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From GLP-1 Breakthrough to Healthcare System Readiness

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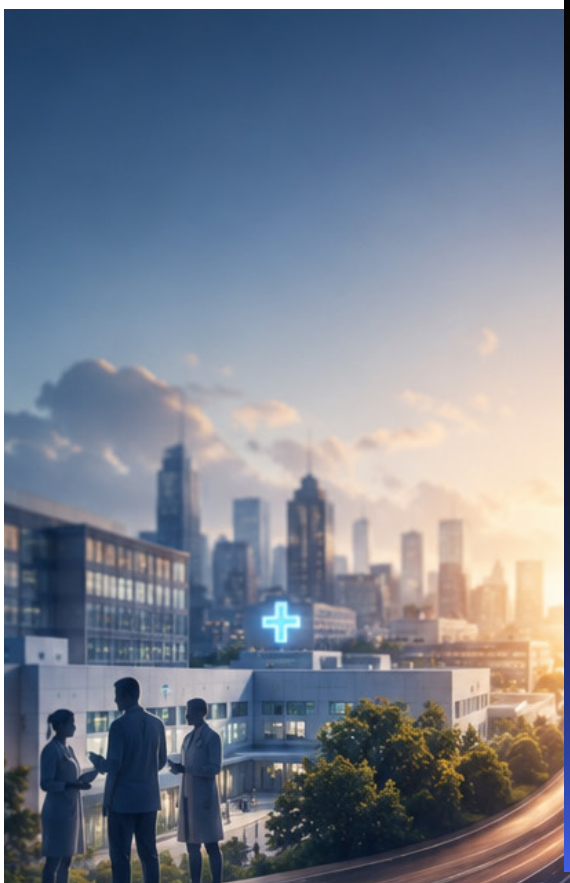

LUCID STRATEGY CONSULTING 2026

FROM GLP-1 BREAKTHROUGH TO HEALTHCARE SYSTEM READINESS

The first wave of glucagon-like peptide-1 (GLP-1) therapies applied beyond diabetes settled one question decisively: *pharmacological intervention in obesity* ***works***. But the challenge has moved on. Pharma companies now face three critical tests: building evidence strategies that demonstrate measurable long-term outcomes as competition intensifies across assets and delivery models; making metabolic care work within healthcare systems that lack the pathways, payor frameworks, and primary care capacity to support it; and engaging patients and clinicians whose expectations are being shaped faster than any company can manage. This will take next-generation, cross-disciplinary business and scientific thinking. Yet *many pharma companies are still operating with the last-generation playbook*.

THE FIELD HAS CHANGED. HAVE THE STRATEGIES?

The first wave of GLP-1 therapies established that meaningful, sustained weight loss was achievable through pharmacological intervention. Regulators have since confirmed broader applications beyond weight loss: approved indications now include cardiovascular risk reduction, metabolic dysfunction-associated steatohepatitis (MASH), obstructive sleep apnea, and obesity-related heart failure. [1,2,3,4]

The next wave of assets brings innovation across multiple dimensions, with dual- and multi-incretin agonists, amylin-based agents, oral small molecules, and longer-acting formulations. [5,6,7] Emerging evidence is also prompting debate around incretin biology in neurodegeneration and addiction – a development that carries significant implications for science, healthcare, and pharma strategy. [8,9]

But the healthcare and socioeconomic systems expected to assimilate these powerful therapies are not keeping pace. From the payor perspective, affordability, appropriate use, and long-term coverage remain fundamentally unresolved. From the healthcare professional (HCP) perspective, primary care is being asked to manage complex, chronic metabolic treatment without the infrastructure or clinical guidance to support it. And from the patient perspective, expectations are being shaped in an information environment that has run well ahead of the clinical reality. As the field diversifies and new approvals further segment a highly comorbid population, headline weight loss will play less of a role in determining which therapies are successful, and the gap between what these medicines can do, and what healthcare systems are ready to deliver, will only widen.

We highlight three key themes for pharma strategists seeking to lead the way in the future of metabolic care.

1. The evidence and value story needs rebuilding

The value proposition for GLP-1 therapies was built on headline weight loss, establishing pharmacological intervention as clinically credible and driving landmark regulatory approvals; however, as a basis for differentiation and value demonstration going forward, that will not be sufficient.

Payors and providers – as well as patient groups and employers – are also asking different questions. What does metabolic intervention do to cardiovascular burden, functional capacity, and long-term disease progression? How does it reduce downstream cost? Who benefits most, under what conditions, and over what time frame? These are not primarily scientific questions; rather, from a pharma company's perspective, they are *questions about evidence strategy, value narrative, and the ability to connect therapeutic data to the outcomes that decision-makers care about*.

