Nine for 2024, Pt 2: Phase change and the challenges of scale

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In the first segment of Nine for 2024, we examined the continued fragility of healthcare systems, global pharmaceutical market infrastructure, and the journey to greater resilience. In this article, we'll examine the trends which will reshape pharmaceutical markets, and healthcare provision, at scale, from 2024 and beyond. The first part of this series for 2024 can be read here.

Oncology became the world's most valuable therapy area by prescription medicine sales way back in 2010, and for over a decade the biggest therapeutic trend of the global medicine market has been the oncology market's positive reinforcement cycle of significant innovation across multiple mechanisms of action, driving outstanding commercial reward, triggering heavy commercial investment, and intensifying competition.

With global annual list price sales of $214bn as at Q3 2023, and a year-on-year growth of 12%, oncology is the lead of three mega-therapy areas, the others being diabetes and immunology, accounting for 40% of global prescription medicines value, and over 60% of list price prescription medicine value growth in the year to Q3 2023. Oncology will comfortably remain the world's most valuable therapy area to 2030, but, from 2024 on, this hegemony will be challenged by the rise of obesity therapeutics, which will

rapidly become a lead driver of value growth and lead the resurgence of innovation in the broader cardiovascular and metabolism (CV-Met) markets.

Scaling Obesity and CV-Met

For the new obesity therapeutics making waves, 2023 was a year of major approvals, with the launch of Zepbound, and high-profile outcomes, along with the readout of Wegovy's SELECT cardiovascular outcomes trial.

2024 will be the year of rapid scaling, with another positive reinforcement cycle of acceleration of uptake, and burgeoning pipeline of new obesity mechanisms of action, presentations, and outcomes data driving exceptionally rapid establishment of a market which will, at some point between 2024 and 2030, very likely become the fourth mega therapy area. The impact of such a rapid rise of a major new therapy area will be profound and unprecedented - whilst Hepatitis C agents rapidly dominated spending growth 2015-17, with Sovaldi the world's top-selling medicine for a single year, as patients were cured Hepatitis C sales value dropped equally rapidly. This will not happen for obesity agents; the sheer number of patients and the chronic nature of the condition mean that obesity will become and will remain a mega therapy area and, as such, an ongoing major element of healthcare system spend.

It's important to note that obesity will be the lead, but not the only, market in the CV-Met revolution. 2024 will likely see the approval of the first Non-Alcoholic Steatohepatitis (NASH) therapy in March. This high prevalence condition, associated with obesity and diabetes, could also be a major new growth market to 2030. Obesity, however, will be where the new paradigms for innovative value in high prevalence primary care conditions will be tested.

How should the vast demand for obesity therapeutics be funded? As insurers and public payers move slowly, a significant out of pocket market is gaining momentum, with the potential scale to shift perspective on out-of-pocket payment for certain types of chronic medication. Disturbingly, rapid growth in fake and unlicensed obesity medications is an accompanying challenge for healthcare systems and regulators in 2024. As the licensed obesity treatments gain scale in usage and are joined by newer treatments, extending the range of mechanisms of action, healthcare professionals and patients must address an intensely complex challenge of optimising their use. Obese individuals are highly diverse and so are their paths to successful treatment. Evidence-based guidance, informed by further outcomes trials and real-world (RW) data will be vital. If the market is split between public and private, RW data across both will become increasingly important.

Joined-up policy solutions for infectious disease in 2024

From 2024, innovation in high-prevalence, non-communicable diseases will, therefore, take on a new importance, but communicable diseases will also see 2024 inflection points.

2024 will be a key policy year to address infectious disease. The United Nation (UN)'s pandemic preparedness treaty is due to be considered in the 77th World Health Assembly, and the antimicrobial resistance (AMR) crisis, with a UN General Assembly high-level meeting on antimicrobial meeting due in 2024. AMR was directly responsible for 1.25 million deaths in 2019, and, unchecked, could reach 10 million annually by 2050. This is the same annual global mortality rate as for cancer in 2020.

The solution to this often-under-appreciated healthcare crisis will not be reached by innovation and commercial incentives alone. Whilst 20 to 30 years ago antibiotics were among the world's bestselling medicines, top-selling innovative antibiotics made 15 times less in global sales in 2022 than those in 2002. The pipeline of novel antibiotics is sparse: three new, active substance launches since 2020, with limited commercial reward, and while six start-ups acquired FDA approval for new antibiotics since 2017, all have now abandoned antibiotic development.

Policy incentivising antimicrobial innovation is needed, but it is not enough. Even were the multiple policies across the US and Europe designed to foster antimicrobial innovation to succeed, if innovation entered the existing environment of mis- and over-use it would fail to achieve the intended goals. The policy solutions of 2024 need to look at the whole picture, encouraging better data collection, analysis, and evidence-based decision making on existing antimicrobial use to let precious innovative agents achieve their right place and optimal use.

Regulating AI for better healthcare

The late 2022 release of Chat GPT3 became the poster child for mass adoption of Generative AI (GenAI), kicking off a 2023 frenzy of use cases, speculation, and strategic development. One of the critical events that will shape the AI story of 2024, and with particular implications for healthcare, happened at the end of 2023, as the EU reached political agreement on the Cross-Sectoral AI Act (AIA) in December.

