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eBook

Billion Dollar Blueprint: The Journey to Blockbuster Status

The industry's top-selling drugs generate billions in revenues each year. Scrip analyzed data on nearly 200 blockbuster drugs, in search of the secret formula for creating the next pharmaceutical behemoth.

May 2024

Foreword

Out of the 487 drugs approved by the US Food and Drug Administration from 2014 to 2023, a staggering 193 are projected to surpass $1 billion in peak-year sales.* This suggests nearly 39% of these new drugs are forecast to reach blockbuster status.

The allure of a blockbuster drug lies not only in its ability to generate billions in revenue, bolstering a company's financial standing, but also in its potential to spur additional investment in research and development initiatives. Success for a company can lead to an enhanced brand image, opening doors to lucrative partnerships and licensing opportunities. It is no wonder that companies commit so much time and resources into the pursuit of the elusive blockbuster.

In this white paper we take deep dive into the dynamics of blockbuster drugs. Scrip surveys the existing field of these top-tier products, examines the role that multiple indications play and the time it takes to reach blockbuster status, and considers whether there is an advantage for developing in-house or external assets.

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*Source Evaluate Pharma

The Life Of A Blockbuster

By Jessica Merrill

Executive Summary

The industry's top-selling drugs generate billions in revenues each year. Scrip analyzed data on nearly 200 blockbuster drugs to see which are forecast to make the most at peak and over a 14-year time horizon.

Developing blockbuster drugs is the prime commercial goal of biopharmaceutical manufacturers, offering the chance to recoup years of investment in drug development and lay a solid financial foundation for the company's long-term future. Building blockbuster brands has never been easy and it has only gotten harder as competitive dynamics have intensified, as certain therapeutic areas have become saturated and as market access headwinds have strengthened. Nonetheless, new drugs reach the market and grow into new blockbuster brands and sometimes even "mega-blockbuster"-sized sellers.

For decades a blockbuster has been loosely defined as a drug that generates more than $1bn in annual sales. But increasingly, drug makers – and their investors – have set sights on bigger and bigger commercial brands, such as drugs that generate $5bn or more in annual sales and can serve as a solid anchor for their pharmaceutical portfolios.

Of the 487 drugs approved by the US Food and Drug Administration from 2014-2023, 193 are forecast by Evaluate Pharma to generate peak-year sales over $1bn. That means about 39% of new drugs are projected to reach blockbuster status.

Among those, the biggest sellers are 17 drugs that are forecast to reach peak-year sales of more than $10bn, while 42 are expected to post peak-year sales of more than $5bn and 114 are expected to bring in peak-year sales of more than $2bn, according to Evaluate data.

Excluding COVID-related products, the five drugs forecast by Evaluate Pharma to generate the most revenue in a single year at their peak are Merck & Co., Inc.'s cancer drug Keytruda ($31.28bn), Novo Nordisk A/S's obesity treatment Wegovy ($22.22bn), Sanofi/Regeneron Pharmaceuticals, Inc.'s immune disease drug Dupixent ($20.02bn), Johnson & Johnson's multiple myeloma drug Darzalex

($16.87bn) and AbbVie Inc.'s autoimmune therapy Skyrizi ($16.1bn).

COVID-19 offered a unique commercial opportunity, and pandemic-related treatments and vaccines are some of the highest-earning products of all time. In the Evaluate dataset, Pfizer Inc./BioNTech SE's COVID-19 vaccine Comirnaty and Pfizer's COVID-19 antiviral Paxlovid would both rank in the top five of peak annual revenues. Comirnaty and Paxlovid have already reached peak year sales, in 2021 for Comirnaty at $41.21bn and in 2022 for Paxlovid at $18.93bn, which means that while the products generated unprecedented revenue upon their launch in the middle of the COVID-19 pandemic, they have had an atypical launch trajectory and are quickly declining.

Keytruda, on the other hand, continues on its path of being a more traditional pharmaceutical success story. The drug is on track to surpass any others in the dataset in generating the most accumulated revenue from its launch in 2014 through 2028, when it will face loss of exclusivity. Keytruda is expected to generate a staggering $251.09bn from 2014-2028, according to Evaluate. The drug has brought in $101.67bn from 2014-2023, meaning it will more than double the revenue it made in its first nine years on the market in the last five before its loss of exclusivity (LOE).

The other drugs that are expected to accumulate the most revenue in the 14-year period from 2014-2028 are Novo Nordisk's Ozempic ($135.28bn), Bristol Myers Squibb Company's Opdivo ($125.55bn), Dupixent ($120.36bn) and Comirnaty ($118.73bn). Comparisons between the brands in terms of accumulated sales figure are challenging because the drugs all launched at different time periods, between 2014 for Keytruda and 2021 for Comirnaty, so some of the drugs have had less time on the market than others.

Nonetheless, the data show just how much revenue a mega-blockbuster can contribute to a drug manufacturer's top line over an extended time period, particularly notable given that the cost of making and selling a drug generally declines the longer it is on the market.

