

White Paper

Achieving Excellence in Commercialising Cardiometabolic Innovation

How commercially successful innovators navigate a uniquely complex opportunity

MARKUS GORES, Vice President, EMEA Thought Leadership, IQVIA KIRSTIE SCOTT, Senior Consultant, EMEA Thought Leadership, IQVIA MARINA KONE, Principal, Strategy Consulting, IQVIA

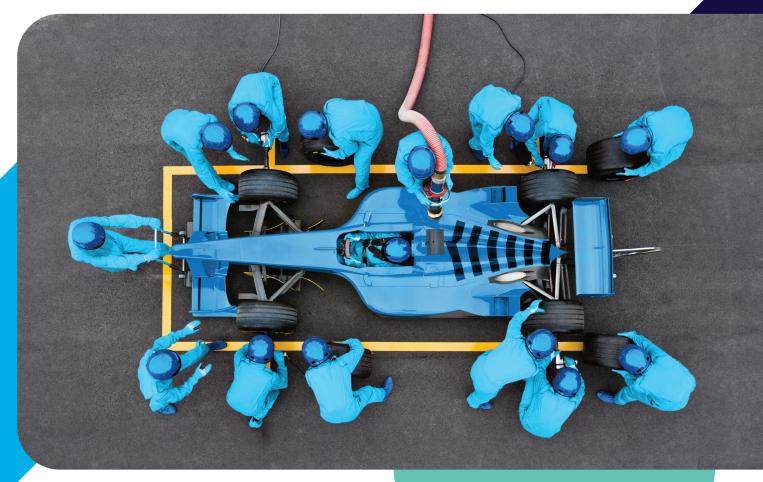


Table of contents

| Introduction | 1 |
|---|----|
| The cardiometabolic opportunity: Uniquely complex | |
| Lessons from cardiometabolic commercial success stories | 6 |
| I. Deep market insight foundation | 8 |
| II. Aligned value propositions and customer engagement strategy | 12 |
| III. High-quality execution and performance management | 15 |
| Organisational implications for cardiometabolic innovators | |
| References | 18 |
| About the authors | 20 |
| Acknowledgements | 21 |



Introduction

We are finding ourselves in the midst of a cardiometabolic renaissance, as the attention of the biopharmaceutical industry returns to an area it largely neglected for most of the past two decades. Obesity undoubtedly dominates the headlines and creates unprecedented excitement within the industry, and among the public at large. However, the industry's renewed interest in cardiometabolic innovation is much broader than obesity and spans a wide range of indications, for example, heart failure, hypertension, coronary artery disease, atherosclerotic cardiovascular disease, chronic kidney disease, dyslipidaemia, (pre)-diabetes or MASH.

Cardiometabolic innovators face unique challenges, such as navigating interdependencies between different indications exhibited as co-morbidities in overlapping patient populations, who are treated by multiple HCP specialties. Furthermore, multi-indication therapies are redefining how cardiometabolic risk is managed, for example incretin mimetics such as GLP-1 and GIP receptor agonists which have shown broader

benefits across multiple morbidities. This adds further complexity to commercialising new products.

In this white paper, we will explore what commercial excellence looks like in the context of cardiometabolic innovation, drawing on lessons from commercially successful brands, and identify what it takes to achieve it.

The cardiometabolic opportunity: Uniquely complex

Cardiometabolic diseases remain among the leading causes of mortality and morbidity globally, collectively accounting for over one third of all global deaths and impacting health-related quality of life by an estimated 500 million Disability-Adjusted Life Years (DALYs).²⁻⁴

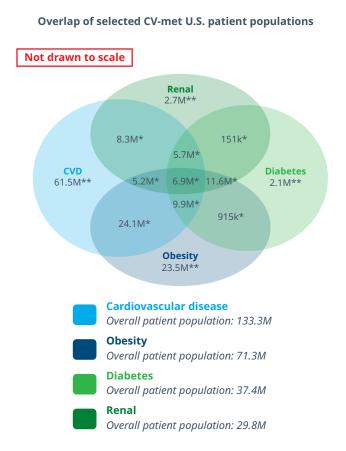
One of the defining features of cardiometabolic diseases is the substantial overlap between different patient populations, because many indications manifest themselves as co-morbidities in the same patient (see Figure 1):

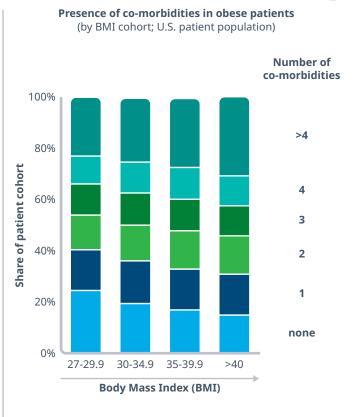
Such interdependencies between different indications make it more difficult to answer key strategic questions, for example, who is the ideal patient benefiting the most from a new therapy? Innovators therefore must have a holistic and granular understanding of patient profiles, including their unmet needs along multiple risk factors, to inform strategic segmentation into target patient groups to guide the target product profile, brand strategy and positioning of new cardiometabolic therapies.

