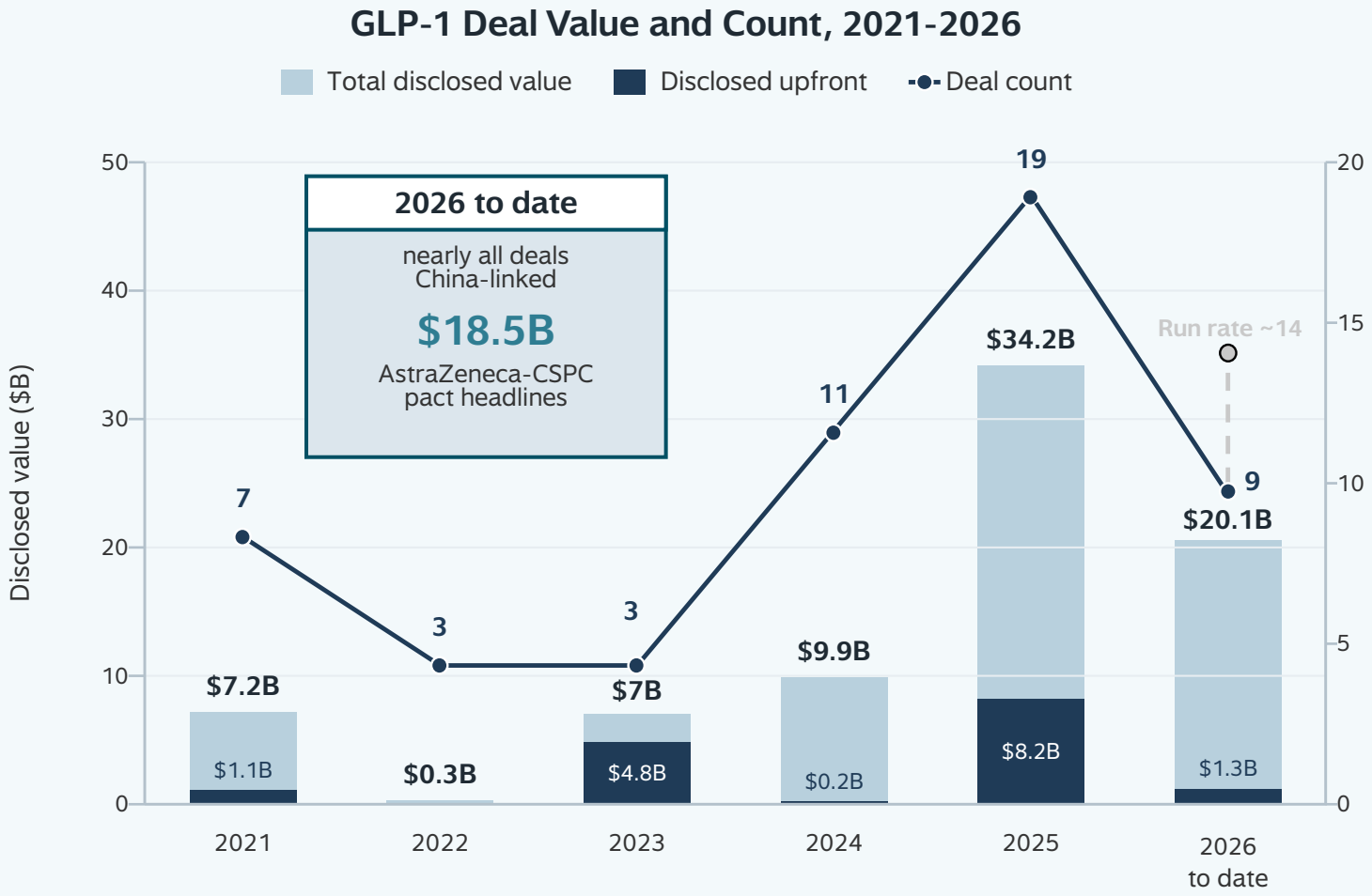
- Semaglutide and tirzepatide keep turning positive readouts into new labels across cardiovascular, kidney, sleep apnea, and MASH
- Challengers chase these adjacencies, but Novo and Lilly run ~74% of late-stage programs, limiting space for smaller entrants
- The late-stage mental health and addiction frontier is led by Lilly, brenipatide in alcohol use and MDD. Treatment area breadth is becoming the incumbent race

Competitive intelligence analysis of GLP-1 and incretin programs pursuing indications beyond core obesity and type 2 diabetes, as of August 2026.

