World Preview 2024: Pharma's Growth Boost



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Foreword

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Obesity drugs loom large over 2030 forecasts. GLP-1 agonists and related incretins are helping drive record overall prescription drug sales growth, propelling leaders Novo Nordisk and Eli Lilly to the top of the company rankings and hogging the lion's share of the 2030 product top-ten. As competition ramps up, more potent compounds, combinations and oral formulations will likely support metabolic diseases' dominance into the next decade and beyond.

Immuno-inflammation and oncology also make 2030's top ten. Sanofi's Dupixent and AbbVie's Skyrizi will be the biggest non-obesity drugs. Resurgent CNS and respiratory are both prominent among most valuable pipeline candidates, as **industry's red-hot innovation engine** drives advances across the board. **New modalities and technologies** continue to open up novel targets and targeting mechanisms: antibody drug conjugates (ADCs), multi-specific antibodies, RNA-based therapies, gene/ cell therapies and radiopharmaceuticals are all expected to grow steeply to 2030. Big Pharma's appetite for Big Drugs for Big Diseases reflects **ongoing patent expiry challenges**, expected to spike the likes of Merck, J&J and Bristol Myers Squibb this decade. Patent expiries are a feature of the landscape, just like the M&A that can help address them. Pharma acquisitions reached a healthy \$124 billion in 2023 and look similarly strong so far in 2024 – welcome news for biotechs, given stubbornly lacklustre public markets.

Pharma cash-piles and expiry pressures should drive even more deals, but pharma **is also having to adapt to other realities**. Inflation and interest rates remain stickier than expected, political uncertainty endures, and new technologies such as AI promise (or threaten) to upend R&D workflows. These factors – plus the M&A upsurge - may already be contributing to slowing forecast pharma R&D spend, whose growth for the rest of this decade is just a third of that seen between 2016 and 2023.

The **US Inflation Reduction Act is bedding into the landscape**. Industry's legal challenges have so far failed, and price negotiations between pharma firms and Medicare/CMS are ongoing. Many implementation details of the Act remain unclear; the forthcoming US election may influence how aggressively (or otherwise) the law is translated into action.

But with payers facing unprecedented numbers of new drugs, and the public lens still firmly focused on drug pricing, it is hard to imagine any US government repealing the IRA.



Pharma's Growth Boost

By Melanie Senior



Big Drugs for Big Diseases

Obesity & inflammation are driving high growth and give us a reinvigorated top 10 – but there is still that patent cliff to contend with.



Big Drugs for Big Diseases

Obesity, inflammation drive higher pharma sales growth

Novo Nordisk and Eli Lilly's respective obesity/ diabetes duos, Wegovy/Ozempic and Mounjaro/ Zepbound, plus inflammatory disease blockbusters Dupixent - from Sanofi - and AbbVie's Skyrizi, will help drive annual worldwide prescription drug sales growth to almost 7.7% over the next five years. That's two percentage points over 2023's forecasts, and significantly outpaces five-year CAGR since 2000. (See World Preview **2023**). In 2030, total pharma sales will top \$1.7 trillion.

Figure 1: Worldwide Total Prescription Drug Sales (2016-230)

Source: Evaluate Pharma© (May 2024)



Metabolic Diseases Drugs Will Dominate Top Product Ranks in 2030 – and Likely Beyond

Five metabolic diseases drugs will by then scoop in over \$100 billion combined, dominating the top ten drug ranking. Those are Novo's Ozempic (semaglutide) and Lilly's Mounjaro (tirzepatide) in diabetes, analogs Wegovy and Zepbound for obesity, plus Novo's follow-on combination Cagrisema (semaglutide and cagrilintide). More than one billion people worldwide – including 50% of all US adults – are classified as obese. These treatments not only help reduce weight but are also shown to cut the risk of related conditions including heart, liver and kidney disease. So \$100 billion may not be the ceiling.

Immuno-Inflammation Not Far Behind: Dupixent and Skyrizi Take 2nd and 6th

Other "big drugs for big diseases" feature prominently in 2030's top ten. This marks pharma's shift away from drugs for rare diseases and cancer in favour of products that can more quickly fill post-patent-expiry gaps, of which there are more to come.