The AIA applies across all sectors with commercial use of AI, but its categorisation of AI use by potential risk makes it especially important for healthcare, because many health applications, due to their use of confidential patient data and their application to people's health, are classified as high-risk. High-risk AI is still to be fully defined in health, but it primarily will include uses which:

- Diagnose patients
- Make therapeutic decisions
- Monitor physiological processes
- Have contraceptive purposes

These will be classified as medical devices and subject to conformity assessment by notified bodies, in addition to the AI Act requirements. The AIA will be enforced from 2026, but the serious scope of penalties for non-compliance, including the possibility of fines of 1.5% - 7% of global turnover, mean that companies must plan from 2024 to ensure compliance.

Life sciences companies should consider an AI governance and compliance strategy building on existing processes, data protection, auditing, and due diligence to establish fit-for-purpose compliance mechanisms. 2024 will also be when the approach that the US, China, and other major regions take to regulating AI will become more apparent, and so strategies should be flexible and future-proofed to regulations coming from other bodies and regions.

Headwinds, part 1 and 2: two pharmaceutical market segments facing stress in 2024

A strong generic and biosimilar sector is key to managing medicines budgets for optimal spend on innovation, and the off-patent opportunity looks strong; $210 – $250 billion of revenue will be newly exposed to loss of exclusivity between 2023 and 2030 in the critical US market alone. Look again, however, and the prospect of optimising savings through the generics and biosimilar markets looks less certain.

Small molecule generics manufacturers are caught in the vice of rising manufacturing costs because of energy and raw materials hikes, and necessary environmental criteria required by health systems to manage their own net zero commitments, and tendering and purchasing policies that recognise purchasing criteria other than cost slowly if at all. Shortages in supply for small molecule generics, especially in hospital medicines with low volumes, will become a critical 2024 concern for all geographies and a core element of regulatory action.

For biosimilars, a void has opened – while the number of biosimilars developed for the major biologics by sales has held up, there's a growing group of smaller sales biologics, often orphans, which have lost exclusivity, but see no biosimilar competitors. Exploring policy approaches to address this will be increasingly critical from 2024 on.

Orphan medicines generally proved resilient in commercial performance during the early years of the pandemic- a combination of agents addressing high unmet medical needs, and health systems motivated to deliver them. However, headwinds will strengthen in 2023. Historically the beneficiaries of successful policies encouraging development of medicines for rare diseases, orphan medicines will increasingly feel the impact of new policies designed to manage medicines spend, which will no longer treat orphan medicines as an exception to the rule.

In the US, orphans with one indication will be protected from price negotiations under the Inflation Reduction Act (IRA), but lose exclusivity with additional indications. In Europe, the EU Pharmaceutical Legislation package will reduce orphan exclusivity from 10 to nine years where regulatory data protection is relevant, and, for Germany, the threshold triggering a "full" benefit assessment for orphans will be lowered from EUR 50 million to EUR 30 million. Orphan medicines will still thrive, but, in 2024, increasingly need to demonstrate cost benefit in the context of the full medicines budget.

Valuations and acquisitions: Phase transition in 2024?

Could a life sciences company ever join the elite group of corporations with a market capitalisation of great than $1 trillion, a value so far attained only by the world's largest technology firms and one petrochemical company? While no life sciences company can achieve that valuation in 2024, the progress of the obesity market in 2024 will be pivotal to whether the most likely life sciences candidates for trillion-dollar valuation, Eli Lilly (valued at over $500 billion by end 2023) and Novo Nordisk (valued at over $450 billion), could achieve this status in the longer term.

To achieve $1 trillion, more factors must go right than the sales of obesity agents – it will require follow-on from a solid pipeline of equally strong blockbusting products, an optimisation of geographic footprint that fully realises the potential of portfolio and pipeline and is resilient to risks across the global healthcare market, cost optimisation to grow EBITDA margins from the current 30%-40% typical of major life sciences companies to 50%, and, finally, an active and effective acquisitions strategy.

One of the major drags on the prospects for life sciences companies of the past two years has been the stuttering of M&A activity, and the challenging climate for IPOs and life sciences investment generally. A hopeful note was struck at the end of 2023, with acquisitions which indicated faith in the future value of mass market, chronic diseases of ageing with, among others, BMS acquiring Karuna, and AbbVie acquiring Cerevel, both in the CNS space.

For 2024, the underlying drivers for further recovery in M&A are strong. Big pharma has amassed a formidable war chest, equating to $0.8 trillion deal capacity among the top 15 companies by 2023, whereas many biotechs will be perilously close to the end of their current funding, with little immediate relief in sight. The impending patent cliff for big pharma provides further incentive to act in 2024. As interest rate rises slow and stall, and the realities of the new pharmaceutical market paradigm – value growth in mass market, chronic areas, and economic challenge across US and Europe – bed in, it may be that 2024 sees a phase transition where the new shape of the pharmaceutical market for years to come becomes apparent.

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