Incumbents buy capabilities while other entrants buy their way in early

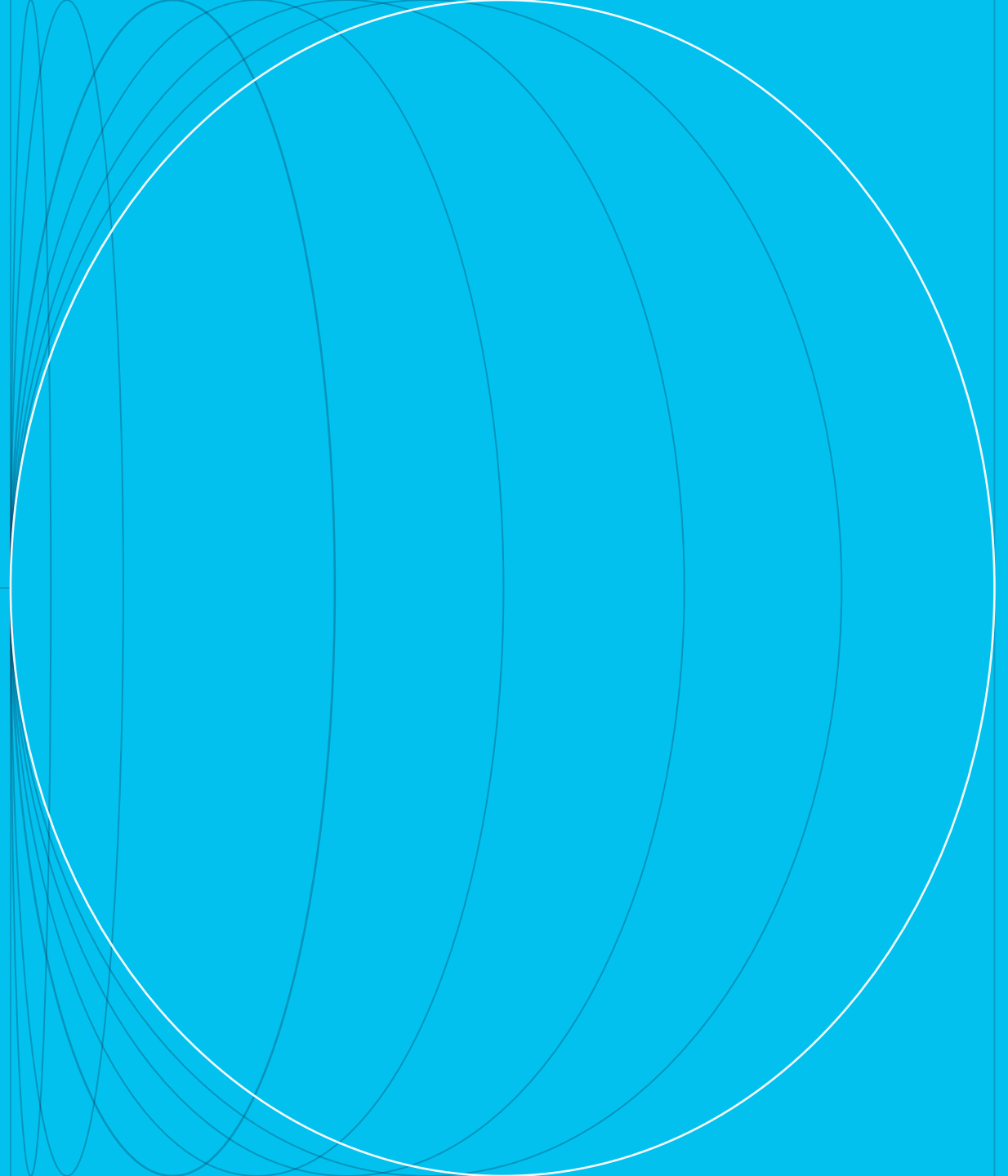
China is now the primary source of GLP-1 dealmaking, most deals since 2024 versus a minority before

- Novo and Lilly buy capabilities, muscle (bimagrumab), oral formats, and long-acting delivery, building on strong portfolios
- Other entrants pay premiums to buy in early on differentiation plays, Pfizer's deal for Phase 2 Metsera
- Buyers pay a $70M median upfront on China-linked assets vs $500M for non-China, yet total deal values match near $2B for both, and the gap holds across development stages.



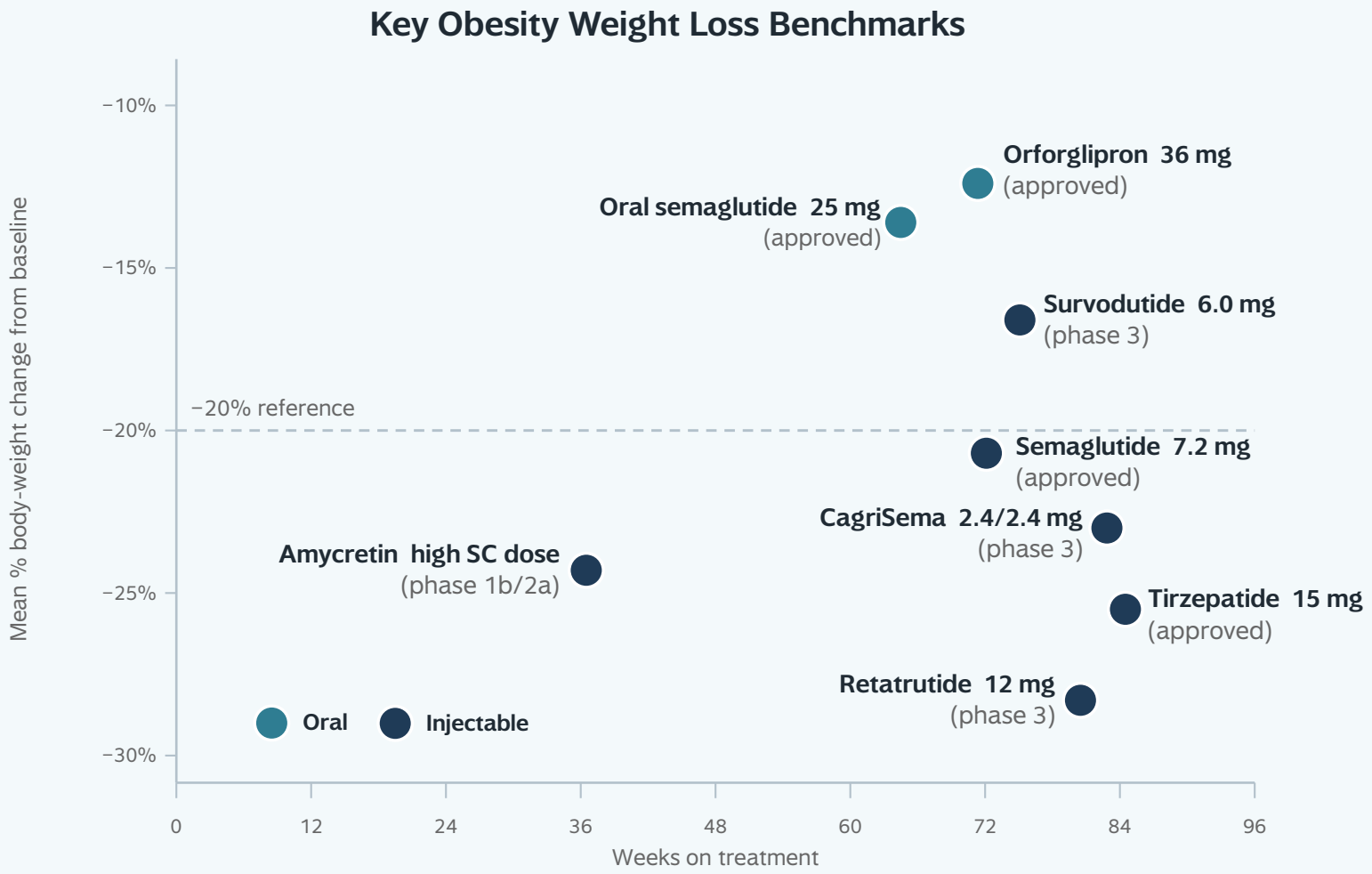
Competitive intelligence analysis of GLP-1 and key-mechanism business-development deals (licensing, collaboration, and acquisition) from 2021 through August 2026.