Ozempic pushes Sanofi/Regeneron's Dupixent

(dupilumab) into second, but the pipeline-inproduct will still sell over \$22 billion in 2030 as it collects approvals beyond asthma, eczema and most recently, eosinophilic esophagitis. The drug's average annual growth of almost 10% banks an anticipated approval in chronic obstructive pulmonary disease: recent Phase 3 data showed the IL-4/IL-13 inhibitor significantly reduces exacerbations and improves lung function in some COPD patients.

Sixth-placed Skyrizi (risankizumab) will grow by over 14% annually on average over the period to reach \$19.5 billion in sales for sponsor AbbVie by 2030. The IL-23 antibody, already approved for plaque psoriasis, psoriatic arthritis and Crohn's disease, is chasing a further win in ulcerative colitis, an inflammatory bowel disease. With sales of once-giant Humira falling steeply as biosimilars deepen their hold, AbbVie is leaning heavily on Skyrizi and JAK inhibitor Rinvoq (upadacitinib), together expected to account for over 40% of AbbVie's 2030 revenue.

Replicating the outsized success of pipelinesin-a-product like Dupixent and Skyrizi will be tough, due to competition and disease segmentation. Auto-immune diseases including psoriasis are increasingly crowded, commanding high promotional spend. Developers now seek differentiation through biomarker-led patient stratification, slicing the market into smaller parts.

Johnson & Johnson's Darzalex (daratumumab) is the largest of the two oncology top-ten



Figure 2: Top 10 Selling Products WW in 2030



candidates, just ahead of Merck's genericising checkpoint inhibitor Keytruda (pembrolizumab). Keytruda's key patent expires in 2028, like that of Bristol Myers Squibb's Opdivo, which has fallen out of the 2030 top ten as a result. J&J's anti-CD38 antibody is anticipated to sell close to \$16 billion across its over half-dozen approvals for multiple myeloma (as part of several treatment combinations and for different disease stages). It only just outsizes Keytruda, whose annual sales will by then have shrunk by over 40% to \$14.6 billion.

Skyrizi and Rinvoq are expected to account for nearly 50% of AbbVie's 2030 revenues.

Patent Risks Persist

Pharma's steepest post-expiry sales drops are yet to come. The high point in terms of worldwide sales at risk – \$100 billion, or 6.6% of total sales – will be in about four years, with Keytruda, Opdivo, BMS/Pfizer's clot-buster Eliquis (apixaban), Pfizer's breast cancer drug Ibrance (palbociclib) and Lilly's Trulicity (dulaglutide) for diabetes all due to lose protection in 2027-8. Last year, those drugs together sold almost \$58 billion.

Figure 3: Worldwide Sales At Risk* from Patent Expiration (2016-2030)

Source: Evaluate Pharma© (May 2024)



Note: Sales at risk refers only to anticipated lost sales in the first year post expiry

By 2030, that sales exposure will have halved.

By company, Merck and BMS are prominent, with JNJ, Novartis and AbbVie's exposure ramping up more steeply toward the end of the decade, as drugs including J&J's Stelara (ustekinumab) and Novartis Cosentyx (secukinumab), both sold for autoimmune conditions, reach the end of their protected lives.

By 2030, Dupixent, Skyrizi and Darzalex will each have spent over a decade on the US market; the oldest, Darzalex, will be 15. This brings them into the penumbra of the Inflation Reduction Act, which stipulates price negotiations on 13-yearold biologics costing Medicare more than \$200 million per year. Life-cycle management strategies thus become even more important. Dupixent's subcutaneous version, Faspro, was launched in 2020 with an added ingredient, hyaluronidase, that enhances the drug's absorption from subcutaneous tissue into the blood. Merck is trying something similar with its subcutaneous Keytruda (MK-3475), which features in Evaluate's top ten most valuable pipeline drugs in 2030 (see below).

Drug sponsors hope that combining their treatments with hyaluronidase may protect from Medicare's price negotiation claws: Medicare counts all drugs with the same active ingredient as the same product for the purposes of the \$200 million cost threshold, regardless of formulation or delivery route. That protection is far from a sure bet, though.