In 2024, cardiometabolic diseases were the focus of 17% of all new clinical trial starts, including phases 1-3, making it the second most investigated therapy area after oncology.5

Figure 1: Substantial overlap between different cardiometabolic populations







^{*} Represents number of patients in each Venn Diagram overlap;

^{**}Represents number of patients in a single TA, i.e. have no comorbidity overlap Patient population sizes include 2022+ data-active patients, or those with Rx or Dx claims in 2022 or 2023; Not shown due to diagram spacing: Obesity and Renal ONLY overlap; Obesity, Diabetes, and Renal ONLY overlap Source: IQVIA LAAD, January 2018 to June 2023



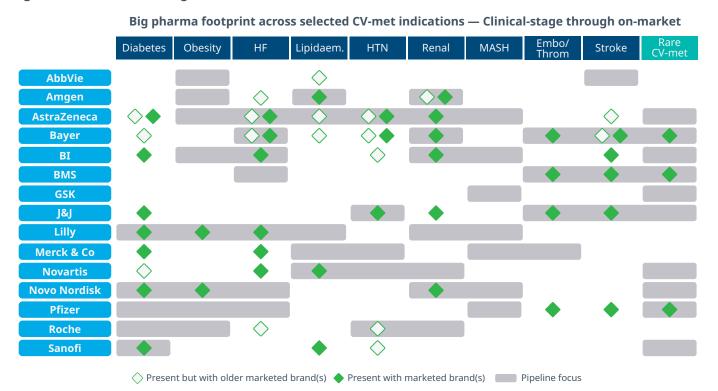
Unsurprisingly, as interest in cardiometabolic innovation rebounds, the competitive landscape is becoming increasingly crowded. Many big pharma companies are making significant investments in building cardiometabolic pipelines to establish, re-establish or expand their presence in this therapeutic space (see Figure 2), while numerous Emerging Biopharma Companies (EBPs) are also pursuing cardiometabolic innovation opportunities.

Among big pharma companies, we find 'portfolio play' a common strategy pursued by many. It is

characterised by companies assembling multi-asset/ multi-indication portfolios to establish a broad presence in the cardiometabolic space. This strategy requires innovators to carefully co-position their different assets to articulate a clear, joined-up, cross-portfolio value narrative.

As portfolios offer multiple value propositions, derived from assets individually and collectively, the ongoing challenge is to address a range of welldefined unmet needs across overlapping, comorbid patient populations.

Figure 2: We are witnessing a cardiometabolic renaissance



Source: IQVIA EMEA Thought Leadership; IQVIA Pipeline Link, September 2024;

RE-DEFINING CARDIOMETABOLIC RISK MANAGEMENT

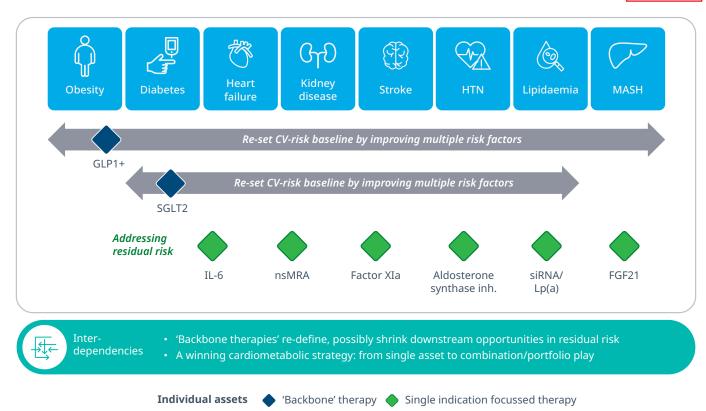
One of the most consequential events for the management of cardiometabolic risk was the arrival of multi-indication therapies, specifically GLP-1 receptor agonists and SGLT2 inhibitors, which have shown favourable effects on multiple risk factors, e.g., blood glucose levels, BMI, blood pressure and kidney function. As demonstrated in a number of cardiovascular-renal trials, e.g., SELECT,⁶ STEP-HF,⁷ FLOW,⁸ SUMMIT,⁹ DELIVER,¹⁰ EMPEROR-Preserved¹¹ and EMPEROR-Reduced,¹² GLP-1s and SGLT2s improved functional endpoints and/or reduced the risk of disease progression or cardiovascular adverse events.

As such, these agents have the potential to transform cardiometabolic risk management. Deployed as backbone therapies, they can re-set a patient's cardiometabolic risk baseline across co-morbidities, while residual risk is managed by additional therapies layered on top that target a specific indication and/ or risk factor, e.g., treatment-resistant hypertension, inflammation linked to heart failure or fibrosis in MASH (see Figure 3).

"Multi-indication therapies have the potential to transform cardiometabolic risk management by re-setting a patient's risk baseline."

Figure 3: Emerging 'backbone therapies' are transforming cardiometabolic risk management

ILLUSTRATIVE



Note: Example MoAs shown for illustration, drawn from a range of CV-met assets in development across the industry;
Source: IQVIA EMEA Thought Leadership; HTN: hypertension; IL-6: interleukin-6 inhibitor; nsMRA: non-steroidal mineralocorticoid receptor antagonist; siRNA: small interfering RNA; Lp(A): lipoprotein (a); FGF21: fibroblast growth factor 21

This has profound implications for innovators who need to understand the impact of backbone therapies on opportunities for managing residual risk. For example, an intervention with a GLP-1 receptor agonist aimed at weight loss, or for controlling diabetes, may shrink the therapeutic opportunity for other treatments by avoiding downstream complications from related comorbidities. Innovators therefore must carefully navigate the interdependencies between different treatment options in this emerging new reality. It also raises the importance of combination approaches, within and between companies' cardiometabolic portfolios.

GO-TO-MARKET COMPLEXITY: THE NEED TO ENGAGE A DIVERSE CUSTOMER BASE

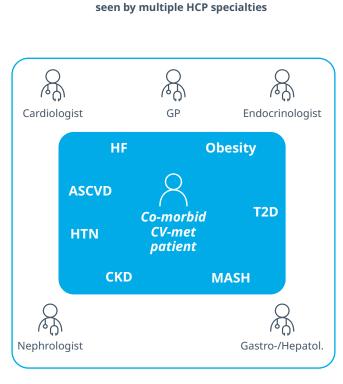
The manifestation of cardiometabolic indications as co-morbidities is a key driver of Go-To-Market (GTM) complexity, because the same patient is

seen by multiple HCP specialties, for example, GPs, diabetologists, endocrinologists, cardiologists, nephrologists, gastroenterologists or hepatologists. In addition, referrals between specialties and fluidity in who ultimately makes particular treatment decisions exacerbate GTM challenges.