Section 2: Sleuth Perspectives



The weight-loss bar is set high, so differentiation is shifting off raw efficacy

Leading injectables cluster at 20 to 28% weight loss, while both orals trail behind at 12 to 14%



- Incumbent GLP-1s continue to push the injectable weight-loss benchmark, increasingly competing on weight differentiation in H2H studies

- **Sleuth Insight:** Injectables set an increasingly high weight loss ceiling, so the white space for future winners hinges on route, dosing, and quality of weight loss

Competitive intelligence analysis of best demonstrated obesity weight loss for leading incretin assets, each the mean percent body-weight change at the highest studied dose under the trial-product or efficacy estimate, from pivotal readouts (TRIUMPH-1, REDEFINE-4, STEP UP, SYNCHRONIZE-1, OASIS-4, ATTAIN-1) through August 2026. Timepoints range 36 to 84 weeks and are labeled per asset; cross-trial comparison is our analytical read, not head-to-head except REDEFINE-4.

Approved GLP-1s expand labels as the late-stage field still proves weight loss

Seven approved-drug catalysts reach new indications while 19 of 23 late-stage assets chase weight loss

Competitive intelligence analysis of forward GLP-1 and incretin catalysts for August 2026 through December 2027, readouts dated by expected trial primary completion. * Tirzepatide mortality (SURMOUNT-MMO), CagriSema cardiovascular (REDEFINE-3), semaglutide retinopathy (FOCUS).

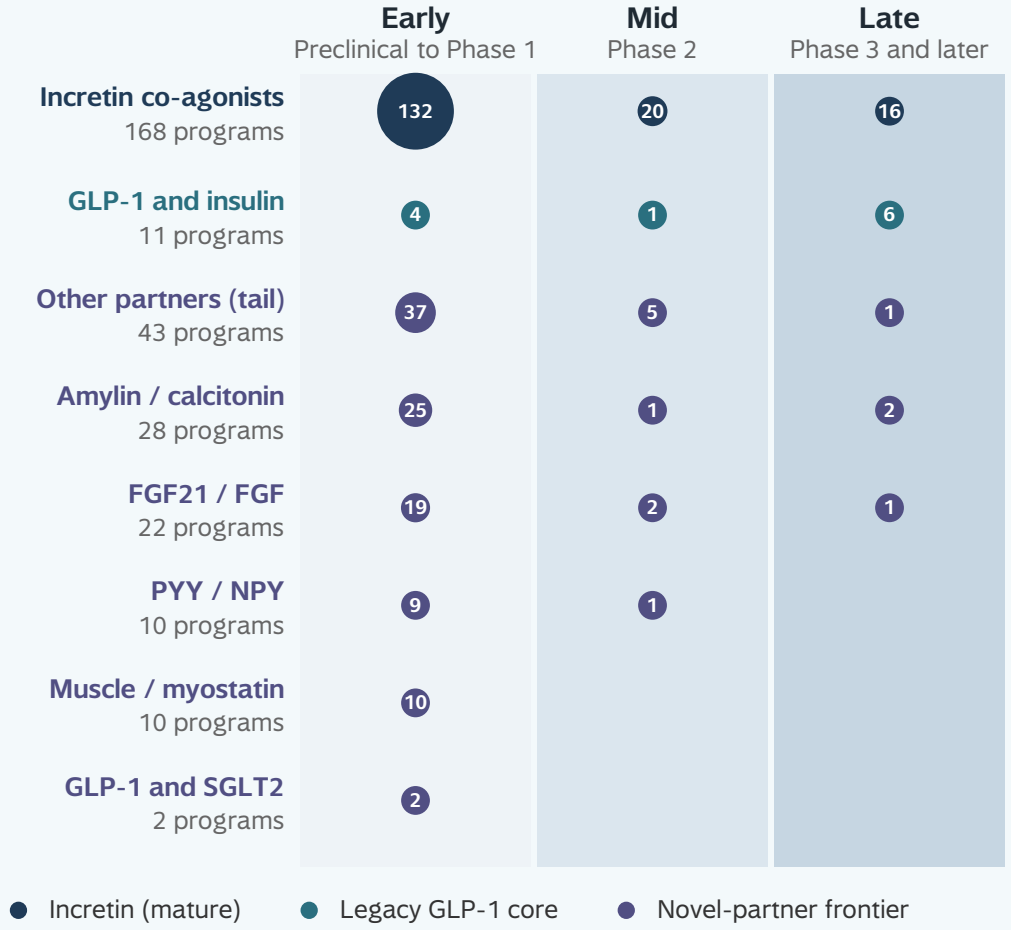
The pipeline is full of combinations, but only incretin co-agonists have matured