Novo and Lilly Catapult to Top Company Spots; AbbVie Third

The GLP-1 agonists will catapult Novo and Lilly to the very top of the company league. Sales of each will grow by over 12% on an average annual



basis, overshadowing even AstraZeneca's anticipated 5%+ growth rate. This is a turn of the tables: neither company had made the top ten at all until their ninth and tenth places last year. (See World Preview 2023). Before that, Novo was categorised as mid-sized. Eli Lilly's market capitalisation at the end of 2020 was less than half that of Johnson & Johnson. Skyrizi helps haul AbbVie into third. Johnson & Johnson and Merck are on similar \$60-70 billion 2030 sales trajectories, so there may be some shuffling. Novo and Lilly, too, may trade places as both continue to face supply issues. (Novo's bid to acquire manufacturer Catalent, currently under Federal Trade Commission (FTC) review, may partially account for Wegovy's lead over Zepbound in the ranking.) Barring major unforeseens, Novo and Lilly will remain at the top of the pile for the rest of the decade and likely beyond. (See chapter: *Wegovy and Zepbound are just the start*).

Figure 4: Worldwide Prescription Drug Sales in 2030: Top 10 Companies



Source: Evaluate Pharma© (May 2024)





Wegovy and Zepbound are Just the Start

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The obesity therapy market is still in its early innings. Wegovy and Zepbound together sold less than \$5 billion in 2023 – a fraction of the \$130 billion Evaluate estimate for the overall GLP-1 space by 2030. The battle for market share has barely begun, and, by the end of the decade, there will likely be more than two in the fight.

Sales of frontrunner Wegovy (semaglutide), a household name barely three years post-launch, are expected to triple over the next five years. Yet it has already been trumped, efficacy-wise, by Eli Lilly's Zepbound (tirzepatide) and other development candidates; three of the top ten most valuable pipeline products are obesity drugs, topped by Novo's own Phase 3 combo Cagrisema.

Zepbound's extraordinary forecast annualised

average growth rate between 2023-2030 – over 90% - is in large part due to its lower baseline: Lilly launched in late 2023, more than 18 months behind Wegovy. The drug has also shown slightly stronger weight loss data than Wegovy, likely because it hits not only glucagon-like

Figure 5: GLP-1 Modulator Sales by Indication (2021-2030)



Source: Evaluate Pharma© (May 2024)

Note: Sales are predominantly in diabetes (purple) and obesity (blue) but by 2028 will include MASH, chronic kidney disease and chronic heart failure.

peptide (GLP)-1, as Wegovy does, but also agonises an additional weight-loss related hormone, GIP (glucose dependent insulinotropic peptide).

But Novo has laid down the gauntlet. When Zepbound arrived, the Danish group launched its Phase 3 head-to-head pitting next-in-line Cagrisema against the highest dose of the Lilly drug. Cagrisema combines long-acting amylin analogue cagrilintide with semaglutide, adding another mechanism that may further potentiate weight loss. In Phase 2, the combination led to 15.6% average weight loss at 32 weeks – possibly faster loss than Zepbound which, at 72 weeks, generated an average 20.9% loss at its highest dose. The drug's net present value of almost \$80 billion makes it the most valuable pipeline candidate. (See Figure 7)

Other Big Pharma like AstraZeneca are buying into the gold rush, and investors are busy writing cheques for next-generation innovators. Going forward, precise percentages shed – even once in-trial comparisons are available – may be less important than route of administration or dosing frequency. Wegovy and Zepbound are onceweekly injections. Many clinicians are excited by the prospect of Lilly's oral GLP-1 orforglipron, silver medalist in the most valuable pipeline projects by net present value. Amgen's Phase 2 MariTide may offer a once-monthly injectable option that's more tolerable. The antibodypeptide conjugate activates GLP-1 and blocks (rather than activates) GIP. Other development candidates seek to improve the quality of weight loss – fat more than muscle – and/or to maintain loss after treatment has ceased.