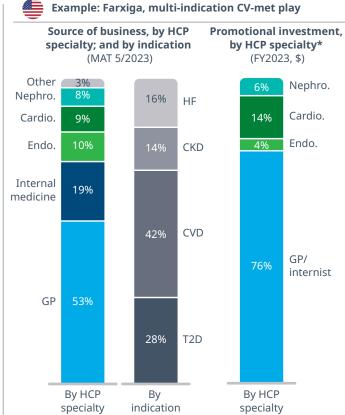
These prescriber specialties have very different needs and value different benefits delivered by a therapy and/or portfolio, which requires a customercentric engagement approach with carefully tailored positioning (see Figure 4).

"The manifestation of cardiometabolic indications as co-morbidities is a key driver of go-to-market complexity."

Figure 4: Go-to-market complexity: Diverse prescriber base treating overlapping, co-morbid patient segments



Patient with multiple CV-met co-morbidities,



Notes: *USD spend on interactive engagements only (details and meetings; including F2F, digital and telephone); Only includes selected specialties Source: IQVIA LAAD, MAT May 2023; IQVIA ChannelDynamics® FY2023 (extracted Feb 2025); IQVIA EMEA Thought Leadership analysis

The need to operate co-existing GTM model archetypes with specific CSFs and capabilities, for different brands and/or indications, depending on innovation novelty, market maturity and competitive intensity, adds further complexity, for example: precision play, targeting unmet need/residual risk in specific patient sub-segments; market transformation, to replace an existing treatment paradigm and set a new standard of care; or market building, which typically requires establishing new care pathways or embedding new diagnostic approaches.

Customer overlap between different parts of a cardiometabolic portfolio necessitates an aligned engagement strategy to avoid internal competition for customers and conflicting messaging, or 'company fatique' by overwhelmed customers. This requires

integrated approaches to customer segmentation, clear brand/indication prioritisation and guidance on messaging, including a coherent portfolio narrative, and the efficient organisation of in-field teams. To make this happen, affiliates will need more guidance from regional and global HQs on how to manage potentially conflicting priorities.

Furthermore, portfolio-level investment and resource planning is needed to maximise the commercial opportunity while capturing synergies.

Given the unique complexity of how the cardiometabolic opportunity presents itself, excellence in commercial execution in this market is elevated beyond being an operational objective to becoming a critical, strategic differentiator for successful innovators.

Lessons from cardiometabolic commercial success stories

Our comprehensive analysis of the performance of cardiometabolic brands over the past 10 years identified three foundational pillars that underpin commercial excellence (see Figure 5):

Figure 5: Three pillars of cardiometabolic commercial excellence



- Comprehensive understanding of market fundamentals and key stakeholders, e.g.,
 - » Cardiometabolic patient profiles and their unmet needs
 - » Patient journeys, treatment pathways
 - » Key HCP specialties, their needs, preferences and prescribing behaviours
 - » Competitive dynamics, treatment landscape, differential brand positioning

Aligned value propositions and customer engagement

- Coherent value narrative with aligned co-positioning across brands/indications
- Clarity on how new therapies fit within cardiometabolic treatment algorithm
- Translated into clear engagement plans, spanning different prescriber specialties
- Guidance on segment-specific, yet aligned messaging across value propositions



High quality execution and performance management

- Precision engagement of target customers with tailored, high-impact campaigns
- Orchestrated omnichannel approach aligned with HCP channel preferences
- Accurate, granular market measurement for performance transparency to instill a competitive mindset, guide execution

Source: IQVIA EMEA Thought Leadership

- 1. Deep market insight foundation: Successfully navigating the complexity of the cardiometabolic opportunity requires a comprehensive understanding of its market fundamentals and key stakeholders, for example: cardiometabolic patient profiles and their unmet needs involving multiple co-morbidities; patient journeys and treatment pathways, including intervention points and the relevant HCP specialties involved, their needs, preferences and prescribing behaviours to inform granular customer segmentation; competitive dynamics, including the evolving treatment landscape, differential brand positioning, sales dynamics and promotional investments.
- 2. Aligned value propositions and customer **engagement:** Overlap of cardiometabolic patient populations and customer segments drives the need for aligned (co-)positioning across brands/ indications, with a coherent value narrative that matches multiple value propositions with distinct needs of patient and HCP segments. Innovators must also articulate where their new therapies, individually and collectively, fit in the cardiometabolic treatment algorithm reflecting the increasing interdependencies in managing risk factors. In turn, this positioning strategy must be translated into a clear engagement plan, typically

- spanning different prescriber specialties. It needs to provide operational guidance on prioritising target customer segments to drive prescriptions, with segment-specific, yet aligned messaging across value propositions, and backed by adequate resourcing levels to ensure a competitive presence in the market.
- 3. High-quality execution and effective performance management: Ultimately, competitive advantage and success are determined by the quality of executing the commercial strategy across brands and indications; for example, precision engagement of target customers with high-impact campaigns through the right channel mix that reflects their preferences. Performance transparency is key for instilling a competitive mindset, making faster, better decisions, optimally directing resources, and to be able to course correct with agility. Accurate market measurement is a pre-requisite, including understanding the sources of business, brand adoption and market share, at patient level, across indications, different segments and channels.

We will now systematically explore best practice for each foundational pillar of excellence in commercialising cardiometabolic innovation, illustrated through relevant case examples.



I. Deep market insight foundation

The foundation for achieving commercial excellence is an in-depth understanding of the uniquely complex dynamics underlying a specific cardiometabolic opportunity to inform strategic and operational decisions.

Successful cardiometabolic brands therefore dedicate significant, early effort to developing critical insight, for example, how an opportunity manifests itself in particular patient profiles with overlapping co-morbidities and in which competitive context; how co-morbid target patients flow through the healthcare system and which prescriber specialties they interact with at different stages along the treatment pathway; or which therapy attributes different prescribers specialties, and sub-segments, value and their channel preference for receiving information.

Such comprehensive, integrated insight must draw on combining multiple data sources, e.g., real-word data such as anonymised, longitudinal patient-level Rx data, claims data or EMR; commercial data, e.g., sales, promotional investment and activity; primary research into patient and HCP behaviours, attitudes and preferences; and intelligence gathered by field teams, including both the sales force and medical affairs.