The pipeline contains 124 unique target combinations, but the novel-partner frontier stays preclinical

- The mature combinations are engineered incretin co-agonists, 168 programs stacking GLP-1 with GIP or glucagon

- **Sleuth Insight:** Beyond incretin combinations, the bets increasingly pair GLP-1 with indication-specific targets like FGF21 for MASH to differentiate, while within obesity they target unmet needs in weight loss, muscle sparing and better dosing

Combination Programs by Mechanism Family and Phase



20 Key Combination Approaches

- **6** **Muscle preservation**
  6 regimens, Phase 2
  Lilly, Regeneron, Scholar Rock
- **5** **Satiety (PYY)**
  5 regimens, Phase 2
- **5** **Liver and MASH**
  5 regimens, Phase 2
- **4** **SGLT2 pairs**
  4 regimens, Phase 3
  only Phase 3, all diabetes

Competitive intelligence analysis of the active GLP-1 and metabolic pipeline catalogued by target combination as of August 2026, across 124 target signatures.

Incumbents are increasingly solving the muscle-loss problem through combinations

Approx. 70 programs claim muscle sparing, the leaders proving it in combination with dedicated muscle agents

- At least 70 programs now message on muscle preservation, with 19 positioning it as their key pillar
- These combinations cut lean-mass loss by half or more and shift weight loss to over 90% fat, in Phase 2
- **Sleuth Insight:** Muscle sparing is becoming a combination race, and the incumbents lead it by adding anti-catabolic agents to their GLP-1s. The battle is shifting from how much weight to how well it comes off

Key Example

Lilly acquired Versanis and its lead asset, bimagrumab, for $1.9B in 2023

Muscle-Sparing Claim-Makers and Phase 2 Proof

EMBRAZE Trial

Scholar Rock

apitegromab + tirzepatide

54.9%

Lean mass preserved vs tirzepatide mono (p=0.001)

COURAGE Trial

Regeneron

trevogrumab + garetosmab + semaglutide

33% to 7.4%

Lean share of weight loss cut, Semaglutide mono to triplet, 92.6% fat

BELIEVE Trial

Lilly

bimagrumab + semaglutide

92.2%

Share of weight loss due to fat mass

QUALITY Trial

Veru

enobosarm + semaglutide

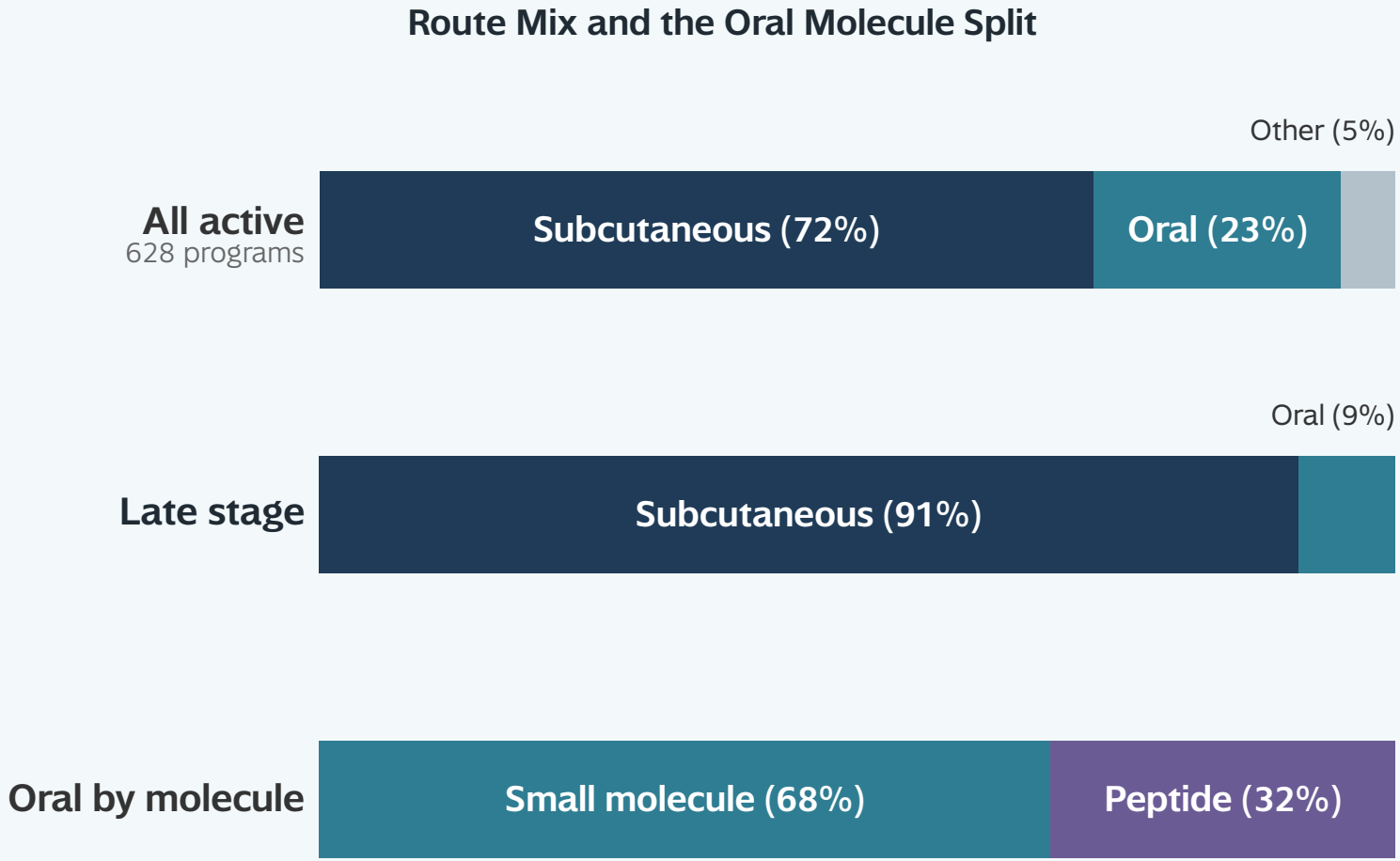
71%

Less lean loss vs semaglutide mono (p=0.002)