Pipeline Captures CNS Revival

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The top ten most valuable pipeline candidates by net present value are projected to collect almost \$65 billion in 2030 sales. Three of the top four address obesity and its sequellae – Novo's chart-topping CagriSema, which combines Wegovy's active ingredient with an amylin analogue, and Lilly's oral GLP-1 hopeful orforglipron and "triple-G" drug retatrutide, which hits GLP-1, GIP and the glucagon receptor (GCGR). Three CNS drugs also feature in the top ten, reflecting significant scientific progress and investor interest in this large under-served category. Bristol Myers Squibb's schizophrenia therapy KarXT, acquired via its \$14 billion acquisition of Karuna in December 2023, combines muscarinic M1/M4 receptor agonist xanomeline with antagonist trospium to create a more tolerable – thus effective – therapy. These aren't new mechanisms, but their intelligent combination lowers risk in a notoriously difficult area. The drug was filed in November 2023 for schizophrenia and Alzheimer's related psychosis and has a September 2024 PDUFA; if approved it would provide a novel therapeutic mechanism for almost three million people in US with schizophrenia.

Lilly's donanemab, an anti-amyloid-beta antibody, could bring similar relief to some patients with early-stage Alzheimer's and their families. An FDA advisory committee in June



Figure 6: Top 10 Most Valuable R&D Projects (Ranked by NPV). Phase III and Filed.

Product	Company	Therapy Area	WW Product Revenues (\$bn) 2030	Today's NPV (\$bn)
Cagrisema	Novo Nordisk	Endocrine/Gl	20.2	80.0
Orforglipron	Eli Lilly	Endocrine/GI	8.3	34.0
Retatrutide	Eli Lilly	Endocrine/GI	5.0	32.3
VX-121 (Vanza Triple)	Vertex	Respiratory	7.7	30.4
MK-3475 SC	Merck & Co	Oncology	8.0	19.7
Datopotamab Deruxtecan	Daiichi Sankyo	Oncology	4.4	17.5
MariTide	Amgen	Endocrine/GI	2.1	12.4
VX-548	Vertex	CNS	2.9	11.0
KarXT	BMS	CNS	3.1	10.5
Donanemab	Eli Lilly	CNS	2.5	9.0
Тор 10			64	256.8
Total			343	957.1

2024 voted strongly in favour of approval, which will likely follow before year-end. It hasn't been an entirely smooth ride for the drug: it was rejected in January 2023 for accelerated approval, following the controversial expedited approval in 2021 of Biogen's Aduhelm which has since discontinued. Peak sales for donanemab are expected to reach just over \$5 billion, tempered by safety concerns, diagnostic challenges, and questions over which patients are most likely to benefit. Biogen/Eisai's frontrunner Leqembi (lecanemab) sold less than \$20 million in the first quarter of 2024.

Vertex's VX-548, a selective sodium channel inhibitor for moderate-to-acute pain, reported positive Phase 3 results in January 2024, setting up an anticipated mid-year filing for what could become the first new, non-opioid drug class for acute pain in over twenty years. Evaluate forecasts nearly \$3 billion in 2030 sales, which may not be the peak.

Vertex Sees Gold with "Vanza Triple"

Another Vertex drug, VX-121 or the "vanza triple"

for cystic fibrosis, was filed in early May with a priority review voucher that could unlock approval within six months. The once daily treatment combines cystic fibrosis transmembrane conductance regulator (CFTR) protein corrector vanzacaftor, similar-acting tezacaftor (already marketed) and CFTR potentiator deutivacaftor, which is a tweaked version of another marketed drug, ivacaftor (Kalydeco). Vertex will owe lower royalties on this combination than it does on existing twicedaily Trikafta, which explains the rush to market. With over \$7.5 billion in forecast 2030 sales, the "vanza triple" also tops Evaluate's list of most valuable pipeline orphan drugs. (See Orphan **Drug report**)







Note: Circle size represents 2030 WW sales (\$bn). Obesity drugs classified as GI, diabetes drugs as endocrine.

Oncology Will Remain Biggest Overall Category in 2030

For all the buzz around obesity, oncology will remain the most valuable therapy area in 2030, with over \$370 billion in forecast sales across all products. That is more than twice the totals for endocrinology (obesity & diabetes), immunology and resurgent CNS. Oncology's 9.8% forecast average annual growth to 2030 has slowed slightly relative to its 2016-2023 CAGR. But it still beats most other categories and is well above total prescription drug sales growth of 7.35%.