"Successful cardiometabolic brands dedicate significant, early effort to developing critical market insight."



PATIENT JOURNEY AND TREATMENT **PATHWAY MAP**

For example, a leading multi-indication, cardiometabolic brand used granular patient journey and care pathway mapping to understand how patients navigate the healthcare system as they begin to experience the onset of multiple co-morbidities, including diabetes, chronic kidney disease and heart failure (see Figure 6).

Cardiometabolic patient journeys are particularly complex due to interdependencies between comorbidities, which manifest themselves at different time points in the natural history of disease, and inevitably lead to an expansion of HCP specialties involved at different stages in a patient's care.

Once the flow of patients through the healthcare system and their touch points were understood, the patient journey was enriched by overlaying the patient experience along the way, e.g., in their interactions with healthcare professionals, facing obstacles along the care pathway, or the burden of living with, and managing, multiple, typically life-long conditions.

Such rich, detailed insight helped sharpen the brand's positioning across its different indications and the communication of patient-relevant benefits, while ensuring the customer engagement strategy was aligned with key intervention points along this complex patient journey.

ILLUSTRATIVE Presentation **Diagnosis** Tx: Initiation and maintenance **Diabetes** Tx Tx ፙ **Asymptomatic** Specialist referral: Ongoing Initiate treatment for T2D/renal impairment monitoring ophthalmologist Intensified therapy T2D Dx Diabetic macular confirmed ᡯ Early T2D oedema symptoms symptoms Endo. CV-met Blood patient CKD/HF glucose test worsen CKD **Early CKD** symptoms worsens CKD Dx Nephro eGFR/ Stage 2 Stage 3 Stage 1 **ACR** test Class 2 Heart Dх failure Ther for Blood/ECG Class 3

Figure 6: Interconnected cardiometabolic patient journey

Source: IQVIA EMEA Thought Leadership

PINPOINTING OPPORTUNITIES IN CO-MORBID **SUB-POPULATIONS**

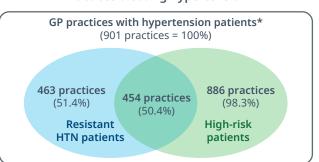
For example, developers of novel therapies for managing blood pressure will need to identify and target specific patient segments with unmet need, such as a high-risk sub-population with CV-risk factors and resistant hypertension. The latter is defined as uncontrolled blood pressure despite the use of three or more antihypertensive drugs of different classes, including diuretics, long-acting calcium channel blockers, ACE inhibitors or angiotensin II type receptor antagonists, at maximally tolerated doses.

Using IQVIA Disease Analyzer (Germany), a representative database of general and specialist practices in Germany, which captures anonymised, patient-level data on diagnoses and treatments based on ICD-10 and ATC codes, IQVIA quantified overlap between patients with resistant hypertension and high-risk hypertension patients with multiple CV co-morbidities. These patient segments were subsequently mapped against GP and cardiology practices, respectively (see Figure 7).

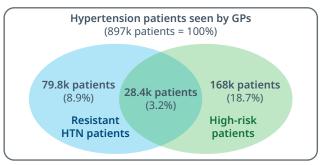


General practitioners

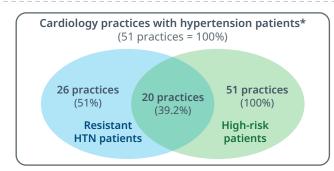
Practices treating hypertension

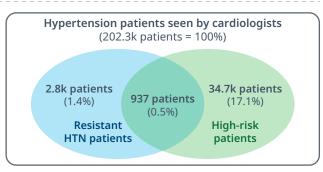


Patient population with hypertension









*Percentages show the proportion of practices that see patients in each segment; Source: IQVA Disease Analyzer (unprojected) | MAT 12/2019 - MAT 11/2023; Notes: HTN - Hypertension, ICD-10 code: I10; high risk HTN patients with CV-comorbidities: heart failure (ICD-10: I50, I11.0, I13.0, I13.2), stroke (I63, I64, G45), CKD (N18).

This analysis highlighted, for example, that ~50% of all GP practices and ~39% of cardiology practices in Germany see high-risk, co-morbid patients with resistant hypertension, while in terms of absolute numbers the majority of those patients are found in the care of GPs. Typically, GPs manage treatment escalation, including initiation of the fourth therapy in resistant hypertension patients. GPs may consider specialist referral when a patient's blood pressure remains uncontrolled.

Such insight forms the basis for granular opportunity pinpointing and integrated HCP/patient segmentation to guide future customer engagement plans. It also informs effectively directing in-field activities at the most important prescribers treating large volumes of high-risk patients with resistant hypertension.

UNDERSTANDING HCP NEEDS AND PREFERENCES

As the cardiometabolic landscape is becoming more crowded and competitive intensity increases in many markets, successful customer engagement must cut through this noise and deliver relevant, personalised content, and services, via an orchestrated omnichannel approach that reflects prescribers' needs and preferences.13

Our analysis of IQVIA ChannelDynamics® data found a significant gap exists between HCPs' channel preference and the promotional reality across EU4+UK markets, which varies by HCP specialty. For example, among relevant HCP specialties for cardiometabolic therapies, nephrologists report the highest level of misalignment, at 43%, followed by endocrinologists and cardiologists at 41% and 40%, respectively, while GPs report the lowest level of mismatch at 33% among this group.

A robust understanding of HCP needs and their communication preferences, at a granular level, is key for closing this gap and to stand out in a crowded field, be heard and build deeper, lasting customer relationships.