Meanwhile, a smaller but still significant blockbuster will generate significantly less over its life. Novartis AG's Cosentyx and Entresto, for example, are both high-growth mega-blockbuster franchises for the company that are expected to peak at under $7bn in peak-year revenues. They are expected to generate substantially less over the 14-year time horizon, $58.26bn and $45bn, respectively, compared to drugs with peak-year sales over $10bn.

It's clear why drug makers are singling out those mega-sized opportunities versus going after more drugs but with smaller market potential. But there are many routes to building a blockbuster. Scrip's continuing series Building A Blockbuster will take a look at how multiple indications help stack up sales, the time it takes to reach $1bn and whether it's better to discover a blockbuster in house or seize an external opportunity.

The Biggest Blockbusters

Rank	Product	Company	Peak Year	Peak Year Sales Forecast ($bn)	2014-2023 Sales ($bn)	2014-2028 Sales ($bn)
1	Comirnaty (tozinameran)	Pfizer, BioNTech	2022	41.21	93.48	118.73
2	Keytruda (pembrolizumab)	Merck & Co	2027	31.28	101.67	251.09
3	Ozempic (semaglutide)	Novo Nordisk	2028	22.22	33.05	135.28
4	Dupixent (dupilumab)	Sanofi	2028	20.02	34.18	120.36
5	Paxlovid (nirmatrelvir/ritonavir)	Pfizer	2022	18.93	20.29	35.40
6	Spikevax (elasomeran)	Moderna	2022	18.44	45.80	70.68
7	Darzalex (daratumumab)	Johnson & Johnson	2028	16.87	34.79	108.29
8	Skyrizi (risankizumab)	AbbVie	2028	16.11	17.81	86.13
9	Wegovy (semaglutide)	Novo Nordisk	2028	15.78	5.64	72.25
10	Biktarvy (bictegravir/emtricitabine /tenofovir alafenamide fumarate)	Gilead Sciences	2028	13.88	44.21	111.29
11	Harvoni (ledipasvir/sofosbuvir)	Gilead Sciences	2015	13.86	31.98	32.26
12	Opdivo (nivolumab)	Bristol Myers Squibb, Ono Pharmaceutical	2027	13.45	62.79	125.55
13	Jardiance (empagliflozin)	Boehringer Ingelheim, Lilly	2027	13.10	26.79	83.59
14	Mounjaro (tirzepatide)	Lilly	2028	12.10	5.65	52.70
15	Zepbound (tirzepatide)	Lilly	2028	10.56	0.18	32.24
16	Enhertu (trastuzumab deruxtecan)	Daiichi Sankyo, AstraZeneca	2028	10.27	5.38	42.13

17	Rinvoq (upadacitinib)	AbbVie	2028	10.12	8.92	49.36
18	Trikafta (elexacaftor/ivacaftor/ tezacaftor)	Vertex Pharmaceuticals	2024	9.25	26.55	65.33
19	Ocrevus (ocrelizumab)	Roche	2026	8.93	30.62	72.07
20	Verzenio (abemaciclib)	Lilly	2028	8.08	9.47	43.21
21	Tagrisso (osimertinib)	AstraZeneca	2028	7.83	27.14	63.10
22	Tecentriq (atezolizumab)	Roche	2028	7.65	17.98	51.62
23	Trulicity (dulaglutide)	Lilly	2022	7.44	36.66	66.49
24	Farxiga (dapagliflozin)	AstraZeneca	2025	7.43	22.16	51.98
25	Entyvio (vedolizumab)	Takeda	2028	7.07	29.29	62.71
26	Vabysmo (faricimab)	Roche	2028	7.07	3.25	31.75
27	Imfinzi (durvalumab)	AstraZeneca	2028	7.00	13.62	44.51
28	Kisqali (ribociclib)	Novartis	2028	6.97	5.73	31.86
29	Entresto (sacubitril/valsartan)	Novartis	2024	6.96	20.39	45.00
30	Ronapreve (casirivimab/imdevimab)	Regeneron Pharmaceuticals, Roche	2021	6.91	7.89	7.89
31	Tremfya (guselkumab)	Johnson & Johnson	2028	6.73	10.91	37.53
32	Hemlibra (emicizumab)	Roche	2028	6.62	15.83	46.67
33	Cosentyx SC (secukinumab)	Novartis	2028	6.52	28.33	58.26
34	Cagrisema (cagrilintide/semaglutide)	Novo Nordisk	2028	6.13	0.00	10.19
35	Shingrix (herpes zoster vaccine)	GSK	2026	6.08	16.30	44.94