Recent approvals and trial data demonstrate that the field is responding by moving toward outcomes beyond weight loss. Semaglutide data in obesity-related heart failure with preserved ejection fraction showed improvements in symptoms, physical limitations, and exercise capacity that go well beyond net weight reduction. [4] Data presented at ADA 2026 reinforced this, with semaglutide and retatrutide analyses spanning sleep apnea, asthma, liver health, osteoarthritis, and glycemic risk.

Comorbidity management and functional outcomes are becoming the next axis of value demonstration in this field. [10,11]

The osteoarthritis data illustrate the breadth of the value case. In primary care, chronic joint pain driven by excess weight frequently becomes irreversible, generating reliance on analgesics that can themselves promote weight gain, increase risk of surgical intervention, and have a compounding impact on mental health. Musculoskeletal conditions and mental health are among the leading drivers of long-term sickness absence and work disability across OECD economies. [12,13,14] If incretin therapies can resolve a root cause rather than manage these downstream consequences, the socioeconomic case may extend well beyond direct healthcare cost, catalyzing new levels of interest from "consumer-patients", employers, and governments.

Approvals in MASH, cardiovascular risk reduction, and obstructive sleep apnea show that regulators are highly receptive to these broader disease-modification claims. As incretins gain approvals in the broader CVRM landscape, this will have profound consequences for pharma companies developing therapies in these areas – products will launch into a more crowded market, with a layered outcome-driven treatment algorithm. [1,2,3] The clinical development implications are significant too. As GLP-1 prescribing becomes more prevalent across patient populations, eligibility criteria, washout requirements, concomitant therapy design, and the real-world relevance of study populations all become harder to manage, a challenge we will look to explore in greater detail in future. Further afield, emerging evidence in neurodegeneration, addiction, and autoimmune conditions suggests the therapeutic scope of incretin biology may extend well beyond metabolic disease. [8,9,15]

The pipeline is also diversifying in ways that will further complicate how value is demonstrated. Amylin and calcitonin receptor agonists target the neurochemistry of appetite regulation directly, while combination approaches such as CagriSema™ are already producing Phase 3 weight-loss data that exceed GLP-1 monotherapy. [16,17] These are not simply more potent versions of existing therapies – they work via different mechanisms, which means their comorbidity profiles, tolerability, and long-term outcomes may differ significantly from approved incretins. A single evidence strategy built around a general conception of the strength of incretin therapies will not be sufficient. Mechanistically distinct assets will require differentiated evidence strategies, potentially tailored to the patient populations and outcomes where that mechanism has the strongest case.

A related question is how treatment selection will evolve. Unlike oncology, where biomarker-driven stratification has become central to treatment choice, metabolic medicine cannot yet predict differential response at the molecular level. [18,19] In the near term, patient–therapy matching will rely in part on convenience, tolerability, and care pathway compatibility. But the longer-term trajectory points toward evidence-based stratification – understanding which patients, with what comorbidity profiles, respond best to which mechanisms. Pharma companies that invest in generating this evidence now will be best positioned to defend their assets as the market becomes more crowded.

One dimension where this kind of evidence-based nuance is overdue is body composition. The *quality of weight change* – not just its amount – is increasingly discussed, but the conversation often conflates a measurement limitation with a pharmacological problem. Sub-analyses reporting that up to 38% of weight lost during GLP-1 therapy is lean mass are based on DEXA scans, which cannot reliably distinguish contractile muscle from glycogen, water, liver fat, or inflammatory fluid. When examined more closely, the clinical picture is different: GLP-1 therapies do not result in disproportionate loss of muscle mass or function compared with calorie restriction; lean mass, after an initial decline, stabilizes over 12 months; a systematic review of incretin therapy versus lifestyle intervention found no significant difference in the proportion of weight lost as lean mass. [20,21,22] Lean mass does decline during treatment, but the nature and clinical significance of that loss appears considerably more nuanced than headline figures imply. [23]

Body mass index (BMI), the primary criterion for treatment eligibility, compounds this problem: it does not distinguish between fat and lean mass or capture visceral adiposity: these are the drivers most closely linked to insulin resistance and cardiometabolic risk. The 2025 Lancet Commission on Clinical Obesity recommended moving beyond BMI alone to confirm excess adiposity through measures such as waist circumference and waist-to-hip ratio, and distinguished between clinical obesity – where organ dysfunction is present – and preclinical obesity, where it is not. [18] If payors and healthcare systems adopt this framework, treatment eligibility will increasingly depend on

functional status and body composition rather than a BMI threshold. Pharma companies whose trials are designed purely around BMI cutoffs risk generating evidence that does not align with how treatment decisions will be made in the clinic.