Johnson & Johnson will top the company league in oncology by 2030, thanks to Darzalex, followed by AstraZeneca, Merck and Roche. Merck's subcutaneous version of Keytruda will be one of just two cancer drugs to make the top ten (though its peak sales of just under \$13 billion are half those of original Keytruda). Cancer's relatively poor showing on this list underscores the challenge of finding genuinely

Figure 8: Oncology Company Rankings

[excludes Gardasil, a vaccine for HPV infection]

Company	2030 WW Sales (\$bn)
Johnson & Johnson	36.8
AstraZeneca	29.5
Merck & Co	25.1
Roche	23.9
Daiichi Sankyo	17.8

2023-2030 CAGR %

new Keytruda-sized therapies: pan-cancer targets are rare, and precision medicines chase ever-narrower mutations.

Still, newer modalities like antibody-drugconjugates (ADCs), bi- or multi-specific antibodies, radiopharmaceuticals and oligonucleotide-based drugs are opening up more targets and targeting mechanisms, offering pipeline-in-a-product opportunities of their own.

Figure 9a: Antibody Drug Conjugate (ADC) sales to 2030



The second top ten most valuable cancer pipeline asset is AstraZeneca/Daiichi Sankyo's ADC datopotamab deruxetecan, under FDA and EU review for lung and breast cancer. This, and the partners' marketed ADC Enhertu, push AZ to number two and the Japanese group up to number five in the oncology company rankings by 2030, a significant jump from Daiichi's 2023 ranking outside the top ten. Datopotamab deruxetecan uses an antibody to direct cytotoxic topoisomerase inhibitors to TROP2,

Figure 9b: Radiopharmaceutical sales to 2030



highly expressed across several cancers including non-squamous non-small cell lung cancers and hormone receptor positive HER2 negative breast cancer. **Top-line overall survival results** from a recent Phase 3 trial fell short of statistical significance, but data had already shown a significant improvement in progression-free-survival (PFS). The ADC is also being tested in triple negative breast cancer.

With a dozen ADCs already marketed, this redhot class has attracted tens of billions worth of deals in the last two years, including Pfizer's \$43 billion acquisition of Seagen and AbbVie's \$10.1 billion Immunogen buy in 2023. ADCs can deliver toxic therapies in a highly targeted fashion offering opportunities to combine existing or new cytotoxics with different antibodies. (**See Evaluating ADCs report**)

Radiopharmaceuticals conjugate toxic radioactive isotopes to targeting ligands, offering similar innovation potential to ADCs and also attracting growing buyer interest and investment. BMS' \$4.1 billion acquisition of RayzeBio is the biggest recent deal, but Eli Lilly, AstraZeneca and Novartis have also each spent over \$1 billion on radiopharma acquisitions within the last six months, respectively buying POINT Biopharma, Fusion and Mariana Oncology. Sales forecasts show a similar upward trajectory to ADCs, albeit at a lower order of magnitude – this is a less mature field. The rapid growth of non-conventional modalities like radiopharmaceuticals, multispecific antibodies or cell and gene therapies helps explain why worldwide shares of biotechnology versus small molecule/ conventional drug sales continue to converge toward 50/50.







Source: Evaluate Pharma© (May 2024)



More M&A as Public Markets Remain Flat

Deals provide a lifeline to cash-strapped biotechs and provide Big Pharma with a route to address loss of exclusivity.



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"The first half of 2024 saw close to \$100 billion worth of Big Pharma M&A, putting this year on track to surpass 2023 – itself one of the topthree strongest M&A years in two decades. The biggest product-focused deals so far this year? Bristol's CNS-focused Karuna buy, and AbbVie's acquisition of ADC company Immunogen, both with on- or close to- market products. (Figures

Figure 11: M&A Combined Deal Values (\$bn)



below include Novo Nordisk's proposed \$16.5 billion deal for CDMO Catalent, which remains under FTC review.)

More M&A is likely as patents expire, obesity/ diabetes drug revenues pile up and as innovation continues to flourish: cutting edge science emerges more often from academia or biotech than from Big Pharma. Smaller, bolt-on acquisitions - like Merck's acquisitions of Harpoon or Abceutics, or Novartis' purchase of auto-immune focused Calypso in early 2024 are increasingly popular as they're easier to integrate and less likely to fall foul of a stillhawkish Federal Trade Commission.