36	Vraylar (cariprazine)	AbbVie	2028	5.87	10.23	35.47
37	Rybelsus (semaglutide)	Novo Nordisk	2028	5.78	5.41	29.53
38	Lagevrio (molnupiravir)	Merck & Co.	2022	5.68	8.06	9.71
39	Veklury (remdesivir)	Gilead Sciences	2021	5.57	14.47	18.71
40	Ibrance (palbociclib)	Pfizer	2021	5.44	35.77	55.24
41	Ofev (nintedanib esylate)	Boehringer Ingelheim	2024	5.31	18.12	32.92
42	Ultomiris (ravulizumab)	AstraZeneca, Alexion Pharmaceuticals	2028	5.18	7.94	30.70
43	Leqembi (lecanemab)	Eisai	2028	4.87	0.06	13.47
44	Genvoya (cobicistat/elvitegravir/ emtricitabine/tenofovir/ alafenamide)	Gilead Sciences	2018	4.74	24.91	33.10
45	Vyndaqel (tafamidis)	Pfizer	2025	4.46	9.69	29.62
46	Kesimpta (ofatumumab)	Novartis	2028	4.17	3.65	21.34
47	Calquence (acalabrutinib)	AstraZeneca	2028	4.02	6.58	24.34
48	Lynparza (olaparib)	AstraZeneca	2027	3.93	12.04	29.62
49	Carvykti (ciltacabtagene autoleucel)	Johnson & Johnson	2028	3.89	0.60	12.72
50	Pluvicto (lutetium Lu 177 vipivotide tetraxetan)	Novartis	2028	3.87	1.25	16.31

Source: Evaluate Pharma (data sourced in February)

Blockbusters By Indication: More Begets More

By Jessica Merrill

Executive Summary

A Scrip analysis of the industry's top-selling drugs examines the power of indication expansion to drive revenue growth.

Pharmaceutical manufacturers have been keen to invest in drugs that have potential in multiple diseases, paving the way for revenue growth through indication expansion. The phrase "pipeline-in-a-pill" has become as ubiquitous in R&D circles as "string of pearls" has become in dealmaking.

An analysis of industry's top-selling drugs underscores the value of indication expansion to drive growth, but also raises questions about whether that pattern will continue at the same pace in the future.

Among 20 of the industry's best-selling drugs that launched since 2014 and are forecast to have the highest peak sales potential, half are approved by the US Food and Drug Administration for three or more indications and seven are approved for five or more.

In this class, Merck & Co., Inc.'s Keytruda (pembrolizumab) – expected to have the highest peak sales – is the poster child with 20 different cancer indications. Keytruda is expected to generate revenues of $31.28bn in peak year sales in 2027, according to data compiled by Evaluate Pharma. Bristol Myers Squibb Company's Opdivo (nivolumab) has the second most indications of the group with 11 cancer indications; peak year sales are forecast at $13.45bn in 2027.

Only one of the 20 drugs with the highest peak sales potential have a single indication – Vertex Pharmaceuticals Incorporated's Trikafta (elexacaftor/tezacaftor/ivacaftor) for cystic fibrosis. Eli Lilly and Company has separate brands for tirzepatide – Mounjaro for diabetes and Zepbound for obesity – each producing blockbuster sales for the same molecule. Mounjaro/Zepbound are newer drugs, however, approved by the FDA in 2022 and 2023, respectively, and are likely to gain new indications.

Biggest Sellers By Number Of Indications

A look at the top 20 bestselling drugs launched since 2014, ordered by 2023 sales.

Drug	Company	Therapy Area	No. Of Indications	2023 Sales ($bn)
Keytruda	Merck & Co.	Oncology	20	18.1
Ozempic	Novo Nordisk	Metabolic	2	13.9
Biktarvy	Gilead Sciences	Antiviral	2	11.9
Dupixent	Sanofi	Immunology	5	11.6
Opdivo	Bristol Myers Squibb	Oncology	11	9.9
Darzalex	Johnson & Johnson	Oncology	8	9.7
Trikafta	Vertex Pharmaceuticals	Respiratory	1	8.9
Jardiance	Boehringer Ingelheim	Metabolic	4	8.1
Skyrizi	AbbVie	Immunology	3	7.8
Trulicity	Eli Lilly	Metabolic	2	7.1
Ocrevus	Roche	Neurology	2	7.1
Farxiga	AstraZeneca	Metabolic	2	6.5
Tagrisso	AstraZeneca	Oncology	4	5.8
Entyvio	Takeda	Gastro-Intestinal	2	5.5
Mounjaro	Eli Lilly	Metabolic	1	5.2
Wegovy	Novo Nordisk	Metabolic	2	4.6
Tecentriq	Roche	Oncology	5	4.2
Rinvoq	AbbVie	Immunology	8	4.0
Verzenio	Eli Lilly	Oncology	4	3.9
Enhertu	Daichi Sankyo/AstraZeneca	Oncology	5	2.6

Note: Top 20 drugs selected by peak year sales. Excludes COVID-19 products and Gilead's hepatitis C drug Harvoni (ledipasvir/sofosbuvir) owing to their atypical launch trajectory, and Lilly's obesity drug Zepbound, which is expected to be a big seller but only launched in December 2023. Source: drug labels and company 10-Ks.

Blockbusters By Indication: More Begets More

It is hard to attain mega-blockbuster status with a single indication, but not impossible as Trikafta has shown, when a drug meets a serious unmet need in a substantial patient population. Cancer has been an especially prime field for growth through indication expansion. A typical launch pattern in oncology sees a drug starting in a hard-to-treat or late-stage disease before expanding into earlier lines of treatment and different indications.