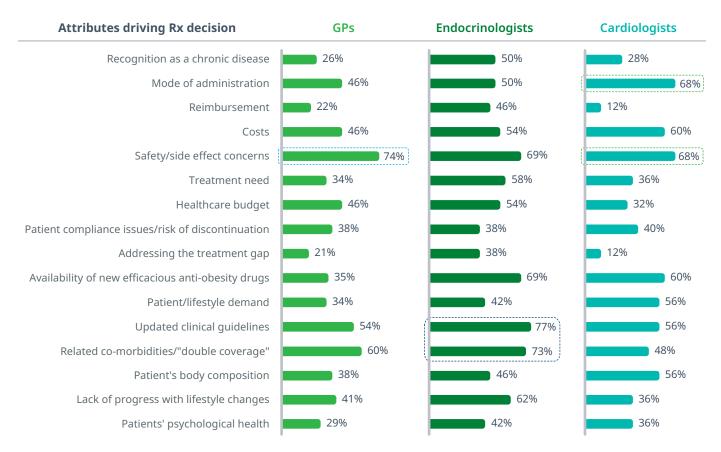
Equally important is insight into the drivers of HCP decisions to tailor the portfolio- and indicationnarratives, and campaigns, for maximum impact. For example, recent IQVIA primary research¹⁴ found great variation among UK GPs, endocrinologists and cardiologists in the attributes that are most important for them when deciding which treatment to prescribe for patients living with obesity (see Figure 8).

A customer profile-guided, orchestrated omnichannel approach must extend beyond commercial teams. 15 Medical affairs' unique depth in understanding diseases and clinical practice, combined with the ability to have peer-to-peer discussions with HCPs, is critical to identify gaps in the standard of care and build advocacy for new therapies. Furthermore, medical affairs is well placed to help prescribers navigate an increasingly complex cardiometabolic landscape, which is at the cusp of seeing cardiometabolic risk management being fundamentally transformed, as we elaborated earlier.

Figure 8: Prescribing decision drivers vary between HCP specialties

Example: Obesity





Questions: Which of the following factors are important to you when making the decision to prescribe a treatment for patients living with obesity?

PMR sample: GPs (n=68), Endocrinologists (n=26), Cardiologists (n=25);

Source: IQVIA Integrated Insights Tracker: people living with obesity, UK report, November 2024

II. Aligned value propositions and customer engagement strategy

When cardiometabolic assets with multi-indication potential secure approval of additional indications, innovators must articulate a broader, coherent value narrative and expand customer engagement to cover all relevant prescriber specialties. This imperative also applies when innovators assemble multi-asset portfolios that target different cardiometabolic indications.

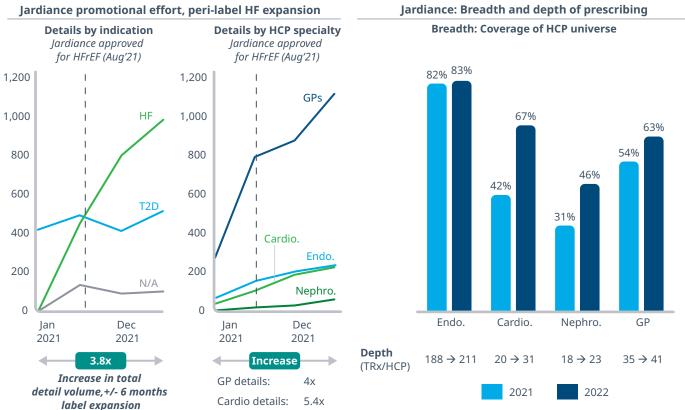
Leading companies treat each new indication as a distinct launch, supported by dedicated teams where critical mass allows, to ensure organisational focus, which is a key prerequisite for achieving outperformance as we demonstrated in IQVIA's extensive Launch Excellence research.16

For example, SGLT2 inhibitor Jardiance, originally approved for T2D, subsequently expanded its label to cover Heart Failure, including both patients with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF), and chronic kidney disease. In preparation for seizing the new commercial opportunities, Boehringer Ingelheim and Lilly significantly stepped up promotional investment around each label expansion, targeting indicationspecific messages, tailored for relevant prescriber specialties, including primary care physicians (PCPs/GPs), endocrinologists, cardiologists and nephrologists. This approach resulted in building important breadth of coverage and depth of prescribing.

During the window of 6 months before and after label expansion in heart failure with reduced ejection fraction (HFrEF), for example, Jardiance increased total detail volume in the U.S. threefold across HCP specialties. Engagement beyond endocrinologists, its original core prescribers, was critical: contacts with GPs and cardiologists increased by a factor of 4 and 5.4, respectively, during this peri-launch period. High levels of prescribing breadth and depth in the primary care setting, achieved via significant in-person engagement with GPs, was particularly important to drive patient volumes (see Figure 9).

Figure 9: Engagement expansion beyond core HCP specialty is critical





Source: IQVIA BrandImpact analysis; IQVIA ChannelDynamics; IQVIA OneKey; IQVIA EMEA Thought Leadership analysis

A verbatims analysis using IQVIA ChannelDynamics with IQVIA AI Assistant illustrates how promotional messages for Jardiance were tailored to audience-specific needs, while joining up cross-indication benefits (see Table 1):

Table 1: Jardiance promotional messages tailored for different HCP specialties

| HCP SPECIALTY | MAIN FOCUS OF PROMOTION | KEY MESSAGES |
|--|--|---|
| Endocrinologists Management of T renal protection | Management of T2D and CV/ renal protection | "Jardiance lowers HbA1c levels and improves glycaemic control in T2D patients" |
| | | "Jardiance provides dual benefits in managing T2D and offering CV and renal protection" |
| | | "Jardiance reduces risk of CV death in T2D patients with established CV disease" |
| Cardiologists | Management of heart failure and CV benefits | "Jardiance significantly reduces CV mortality and hospitalisations for HF patients" |
| | | "Jardiance has proven efficacy in both HFrEF and HFpEF as demonstrated in the EMPEROR trials" |
| | | • "Jardiance provides CV protection in patients with or without diabetes" |
| Nephrologists Management of CKD and renal protection | "Jardiance slows progression of CKD and reduces risk of end-stage renal disease" | |
| | "EMPA-KIDNEY trial shows Jardiance reduces risk of CKD progression and CV death by 28%" | |
| | "Jardiance is effective in patients with varying degrees of renal impairment, including those with low eGFR" | |
| GPs Comprehensive patient management across multiple indications | | • "Jardiance is indicated for T2D, HF and CKD" |
| | • "Jardiance offers a safe, once-daily dosing regimen" | |
| | • "Early intervention and routine screening are crucial for at-risk patients" | |