Competitive intelligence analysis of muscle-preservation positioning across, layered with Phase 2 body-composition readouts from the leading muscle-preserving combinations. Muscle-preservation positioning is scored per program from public materials: 70 programs reference it, 19 as a core pillar of their positioning and 51 mentioning it.

Small molecules make oral scalable and convenient, but efficacy lags injectables

The oral race is consolidating around small molecules that solve bioavailability and manufacturing



- Small molecules are the majority orals; orforglipron reaches 79% bioavailability with no food rules versus near ~1% for peptides
- As injectable efficacy plateaus, oral scale and route could win a growing segment (e.g., needle aversion for 14 - 38% of adults pulls oral demand), but GI tolerability stays the open question
- **Sleuth Insight:** A scalable, convenient oral could garner demand, with injectables as the higher-efficacy step-up, though the question becomes whether RoA alone can break through Novo and Lilly's entrenched portfolio contracts.

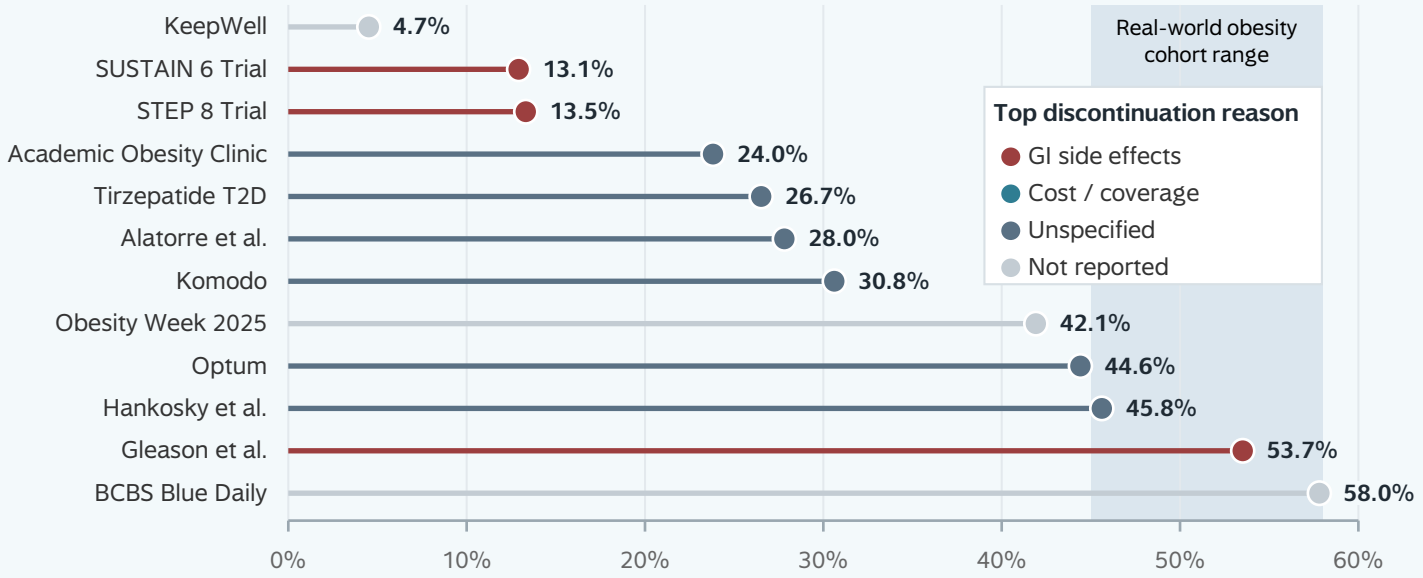
Competitive intelligence analysis of program route of administration (RoA).

Efficacy is proven, but real-world persistence collapses within the first year

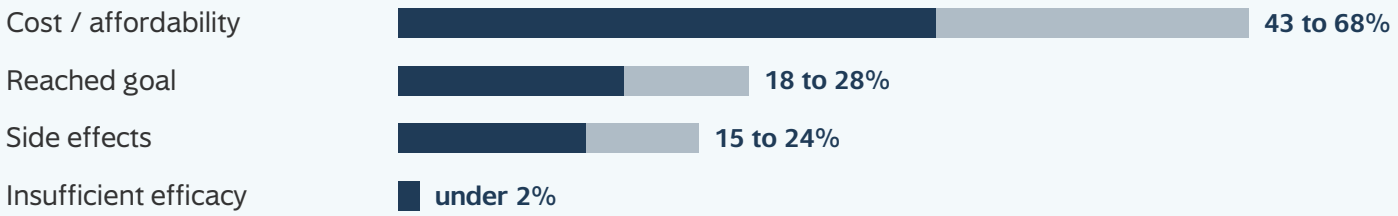
About half of obesity patients stop within six months, and only 8 to 14% persist at three years

- Patients enter intending to stay beyond a year, per Morgan Stanley's 2026 AlphaWise user survey, but cost, tolerability, and access friction end it within months
- Cost is the top driver at 43 to 68%, but side effects also push exits, so cheaper prices alone may not restore persistence
- **Sleuth Insight:** The unmet need is durability, not efficacy, and the extent to which rising cash-pay channels ease durability barriers remains an open question