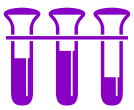
Of the 20 drugs launched since 2014 that have the highest peak sales forecasts, seven are cancer drugs; all seven are approved for at least four indications.

Indication Expansion Slowdown Ahead?

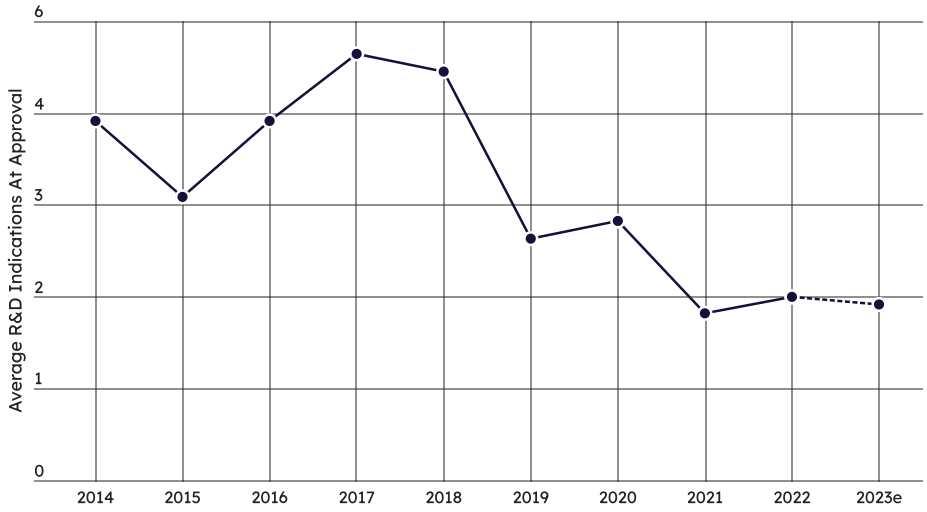
Indication expansion has been a big area of industry focus over the past decade, but the rollout of the Inflation Reduction Act in the US, which introduces Medicare drug price negotiation, is believed to undermine that model of drug development. (Also see "US Pricing Reform Puts Cancer Drug Innovation At Risk, Drug Leaders Warn" - Scrip, 2 Nov, 2022.) Evaluate Pharma's forecasts also trend downwards. For drugs approved in 2019 and after, for drugs that have not yet had a full five years on the market, the five-year supplemental approval averages fall from 2.5 to a forecast of 1.8 from 2023-2028.

Diving deeper and looking at blockbusters with forecast supplemental approvals in indications for which they are still in clinical trials also shows a move toward fewer indications. Blockbusters approved in the US in 2018 were in the clinic for an average of 5.5 additional conditions, while blockbusters approved in 2022 were, on average, only being studied in 2.3 other conditions on average, a decline of nearly 60%.

Indication Expansion In The Clinic



Average clinical-stage indications underway for blockbuster drugs at initial US approval



These analyses take as their basis all the drugs approved in the US in the past decade that are either already blockbusters or are predicted to achieve this status by 2028. This is dated from the first US approval, but sales from subsequent approvals are included in the total. Source: Evaluate Pharma (data as of February)

Blockbusters By Indication: More Begets More

The saturation of the market with checkpoint inhibitors is likely a contributor to that downward trend. Keytruda, for example, was in the clinic for 20 additional tumor types in 2014, the year it was approved for melanoma.

Of 17 drugs that are forecast to become blockbusters that gained an initial US approval in 2023, meanwhile, six of them are not in the clinic for any other diseases. RSV vaccines like GSK plc's Arexvy and Pfizer Inc.'s Abrysvo are in this category as they are not applicable to any other infection.

Nonetheless, big pharma's interest in the pipeline-in-a-pill strategy doesn't appear to be waning. Indication expansion opportunities have been a cornerstone of some recent high-profile business development deals like Pfizer's acquisition of Velsipity (etrasimod) with the buyout of Arena Pharmaceuticals, Inc. in 2021 and Merck & Co.'s addition of Winrevair (sotatercept) with the 2021 acquisition of Acceleron Pharma, Inc. (Also see "Pfizer Buys Arena For $6.7bn In Bid To Diversify In Inflammation & Immunology" - Scrip, 13 Dec, 2021.) and (Also see "Merck's $11.5bn Acceleron Buy Partially Fills Future Keytruda Revenue Gap" - Scrip, 30 Sep, 2021.)

An area of R&D that will likely drive continued indication expansion is antibody-drug conjugates (ADCs) for cancer. One pioneering ADC is blazing that trail already: Daiichi Sankyo Co., Ltd./AstraZeneca PLC's Enhertu (fam-trastuzumab deruxtecan), which is approved in five cancer types and in trials in 11 more. The partners are also developing a second ADC, datopotamab deruxtecan, which is expected to be approved this year and forecast to become a blockbuster in its first indication, non-small cell lung cancer, but is also in the clinic in 12 more tumor types.