In addition to promotional activities, both Boehringer Ingelheim/Lilly and in-class competitor AstraZeneca, invested in extensive, early RWE generation to support their respective SGLT2 brands, Jardiance and Farxiga, for example:

- AstraZeneca's CVD REAL landmark observational study, involving 300,000 T2D patients with atherosclerotic CV disease across 6 countries, assessed Farxiga for risk reduction in CV death and hospitalisation for heart failure.¹⁷
- A second analysis (CVD REAL 2) assessed data from 400,000 T2D patients across 6 countries with or without established CV disease and receiving treatment with SGLT-2 inhibitors, including Farxiga, for risk of all-cause death, hospitalisation for heart failure, myocardial infarction and stroke.¹⁸
- Boehringer Ingelheim's/Lilly's EMPRISE real-world evidence study involving 200,000 U.S. patients compared Jardiance vs. DPP-IVs for risk reduction in hospitalisation for heart failure in T2D patients.¹⁹

Some of these major programmes were initiated over 3 years before label expansion and ran alongside key CV-outcomes trials, such as Jardiance's EMPA-REG OUTCOME or Farxiga's DECLARE. Collectively, these evidence generation efforts focused on demonstrating real-world CV outcomes, characterising the target patient populations that benefit the most, and quantifying impact on healthcare resource utilisation and potential cost off-sets, with the findings being disseminated via early medical affairs engagement to build awareness and advocacy for the new indications.

Incretin mimetics, such as semaglutide, tirzepatide or survodutide, will face similar challenges of managing increasing complexity while entering highly competitive markets as they pursue multi-indication opportunities, e.g., with semaglutide already being approved for T2D, obesity, chronic kidney disease and CV risk reduction, with additional indications in heart failure and MASH likely to follow in the near future.



EXTENSIVE MARKET SHAPING

Recent breakthroughs in cardiometabolic innovation have led to pharmacotherapies becoming available in indications that previously had no treatment options, for example metabolic dysfunction-associated steatohepatitis (MASH). Ensuring health system and care pathway readiness is a key prerequisite for the broad and effective adoption of such novel therapies within the eligible patient population.

In March 2024, Madrigal's Rezdiffra became the firstever therapy specifically approved for the treatment of MASH in patients with moderate or severe liver fibrosis, consistent with fibrosis stages F2 and F3 disease. In preparation for a successful launch, it was critical for Madrigal to dedicate significant, early effort to market shaping to address challenges such as limited disease awareness, low diagnosis rates and the absence of established care pathways for MASH.²⁰

Specifically, Madrigal's extensive market shaping activities²¹ for its U.S. launch included:

• Identifying 14,000 target physicians in total, with a primary focus on engaging 6,000 hepatologists and gastroenterologists, who treat the majority of the 315,000 diagnosed F2-F3 stage MASH patients. Initial focus on liver-specialists was aimed at capturing patients already diagnosed and under care, while gastroenterologists, who far outnumber hepatologists, are typically less familiar with MASH but will be critical prescribers for driving future growth.

- Educating physicians and payers about MASH, the benefits of Madrigal's new therapy and the use of non-invasive diagnostics to identify eligible patients.
- · Creating treatment pathways, broadening access and supporting practices with administrative requirements for securing reimbursement or acquiring imaging diagnostics.
- Supporting patients along their MASH treatment journey.

Madrigal's efforts are paying off, as Rezdiffra is going from strength to strength, delivering impressive revenue growth and beating consensus expectations in each of its first three quarters on the market.

As more late-stage assets in development for MASH progress towards regulatory approval, including several incretin mimetics, e.g., semaglutide, tirzepatide and survodutide, and other candidates with different MoAs, market development continues to be critical to unlock the sizeable, untapped potential of an immature, underserved MASH market.

III. High-quality execution and performance management

Performance transparency is critical to succeed in highly competitive, fast-moving and complex cardiometabolic markets, where overlapping, co-morbid patient populations are served by competing, increasingly multi-indicational products.

It drives accountability, focus on competitiveness and high-quality execution, and enables agility by guiding timely business decisions, e.g., directing the deployment of resources, or informing in-field tactics including when and how to course correct.

"Performance transparency is critical to succeed in highly competitive, fast-moving and complex cardiometabolic markets."

Given the sheer scale of potential cardiometabolic patient populations and target prescriber universes to engage, which can be orders of magnitude higher than for typical specialty care indications, fit-for-purpose market measurement becomes elevated to a high priority; for example, to understand the sources of business, and market share, at patient level, across indications, for different patient and prescriber subsegments and channels. Additionally, in obesity, it will also be important to accurately measure performance across both the private, consumer-led market and in the reimbursed setting.

Granular, timely market measurement forms the basis for defining effective incentives that drive focus on priorities and instil critical behaviours and ways of working.

For example, a leading cardiometabolic innovator, with a multi-indication brand competing in several crowded market segments, partnered with IQVIA to implement best-in-class performance management to sustain its competitive advantage.

To accurately track brand performance and patient dynamics at indication level in ex-US markets, IQVIA developed an AI-algorithm, trained on medical history and treatment patterns in the target population using representative longitudinal, anonymised patient-level EMR data. The algorithm was applied to longitudinal prescription data collected at pharmacy level to measure performance by indication. Feeding the latest EMR data into the learning model ensured continuous improvement of the algorithm.

This approach delivered accurate performance transparency on several key metrics at indication level (see Figure 10), e.g., TRx, NBRx, acquisition of treatment naïve patients or patient switches between brands.