Most patients discontinue within six months



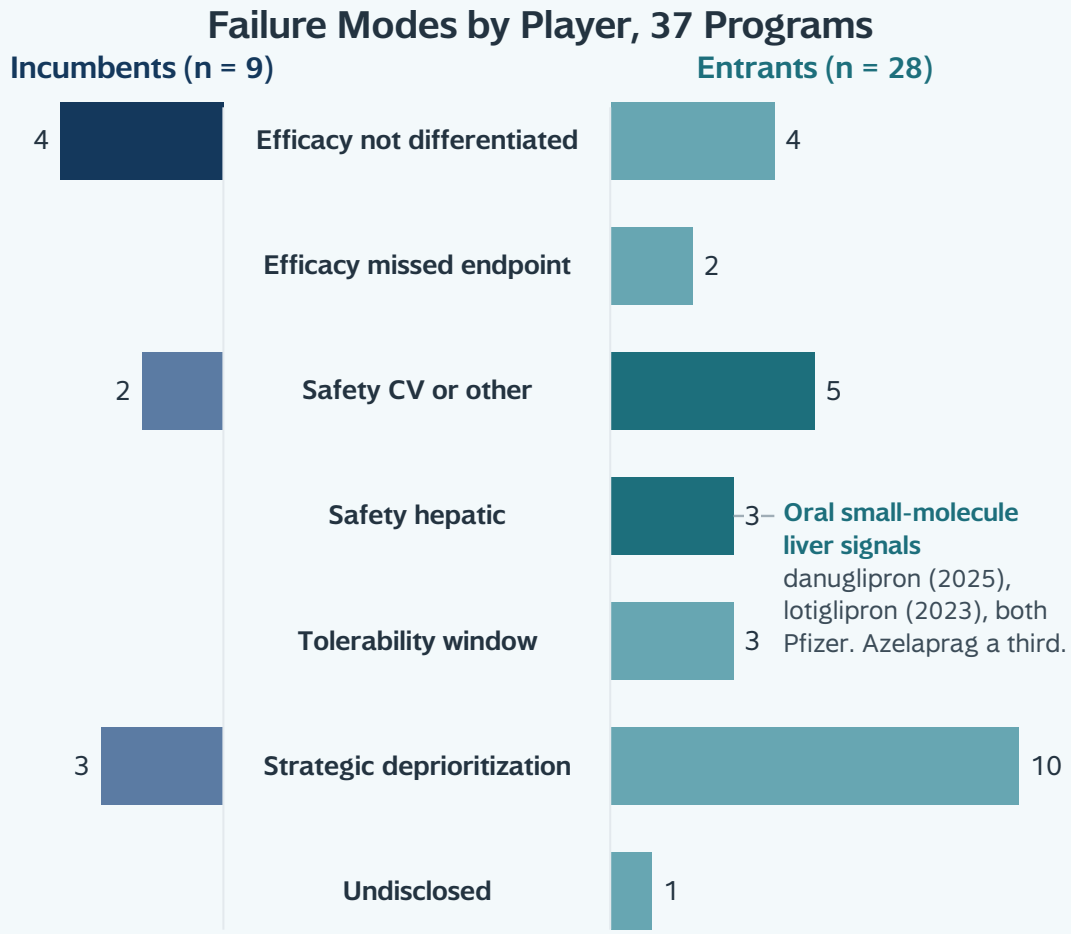
Drivers of discontinuation (share)*



Competitive intelligence analysis of real-world persistence and discontinuation across a consolidated six-month discontinuation evidence set (43 studies). Persistence, discontinuation-driver, restart, and weight-regain figures are cited to primary real-world and claims-based studies.
*Drivers of discontinuation: cost 43 to 68% (Navitus 68%, KFF 53 to 54%, Cleveland Clinic 47.6%, EBRI 43%); side effects or GI ~15 to 24% (EBRI 24%, Cleveland Clinic 14.6%); achieved goal ~18 to 28% (EBRI 28%, Omada 18%); insufficient efficacy ~2% (Cleveland Clinic).

Incumbents prune on efficacy; entrants must clear a higher whole-profile bar

Failure modes signal that entrants face a much higher clinical and commercial bar



Oral small-molecule liver signals
danuglipron (2025), lotiglipron (2023), both Pfizer. Azelaprag a third.

The commercial bar entrants must clear

Broad, entrenched payer access
Entrenched formulary positions and portfolio contracts set barriers for novel entrants

Broad market shaping / brand recognition
A clean clinical profile alone does not open the market

- Incumbents are competing on increasingly high efficacy data, even CagriSema missed non-inferiority to tirzepatide at 23.0 versus 25.5%
- Entrants differentiate on route or modality, yet oral small molecules still carry tolerability concerns, as Pfizer's danuglipron showed in 2025
- **Sleuth Insight:** Novo and Lilly are racing to fill the gaps entrants seek to fill, and growing incumbent volume makes them even harder to dislodge. Clinical parity no longer opens the market

Competitive intelligence analysis of 37 discontinued or deprioritized GLP-1 and metabolic programs, normalized to a six-bucket failure-mode taxonomy and split by incumbent (Novo, Lilly) versus entrant. Named-example clinical details are cited to primary company and regulatory disclosures.