Winning Therapeutic Areas

Over the past 10 years from 2014-2024, cancer has reliably been where the money is, with anti-infection drugs coming behind, according to Evaluate data.

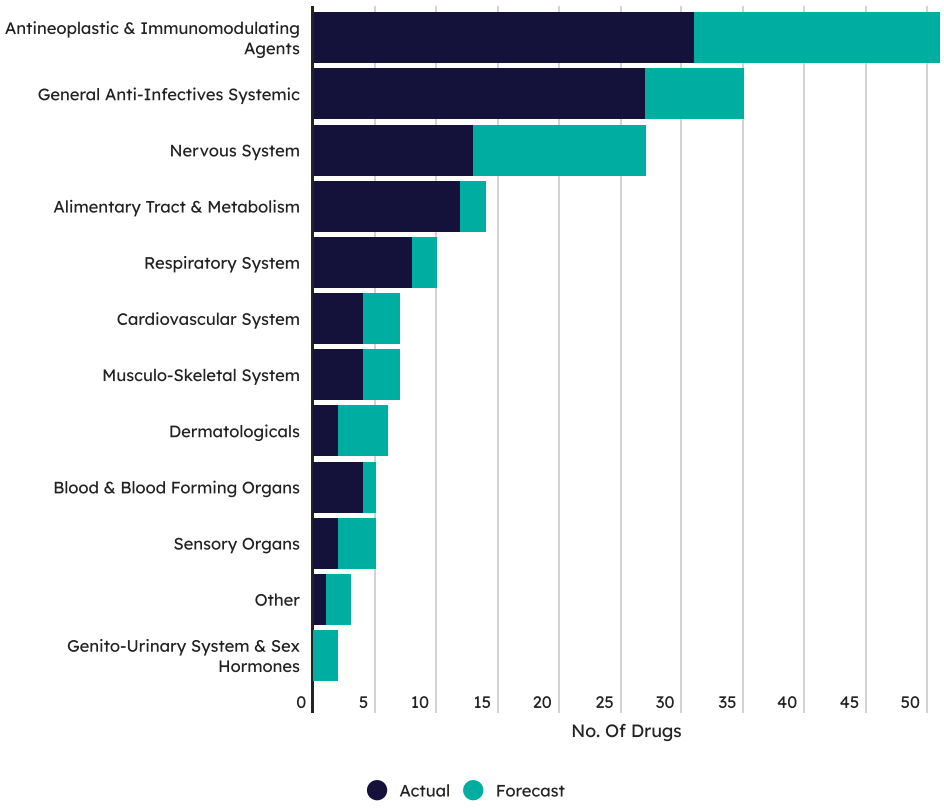
Looking at drugs by therapeutic area shows cancer has led the blockbuster field. Of the 51 drugs classified as antineoplastic and immunomodulating agents – the categories most often used to treat cancer – approved in the US between 2014 and 2023, 31 are already blockbusters. A further 20 cancer drugs are forecast by Evaluate to hit $1bn in sales over the next four years, including Bristol Myers Squibb's CAR-T therapy Abecma (idecabtagene vicleucel), Johnson & Johnson's Carvykti (ciltacabtagene autoleucel) and Roche's Polivy (polatuzumab vedotin).

The anti-infective category is not far behind cancer when it comes to existing blockbusters, with 27 drugs approved in the past decade generating $1bn or more. Perhaps surprisingly, COVID-19 does not play as large a role as might be expected. True, big names like Comirnaty from BioNTech and Pfizer, Moderna's Spikevax and Pfizer's therapy Paxlovid (nirmatrelvir/ritonavir) are represented. But the majority of the past decade's existing anti-infective blockbusters predate the pandemic.

Gilead is the big name in this category, with its HIV and hepatitis franchises, along with its COVID-19 therapy Veklury (remdesivir), accounting for seven of the 27 existing blockbusters. Looking ahead, the respiratory syncytial virus (RSV) category is poised to be a lucrative one, with vaccines like GSK's Arexvy and Pfizer's Abrysvo and AstraZeneca/Sanofi's monoclonal antibody treatment Beyfortus (nirsevimab) positioned to be big sellers.

Blockbusters By Therapy Area

Actual and forecast blockbuster drugs approved between 2014-2023.



These analyses take as their basis all the drugs approved in the US in the past decade that are either already blockbusters or are predicted to achieve this status by 2028. This is dated from the first US approval, but sales from subsequent approvals are included in the total. Products are categorised by EPHMRA code. These were devised by the European Pharmaceutical Market Research Association (EPHMRA) to classify products according to their indications and therapeutic use. Source: Evaluate Pharma (data as of February 2024).

Rapid Rise Or Slow Roll: How Long Does It Take To Become A Blockbuster?

By Jessica Merrill

Executive Summary

Scrip analyzed data on top-selling drugs to see how long it takes to surpass $1bn in revenues and grow into $5bn and even $10bn brands.