Deals of any size have become a lifeline for biotechs, struggling in a longer-than-usual down-cycle during which public markets have remained stubbornly shut. This year has seen fewer than a dozen biotech IPOs, with many trading below their list price. CNS-focused Rapport Therapeutics, which went public in June, is a notable exception. Many other companies have filed IPO documentation, but the outlook is uncertain – Australian radiopharmaceutical company Telix withdrew a planned Nasdaq listing in mid-June. M&A is really the only reliable exit option for investors and has turned Big Pharma into a very important friend to biotech and its backers. Venture capitalists are eking out support for portfolio companies that pharma hasn't bought, but the money's running short. Raising new funds is much tougher, too, since many of VCs' own limited partner investors have seen paltry returns.



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Pharma R&D Spend Grows More Slowly

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Pharma R&D spend is forecast to grow significantly more slowly in the second half of the decade than it did in the first: CAGR of over 9% in 2016-2023 shrinks to below 3% between 2023-2030. Combined R&D spend of over \$300 billion in 2024 (27% of sales) falls to 21% of sales in 2030.

Why? Various factors may be in play. Many pharma are streamlining pipelines and operations as commercial pressures continue to build. M&A may be playing a relatively greater role given some pharmas' need to replace genericising blockbusters. Al promises to boost R&D and operational efficiency, though it's too

Figure 12: Worldwide Total Pharmaceutical R&D Spend in 2016-2030



early to quantify to what extent. Forecasts of the technology's impact may be somewhat optimistic.

Geopolitical tensions also add uncertainty to spending plans. The US Biosecure Act seeks to bar biopharma firms from contracting with Chinese players such as Wuxi AppTec and Wuxi Biologics, key CDMO partners. The act hasn't yet made it into law, but industry association BIO recently U-turned to join the government in backing it and experts predict that it will eventually pass.

Continued macroeconomic malaise adds to a more general "risk-off" attitude among investors, helping explain the lacklustre performance so far this year of the XBI, a basket of US-listed biotech stocks.

Inflation Reduction Act Beds In

Then there's the Inflation Reduction Act. Pharma C-suites are less vocal about it these days, even though aspects of the Act – including the unequal treatment of small molecules and biologics – remain controversial. Battles could re-ignite as the IRA provisions roll out, and forecasts may change as the true shape of the law is revealed. It is difficult to gauge whether – or how much – IRA is influencing pharma's choice of modality and/or indication.

Price negotiations are underway for products including clot-busters Eliquis (BMS) and Xarelto (JNJ) and diabetes meds Jardiance (Lilly/ Boehringer Ingelheim) and Januvia (Merck). They will come into effect in January 2026. At the start of 2025, Medicare will select up to 15 more drugs for negotiations. Novo's semaglutide – the active ingredient in Ozempic and Wegovy – is expected to fall into IRA's crosshairs by the end of the decade; it was first launched in 2017. Ozempic and Wegovy sales will be combined to determine when the Medicare cost threshold is reached. Novo is banking on Cagrisema to have by then been approved as an even more effective alternative.

Medicare doesn't, by law, cover drugs for obesity. But the picture may change if these treatments continue to show benefits across related conditions including cardiovascular and kidney disease, of liver fibrosis (Lilly recently reported promising Phase 2 results for tirzepatide in metabolic dysfunction-associated steatohepatitis (MASH)). Wider approvals could turn GLP-1 drugs into one of the most impactful health interventions since the statins. But they will also squeeze already limited health budgets, leaving less room for the flurry of newer modalities in other areas – including much rarer diseases. (See Orphan Drugs report).

US Elections May Influence Pharma Fortunes

A Trump win in the US presidential elections in November 2024 may boost stock markets and, with it, the biotech sector, according to Tim Opler, managing director at investment bank Stifel. It could also take some of the sting out of IRA's implementation. But drug pricing pressure will remain whoever is in the White House. Flourishing biopharma innovation plus ageing populations make that almost certain.

"

IRA price curbs are unlikely to radically change obesity company rankings or sales forecasts for now, since most sales are in the private market.





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