China is now the fast-follower engine the West sources its next GLP-1s from

China's fast-follower entries jumped from 2 to 13 a year, and the West is now licensing them back

GLP-1 Fast-Follower Chain, End to End

	Steps	Key Data	Description
1	**Originate** U.S. and Western catalysts	**2** non-Chinese originators	Novo Nordisk and Eli Lilly validated the class with semaglutide (2021) and tirzepatide (2022); Chinese fast-followers surged once the targets were proven.
2	**Fast-Follow** China develops in parallel	**69** programs, 44 developers	A concentrated field led by Hengrui, Hansoh, and CSPC, each building a fast copy of a validated incretin. Entries rose from 2 to 13 a year.
3	**License-Back** assets return West, priced	**~$2.0B** median total per deal	13 of 15 deals carry disclosed terms and licensed assets back, with Novo and AstraZeneca among buyers; a $106M median upfront against the $2.0B total, and 8 of 15 signed in 2025.
4	**Capital** funding, both sides	**66% / 3%** China-domestic / direct US	Across 368 funding rounds, U.S. money is mostly indirect: about 66% is Chinese-domestic and only ~3% direct U.S. equity, with Western capital present as co-investment.

- The West has licensed 13 Chinese assets back across 15 deals since 2021 at a median $2.0B, with 8 signed in 2025 alone
- The assets reach the West two ways, direct out-licensing and venture NewCos, Kailera, Verdiva, and Sidera at $920M
- **Sleuth Insight:** China has become the fast-follower engine of the class, yet the copies are Chinese-funded, with barely 3% of rounds direct US equity. For an entrant the question is no longer whether to tap China, but on which channel and how early

Competitive-intelligence analysis of China-origin GLP-1 and incretin fast-follower activity, 2018 to 2026. The license-back set is 15 deals covering 13 distinct assets at a median total value of about 2 billion dollars, 8 of them signed in 2025. The three venture NewCos raised about 920 million combined. The funding read covers 368 rounds, about 66 percent Chinese-domestic and about 3 percent direct United States equity, with Western capital present on both sides as co-investment rather than a proven flow.

Sleuth predictions

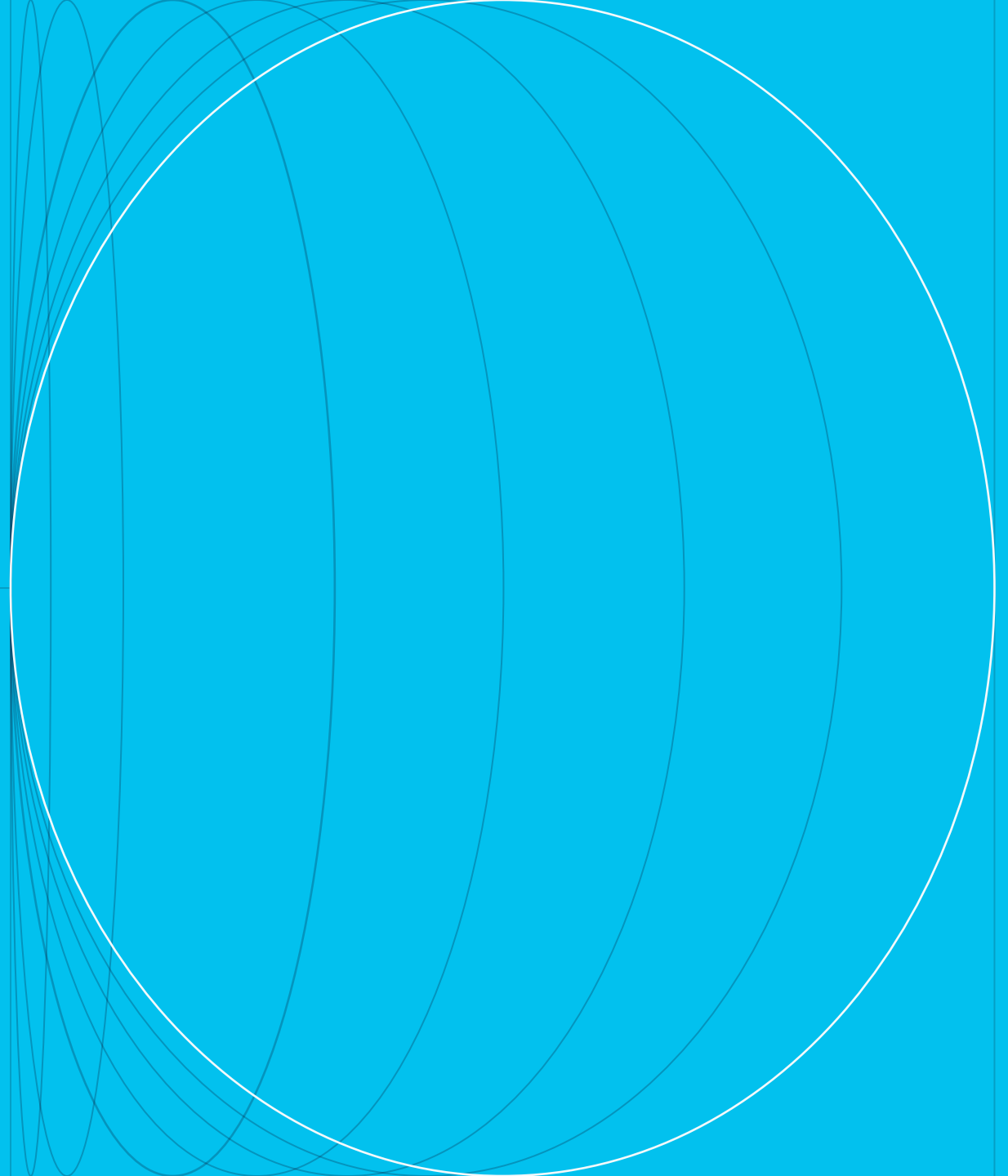
Our read when we look beyond the data

1. **Quality of loss displaces raw loss as the benchmark:** By 2027 quality of weight loss displaces raw loss as the benchmark, with muscle-sparing endpoints as an integral portfolio play