A new drug that is quick to reach blockbuster status – or $1bn in revenues – is often a sign of a mega-blockbuster in the making. Launch trajectories are a closely watched metric to evaluate a new drug's likelihood of long-term commercial success.

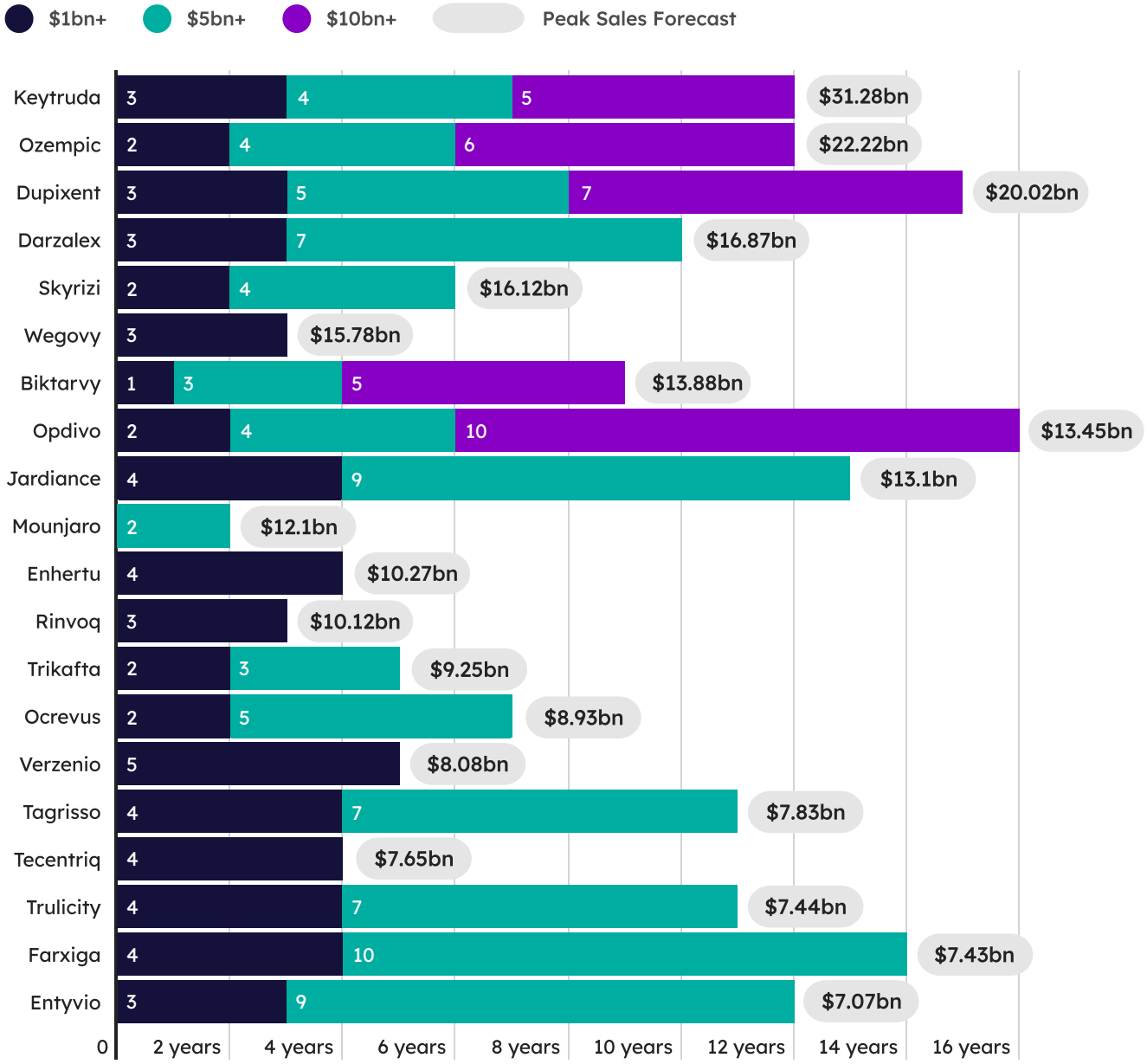
Historically, $200m in first year sales for a new drug has been a benchmark for predicting an eventual blockbuster-sized seller, though in some therapeutic areas like oncology and immunology, launch trajectories have lengthened as the categories have grown more competitive and market access has taken longer to secure.

In rare instances, new drugs burst out of the gate, addressing a critical unmet need or a big market opportunity, and in those cases a new drug can generate close to $1bn in sales in its first year, a sign the drug is on its way to becoming a mega-blockbuster-sized commercial winner.

Of 20 top-selling drugs that launched since 2014, it took an average of three years for drugs to generate $1bn or more in sales. It took 5.5 years on average for the 15 drugs that surpassed $5bn in sales to reach that threshold and it took an average 6.6 years for the five drugs that reached $10bn or more in sales to hit that marker, according to Evaluate Pharma.