In addition to monitoring commercial outcomes metrics such as brand sales, prescriptions, market share or number of patients acquired, it is important to track execution metrics that are more directly linked to underlying activities that drive performance. For example, as we discussed in another IQVIA publication, the quality of HCP engagement is a strong predictor of launch success.²² Therefore, visibility of execution metrics enables swift, purposeful changes in tactics, e.g., HCP targeting, omnichannel call plans, or message prioritisation and delivery.

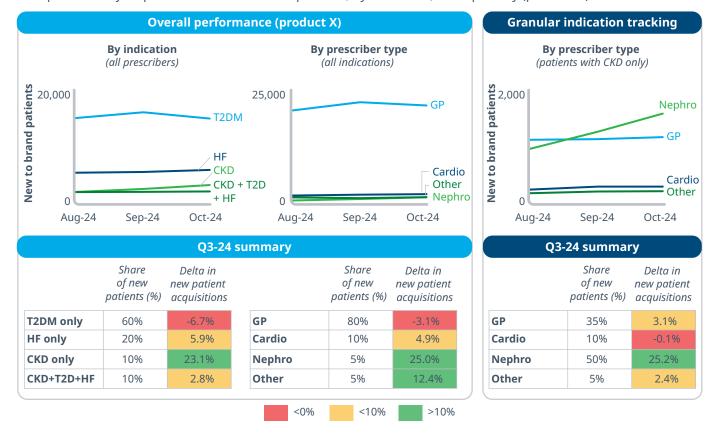
As competition is heating up, innovators must relentlessly focus on consistent, high-quality commercial execution which makes or breaks a successful cardiometabolic franchise.

"Innovators must relentlessly focus on consistent, high-quality commercial execution which makes or breaks a successful cardiometabolic franchise."

ILLUSTRATIVE

Figure 10: Effective market measurement and performance tracking

Example: Monthly acquisition of new-to-brand patients, by indication, HCP specialty (product X)



Source: IQVIA EMEA Thought Leadership analysis supported by Real-World Analytics and Insights; Illustrative based on IQVIA LRx data in a European country

Organisational implications for cardiometabolic innovators

How do organisations achieve excellence in cardiometabolic innovation, what mindset, operating model, and capabilities are required to succeed?

Faced with the formidable challenges discussed earlier, cardiometabolic innovators must address three organisational priorities:

1. Portfolio mindset: Maximising the overall cardiometabolic commercial opportunity requires a vision and mindset that rise above individual assets and indications. This allows a holistic view across interdependent opportunities, and how they fit together, to articulate a coherent, crossportfolio value narrative vs. a collection of disparate value propositions. A portfolio mindset is also essential for joined-up strategic planning, including opportunity prioritisation, optimal investment and

resource allocation, and the capture of synergies, e.g., due to customer overlap. Note, we consider a multi-indication asset a 'portfolio in a product' in this context.

2. Structure and governance provide the mechanisms for translating a portfolio mindset into operational reality. Pan-cardiometabolic governance, supported by consistent frameworks and effective, crossfunctional processes with clearly defined decision rights, is crucial to drive organisational alignment around the cardiometabolic strategy, portfolio priorities and critical success factors. It facilitates joined-up decisions above individual assets and indications as a prerequisite for resolving conflicting priorities and internal competition for resources or customers, avoiding duplication of efforts and orchestrating seamless execution by in-field teams. Moreover, efficient decision making and planning processes enable organisational agility, which is critical for playing in complex, fast-moving markets.

3. Enablers: Advanced analytics capabilities are fundamental for successfully navigating the complex and highly competitive cardiometabolic landscape. These include sophisticated, data-driven planning tools for portfolio-level prioritisation, such as OPEX modelling and quantifying the P&L impact of trade-offs (see Figure 11), e.g., contribution margins by brand, and indication, under different investment allocation scenarios; and data-driven tools that enable rapid decision making and personalised, high-value customer engagement, e.g., AI digital twins for tactical resource optimisation, dynamic customer targeting or agile, customer-centric omnichannel call planning across assets, indications and HCP specialties, to enable precision engagement at scale.

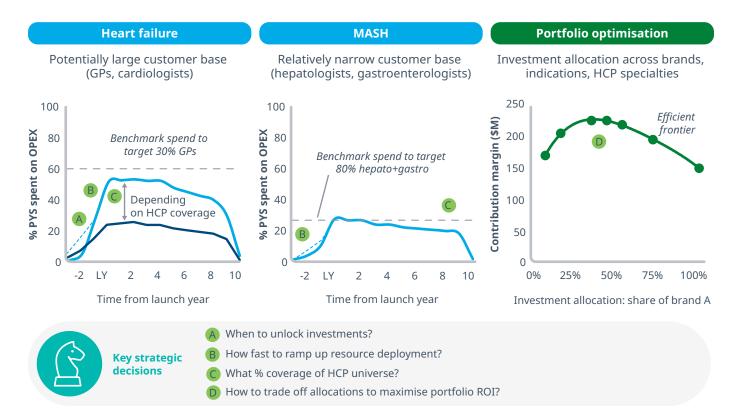
Innovators at the heart of the cardiometabolic renaissance must overcome uniquely complex challenges to seize a tremendous commercial opportunity. This requires evolving their operating models to compete successfully by delivering commercial excellence at the next level.

"Commercial excellence in this uniquely challenging market is elevated beyond an operational objective to becoming a critical, strategic differentiator for successful innovators."

Figure 11: Data-driven, portfolio-level investment planning

Example: OPEX modelling and portfolio ROI optimisation

ILLUSTRATIVE



*LY: launch year; PYS: peak year sales;

Source: IQVIA proprietary OPEX benchmark and portfolio optimisation models; IQVIA EMEA strategy consulting.