However, the evidence challenge is only part of the problem. GLP-1s drive faster, larger weight loss than lifestyle change alone, and the appetite suppression that drives this can sharply reduce dietary quality and protein intake. Data presented at ENDO 2026 showed that patients on GLP-1 therapy also significantly reduce their physical activity. [24] These are consequences of inadequate wraparound care, not of the molecule itself. Pharma companies will need to pair sharper evidence strategies with care models that address broader drivers of adverse outcomes, including poor nutrition, inactivity, and inadequate clinical support.

Taken together, these shifts demonstrate the need for pharma companies to rethink how they articulate value in metabolic care. But as the evidence above makes clear, even the sharpest evidence strategy will not deliver sustained outcomes without the operational infrastructure to support it.

2. In the real world, sustained value depends on more than the asset

Metabolic medicine has moved faster than almost any therapeutic area in recent history, carrying enormous promise for patients and healthcare systems. But the widening evidence landscape described above will only translate into sustained outcomes if a robust implementation framework is there to reinforce it. As oral formulations reshape how treatment is initiated and dual agonists raise the bar for efficacy, the systems surrounding these medicines, and not just the molecules themselves, will determine which pharma companies deliver lasting value.

Most pharma companies built their metabolic pipelines and capabilities in a world where obesity treatment was specialist led. However, metabolic therapies have already shifted toward primary care, telehealth platforms, online prescribing pathways, and pharmacy-linked models – and increasingly, in many markets, into direct-to-consumer channels that bypass the prescriber and payor relationships that commercial models have historically been built around.

In the UK, NICE's approach to tirzepatide, with defined initiation criteria, structured review points, and explicit stopping rules, signals that healthcare systems are treating these medicines as components of managed long-term care. [25] NHS England's commissioning guidance goes further, emphasizing operational readiness in primary care, and online prescribing safeguards. [26] What these frameworks do not yet address consistently is the behavioral dimension. Commissioning attention remains overwhelmingly focused on drug cost, with little provision for the lifestyle and psychosocial support needed to sustain long-term benefit. As discussed in the previous section, in practice, medication efficacy can paradoxically reduce a patient's motivation to maintain diet and exercise – the very behaviors that underpin durable outcomes in muscle mass, bone density, and nutritional status. Private digital health providers are starting to build behavioral interventions to address this, including nutrition coaching, activity tracking, and adherence support, but these sit mainly outside the traditional reimbursed clinical pathway. Pharma companies that find ways to embed behavioral support alongside pharmacological management will close a gap that many commercial models are yet to solve.

The MHRA's June 2026 approval of oral semaglutide as the first GLP-1 tablet for weight loss in the UK came with an explicit note that the product is not yet available on the NHS. [27] Meanwhile, Novo Nordisk reported that approximately half of early Wegovy® pill sales came through direct-to-consumer routes, with over 80% of new prescriptions going to patients previously untreated with GLP-1 therapy. [28] Alongside the increased convenience of a pill formulation, this could also reflect the "unlocking" of a psychological barrier: for many patients, injectable treatment carries associations with more severe conditions, and the availability of a pill changes who is willing to engage with pharmacological weight management. Oral formulations are not just opening new commercial channels; they are reaching patient populations that existing infrastructure and engagement models were not designed to serve.

Access is only one part of the operational challenge. Data from the STEP 1 trial extension – the landmark study of semaglutide in obesity – showed that patients who stopped semaglutide regained the majority of their weight within a year of discontinuation. [29] Similarly, a meta-analysis of 37 studies found that weight regain is accompanied by a reversal of the cardiometabolic benefits achieved during treatment, including improvements in blood pressure and cholesterol. [30] The consequence

of these findings is reflected in maintenance trial designs for tirzepatide and emerging oral agents. [31, 32] The parallel with other chronic conditions is instructive: withdrawing antihypertensive medication once a patient's blood pressure normalizes, only to watch it deteriorate, would be considered clinically indefensible. Yet the commercial and operational models around obesity treatment have not yet fully taken on the same logic. Modeling from Goldman Sachs anticipates that one in two patients will discontinue therapy, with between 60% and 64% of those citing cost or lack of coverage as the primary reason. This is a discontinuation profile that no commercial model built around treatment initiation is designed to address. [33]

Consider what a metabolic-ready commercial model actually requires: Field teams capable of supporting primary care physicians through the complexity of long-term management decisions, not just product education at launch; digital infrastructure built around patient retention and structured review; and Medical Affairs functions equipped to engage healthcare systems on care pathway design. Most pharma organizations have none of these at the scale metabolic care will demand.

Companies that can demonstrate credibly that they know how to support long-term metabolic care, through primary care partnerships, structured patient support programs, and clinically grounded switching and sequencing guidance, will build a *sustainably differentiated position in the market that the asset alone cannot deliver*.