Years To Blockbuster Status

A look at how long it took some of the industry's best-selling drugs to pass $1bn, $5bn and $10bn in annual revenues.



Note: Data includes year of launch as year one. Selected drugs are those that launched in the last 10 years and ranked by peak year sales forecasts, excluding COVID-19 products and Harvoni due to the unusual sales trajectory, and Zepbound, which only launched in December 2023.

Source: Evaluate Pharma

Rapid Rise Or Slow Roll: How Long Does It Take To Become A Blockbuster?

The analysis counts the year of launch as the first year on the market even when the launch occurred late in the year. Each of the drugs launched at different times so it is not possible to draw any direct commercial comparisons, but all of the drugs included are expected to be among the industry's top sellers based on peak sales forecast by Evaluate Pharma.

The analysis excludes COVID-19 products and Gilead Sciences, Inc.'s hepatitis C drug Harvoni (ledipasvir/sofosbuvir) due to their atypical launch trajectory and Eli Lilly and Company's obesity drug Zepbound (tirzepatide), which is expected to be a big seller based on peak sales forecasts but only launched in December 2023.

Of the drugs included in the analysis, Lilly's Mounjaro, the same active ingredient used in Zepbound but approved for type 2 diabetes, stands out as the fastest mega-blockbuster-sized seller. Mounjaro surpassed $5bn in revenues in only its second year on the market, generating $5.16bn in 2023, powered presumably by off-label use in obesity.

Novo Nordisk's Wegovy (semaglutide) – another notable seller – would have presumably experienced a similar rocket-fueled launch if the company had not faced supply constraints the first two years after approval by the US Food and Drug Administration. The drug generated much less in its first two years on the market, $200m and $888m, respectively in 2021 and 2022. Demand for the drug has continued to outstrip supply through 2023, but it did achieve blockbuster sales as of Q1 2024. (Also see "Competition Forces Price Cuts, But Novo Nordisk Is Unstoppable" - Scrip, 2 May, 2024.)

Gilead's HIV pill Biktarvy (bictegravir/emtricitabine/tenofovir) is another notable standout, surpassing blockbuster status its first year on the market, generating $1.18bn in 2018 and becoming a $10bn-plus seller in 2022, five years after launching. The combination pill, however, is built on the back of older, well-known medicines, so the launch trajectory is not necessarily similar to that of a brand new medicine.

Drugs that fit a typical launch model that generate more than $1bn in sales in the first year on the market are rare indeed. In addition to Mounjaro, which achieved that milestone, other drugs that have come close to hitting the mark include Regeneron's Eylea (aflibercept) for wet age-related macular degeneration in 2012, Biogen's MS drug Tecfidera (dimethyl fumarate) in 2013, Bristol Myers Squibb's Opdivo (nivolumab) for cancer in 2015 and Roche's multiple sclerosis drug Ocrevus (ocrelizumab) in 2018.

Development Versus Dealmaking: How To Obtain A Blockbuster

By Elizabeth Cairns

Executive Summary

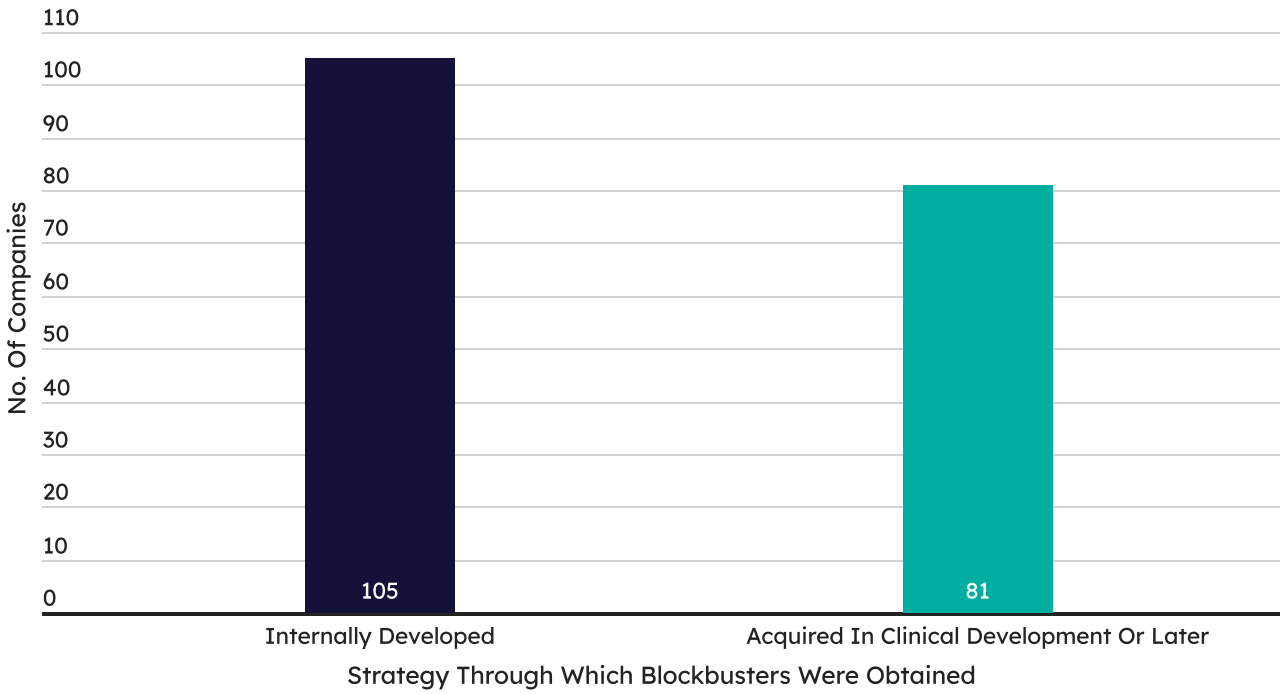
Most of the companies with blockbuster drugs approved over the past decade oversaw their clinical development internally. Lilly holds the lead with eight blockbusters developed in-house.