2. **A small-molecule oral takes double-digit share of new starts:** Orforglipron takes double-digit share, driven by a combination of incumbent contracts, oral demand, and indication expansion surge (e.g., OSA, hypertension)

3. **By 2028, maintenance becomes its own race:** As persistence collapses inside 6 months and ~2/3 of weight returns off drug, the next impactful readouts move from peak loss to tolerability-first, stay-on regimens led by the amylin agonists

How Sleuth can help



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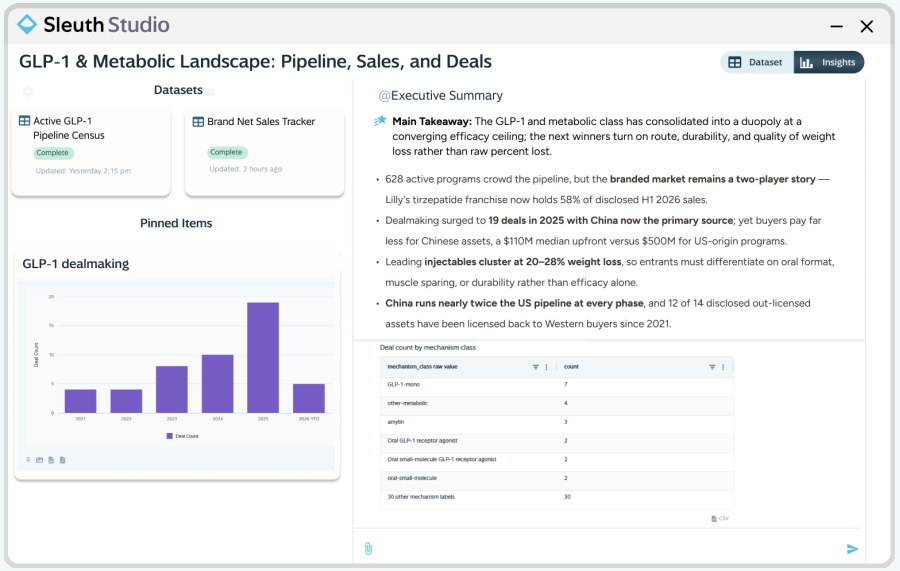
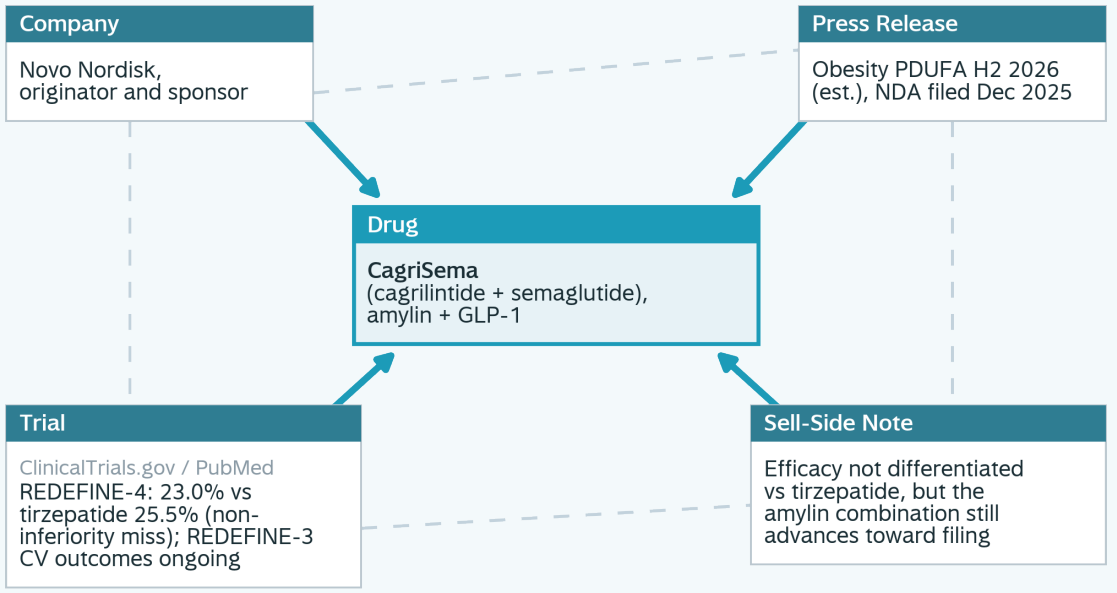
Main Takeaway: The GLP-1 and metabolic class has consolidated into a duopoly at a converging efficacy ceiling; the next winners turn on route, durability, and quality of weight loss rather than raw percent lost.



Intelligence you can stand behind

Bring Sleuth your questions, and pre-connected intelligence surfaces automatically. Our knowledge graph connects data across the landscape, with full traceability.

Illustrative knowledge graph for CagriSema



Case study: Epana Bio indication prioritization

What happens when you evaluate 167 indications with the same effort as six? Read the full case here.

Stakes: Epana Bio needed to make a high-stakes decision on which indications to pursue first for their targeted cell depletion therapeutics.

Challenge: Standard evaluation is often limited by bandwidth, forcing teams to choose from just a few familiar diseases.

Approach: Epana ran a comprehensive evaluation of 167 indications, using an iterative framework to challenge scores and pressure-test every assumption.

Outcome: Leadership built the conviction needed to select lead indications and raise capital with an investor-ready narrative.

167	Indications evaluated
25	Evaluated with a tailored Epana focus that most processes never reach
4	Shortlisted for deep commercial diligence
1	Optimized basket

"All the strategy that used to be proprietary to pharma — the 'game within the game' that actually drives strategic decisions — Sleuth made that accessible to a nine-person biotech. **I think it's the most disruptive, amazing thing for small organizations like ours.** A massive, massive unlock."

Danny Wells, PhD
CEO, Epana Bio