3. Trust and experience will shape long-term value

The information environment around metabolic health has changed fundamentally. Patients are forming expectations before they encounter a clinician – through social media, AI-generated health content, peer networks, and digital clinics, but also mainstream media coverage. Recent surveys suggest that growing proportions of patients now consult AI tools before, after, or sometimes instead of, seeing a clinician, and in practice, many arrive at appointments with AI-generated summaries and preprepared questions, all of which can have profound consequences for patient expectations. [34,35] Nor is this limited to patients: platforms like OpenEvidence are increasingly the first reference point for HCPs seeking clinical guidance, which changes what field-based education and promotional engagement need to offer to add value. Compounded GLP-1s, unregulated online pathways, and a fragmented conversation about side effects, weight regain, and long-term safety have complicated the task of building informed, realistic patient expectations. [36, 37]

Unlike most therapeutic areas, where reporting tends to defer to clinical authority, incretins have generated active public debate, oscillating between "miracle drug" enthusiasm, celebrity association, and moral concern about medicalizing weight. This misalignment of expectations means patients may enter treatment with inflated expectations, incomplete understanding of tolerability, or no clear picture of what happens when treatment stops, and therefore could be more likely to discontinue treatment. Discontinuation undermines clinical outcomes and the commercial model simultaneously.

The trust challenge extends to institutional stakeholders. Employers and payors are weighing near-term affordability against long-term benefit, appropriate use against utilization risk, and the credibility of manufacturers' value claims against a broader information environment that has not always served patients well. The FDA's recent actions against telehealth companies marketing compounded GLP-1s illegally suggests that regulatory scrutiny of the information environment is increasing, and that brand trust will be a meaningful strength as the market matures. [36, 37]

None of this is entirely new. What is different here is the scale and pace. The speed at which incretin therapies have moved from clinical trials into mainstream clinical conversation, and the volume and diversity of information sources now shaping patient and HCP understanding, create a communication and engagement challenge that conventional medical education and promotional models were not designed for. As we will discuss in future articles, *the end of the controllable, click-through internet* means pharma companies can no longer communicate with patients and clinicians at chosen moments; they need to understand and engage with holistic patient–clinician dialogue as it forms, across platforms where they have limited control.

Building credible, sustained engagement among patients, HCPs, and institutional stakeholders in this environment requires more than a communications strategy. It demands deep insight into how behavioral barriers form and can be broken down, and how the narrative around metabolic care is constructed, and reconstructed, across a fragmented, digitally mediated information landscape.

WHAT THIS MEANS FOR STRATEGY

The challenges differ across evidence, operations, and trust, but the underlying pattern is the same: *the science has outrun the system and strategies to support it*. Across all three dimensions, models designed for a first generation of metabolic therapies are being asked to do things they were never built for.

- **On evidence:** Headline weight loss can no longer carry differentiation on its own. As mechanisms and modalities diversify, value strategies need to be rebuilt around specific patient populations and specific outcomes – comorbidity impact, functional capacity, and the quality of weight loss – with evidence strategies geared to the mechanisms and populations where each asset has the strongest case. The advantage will be with companies that do this deliberately rather than trying to retrofit first-wave evidence claims across a diverging portfolio
- **On operations:** A strong asset is necessary but not sufficient. Sustained outcomes will depend on Commercial and Medical functions built for long-term chronic care, patient retention, and behavioral support, rather than for launch alone. Few organizations have these today, which makes building them a genuine source of advantage
- **On trust:** Expectations are forming faster than they can be managed, in an environment pharma does not control. Durable engagement will come from behavioral insight and a coherent narrative across a fragmented landscape. Built deliberately, trust becomes a commercial strength as the market matures

The field has moved fast. GLP-1s are continuing to redefine healthcare. As they do so, the question now is not only which companies have the right strategy, but which can move beyond strategic ambition and deliver the evidence, operations, engagement and care models needed to keep pace.

These are the types of challenges Lucid Strategy Consulting works on with our clients. We are also taking these important topics further across future articles: how to deliver sustained value, how far incretin biology could extend and what widespread GLP-1 prescribing means for trial design, and how the healthcare information environment is evolving. If you would like to work with us or contribute to these articles, please do reach out via the contact details over the page.

ABOUT LUCID

At **Lucid Strategy Consulting**, we combine strategic insight with deep life sciences expertise to deliver impact for our clients. We help leaders unlock the full potential of their assets, transform their functions across development and commercial, and create new value for their customers and patients. Our capabilities include ecosystem mapping, clinical program strategy, evidence generation, launch readiness, and real-world insights.

Lucid Group transforms bold science into market impact by bringing together scientific, strategic, commercial, creative, and human expertise, powered by our real-world data platform, to uncover the Lucid Truth: critical insights on the change necessary for successful asset adoption. Through bold, behavior-changing interventions, Lucid helps clients drive outstanding commercial performance and meaningful patient impact.

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