References

- A renaissance for cardiometabolic innovation; IQVIA white paper, June 2023: A renaissance for cardiometabolic innovation - IQVIA
- 2. Global health estimates: Cause-specific mortality, 2000–2019; leading causes of death; The Global Health Observatory, WHO: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ ghe-leading-causes-of-death
- 3. Global health estimates: Disease burden, 2000–2019; leading causes of DALYs; The Global Health Observatory, WHO: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ global-health-estimates-leading-causes-of-dalys
- Vaduganathan M, Mensah G, Turco J, et al. The Global Burden of Cardiovascular Diseases and Risk. J Am 4. Coll Cardiol. 2022 Dec, 80 (25) 2361–2371; https://doi.org/10.1016/j.jacc.2022.11.005
- 5. Global trends in R&D 2024; IQVIA Institute report, February 2024: https://www.iqvia.com/insights/theiqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2024
- Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes; N Engl J Med 2023;389:2221-2232; https://www.nejm.org/doi/full/10.1056/NEJMoa2307563
- Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity; N Engl J Med 7. 2023;389:1069-1084; https://www.nejm.org/doi/full/10.1056/NEJMoa2306963
- 8. Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes; N Engl J Med 2024;391:109-121; https://www.nejm.org/doi/10.1056/NEJMoa2403347
- 9. Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity; N Engl J Med 2024; https:// www.nejm.org/doi/full/10.1056/NEJMoa2410027
- 10. Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction; N Engl J Med 2022;387:1089-1098; https://www.nejm.org/doi/full/10.1056/NEJMoa2206286
- 11. Empagliflozin in Heart Failure with a Preserved Ejection Fraction; N Engl J Med 2021;385:1451-1461; https://www.nejm.org/doi/full/10.1056/NEJMoa2107038
- 12. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure; N Engl J Med 2020;383:1413-1424; https://www.nejm.org/doi/full/10.1056/NEJMoa2022190
- 13. Time to Take Omnichannel Action, IQVIA white paper, June 2024: https://www.iqvia.com/locations/emea/ library/white-papers/time-to-take-omnichannel-action
- 14. IQVIA obesity tracker, data collection via online HCP survey, October 2024
- 15. Medical Affairs' Next Frontier: Unlocking Omnichannel Engagement, IQVIA white paper, December 2022: https://www.iqvia.com/library/white-papers/medical-affairs-next-frontier-unlocking-omnichannelengagement

- 16. IQVIA Launch Excellence I-VIII series of bi-annual publications, 2007-2023
- 17. Kosiborod M, et al. Lower risk of heart failure and death in patients initiated on SGLT-2 inhibitors versus other glucose-lowering drugs: The CVD-REAL Study, 2017; https://doi.org/10.1161/circulationaha.117.029190
- 18. CVD REAL 2 analysis, AstraZeneca press release, 12 March 2018: https://www.astrazeneca.com/media-centre/press-releases/2018/new-data-from-landmark-cvd-real-study-of-patients-with-type-2-diabetes-confirms-cv-benefits-associated-with-sglt-2-inhibitors-12032018.html#
- 19. EMPRISE real-world evidence study, Boehringer Ingelheim press release, 5 November 2018:

 https://www.boehringer-ingelheim.com/us/media/press-releases/initial-results-emprise-real-world-evidence-study-show-jardiance-was-associated-reduced-risk
- 20. IQVIA white paper, January 2024: Emerging from the Shadows: A New Era for NASH IQVIA
- 21. Madrigal quarterly earnings reports, Q2-Q4/2024
- 22. No More Surprises: Understanding Predictors of Launch Success, IQVIA white paper, June 2021: https://www.iqvia.com/library/white-papers/no-more-surprises-understanding-predictors-of-launch-success

About the authors



MARKUS GORES Vice President, EMEA Thought Leadership, IQVIA

Markus has over 20 years of experience in life sciences, advising

clients in all major geographies on a broad range of topics, including real world evidence strategy, launch readiness, go-to-market models, brand and commercial strategies, and building enabling organisational capabilities. Markus is a frequent speaker on the latest industry trends and regularly engages with senior leadership teams of pharmaceutical companies. Prior to his current role in Thought Leadership, he has held leadership positions within IQVIA Real World Solutions and QuintilesIMS Consulting Services (formerly the IMS Consulting Group). Markus holds a PhD in Pharmaceutical Chemistry from the University of Hanover and has completed post-doctoral research at the University of California.



KIRSTIE SCOTT Senior Consultant, EMEA Thought Leadership, IQVIA

Kirstie is a Senior Consultant in IQVIA's EMEA Thought Leadership

team, based in London. She has experience preparing white papers and delivering presentations across a range of priority healthcare topics such as Launch Excellence, the availability of medicines, and the impact of biosimilars in Europe. A particular recent focus is how companies with new launches can overcome the challenging post-pandemic environment to achieve launch success. Kirstie has 8 years' experience in healthcare and life sciences, previously providing clinical and commercial competitive insights for pharmaceutical companies, and working to support industry associations to influence health policy. She holds a degree in Neuroscience from the University of Nottingham.



MARINA KONE Principal, Strategy Consulting, **IQVIA**

Marina is a Principal with IQVIA's Strategy Consulting team based

in London. She has over 12 years of consulting experience and advises both big pharma and emerging biopharma clients on a wide range of business issues, including commercial strategy (asset or portfolio), innovative go-to-market models, launch excellence, and organisational design and capability building to support operational excellence. She has deep expertise within the cardiometabolic space, with a particular focus on obesity and T2D. Prior to joining IQVIA, Marina gained experience in medical sales with Novartis Pharma Services Inc., Cyprus, focussing on their cardiometabolic portfolio. She also spent time in academia, researching new potential targets for maintaining pancreatic β-cell function in some forms of diabetes. Marina holds a MRes in Structural Molecular Biology and a BSc in Biochemistry, both from Imperial College, London.



Acknowledgements

This white paper was supported with expertise from IQVIA Real World Analytics and Insights, IQVIA Integrated Research, and IQVIA Brand and Commercial Strategy. In particular, the authors would like to thank Andrea Seltmann, Anna Ostermeier, Cristina Alzaga-Chaudhry and Annabel Taylor for their valuable contributions to the development of this publication.



CONTACT US iqvia.com