Considering that an actual or potential blockbuster developed by a smaller biotech is catnip to big pharma, obtaining a blockbuster by buying it might be expected to be the most common strategy. But according to data from Evaluate Pharma, only 81 companies with blockbusters gained them through dealmaking – at least when the parameters are limited to clinical stages.

Meanwhile, 105 drug companies either discovered blockbusters internally or bought them before clinical trials had started. Many companies that developed blockbusters in-house are big pharmas or big biotechs, including big names like Novo Nordisk A/S, which discovered and developed Ozempic (semaglutide) and Johnson & Johnson, which developed Tremfya (guselkumab).

There are also some niche products that are out-licensed but are only expected to yield blockbuster numbers for the originator. One such is Sarepta Therapeutics, Inc.'s Duchenne gene therapy Elevidys (delandistrogene moxeparvovec), partnered with Roche Holding AG. Elevidys is forecast to earn $2.4bn for Sarepta in 2028, down from a peak of $3.0bn in 2026. The same year, just $489m will accrue to Roche, according to Evaluate's forecasts.

Strategy Of Company - Blockbusters Approved 2014-2023



Note: "Internally Developed" includes assets acquired or licensed while still preclinical

Source: Evaluate Pharma

Who's In The Lead?

One of the companies with the most blockbusters approved in recent years is Eli Lilly and Company – currently the world's biggest pharma company by market cap.

From the start of 2014 to the end of 2023 170 drugs were approved in the US that, as of February 2024, had earned (or were forecast to earn) total sales of more than $1bn in any year up to 2028. This analysis counts only those drugs with blockbuster revenues that will accrue to a single company. For example, a partnered drug poised to earn $600m for company A and $600m for company B, is excluded from the analysis.

Conversely, a product that earns over $1bn for more than one company – such as Enhertu (trastuzumab deruxtecan), the cancer drug that has made blockbuster numbers for both Daiichi Sankyo Co., Ltd. and AstraZeneca PLC – is counted twice.

Lastly, if a product deal is done while the asset is still preclinical, it is counted as internally developed by the buyer. A clear example is Keytruda (pembrolizumab), the checkpoint

inhibitor discovered by Organon and, through nested acquisitions, ultimately landed with Merck & Co., Inc.. Since Merck obtained pembrolizumab before the asset entered the clinic, and funded its clinical development, Evaluate counts it as an internal Merck product.

The Different Routes Blockbusters Take To Market

Changing hands when preclinical – Keytruda

The asset that later became the mega-blockbuster Keytruda, the PD-1 inhibitor pembrolizumab, was initially discovered by scientists at Organon. This group was bought by Schering-Plough in November 2007 for $14.4bn; at this point pembrolizumab was still preclinical.

Schering-Plough was itself taken out by Merck & Co. in November 2009, for $41.1bn. Pembrolizumab had not yet reached the clinic, and Merck showed little interest in the program until 2011, when it pushed the drug into Phase I in metastatic carcinoma, melanoma, or non-small cell lung cancer. Keytruda was first approved for melanoma in 2014, and became a blockbuster in 2016.

Changing hands in clinical trials – Opdivo

Bristol Myers Squibb's rival PD-1, Opdivo (nivolumab), also arrived via acquisition, BMS's purchase of Medarex for $2.4bn in 2009. Medarex started the first clinical trial of nivolumab in 2006, but it was not the originator.

Nivolumab initially came from the labs of Ono Pharmaceutical, and it was still in early research when Medarex licensed it from Ono.

Opdivo was first approved for melanoma in December 2014, and achieved blockbuster status the year after.

Changing hands when marketed – Ultomiris

When AstraZeneca obtained the paroxysmal nocturnal hemoglobinuria therapy Ultomiris, via the $13.3bn acquisition of the drug's originator, Alexion Pharmaceuticals, in July 2021, the product had been on the market for two years.

Though it did not become a blockbuster until 2022, the drug already carried billion-dollar forecasts, and the lure of adding a blockbuster would have been a major factor in AstraZeneca's decision to buy Alexion.

Never changing hands at all – Ofev

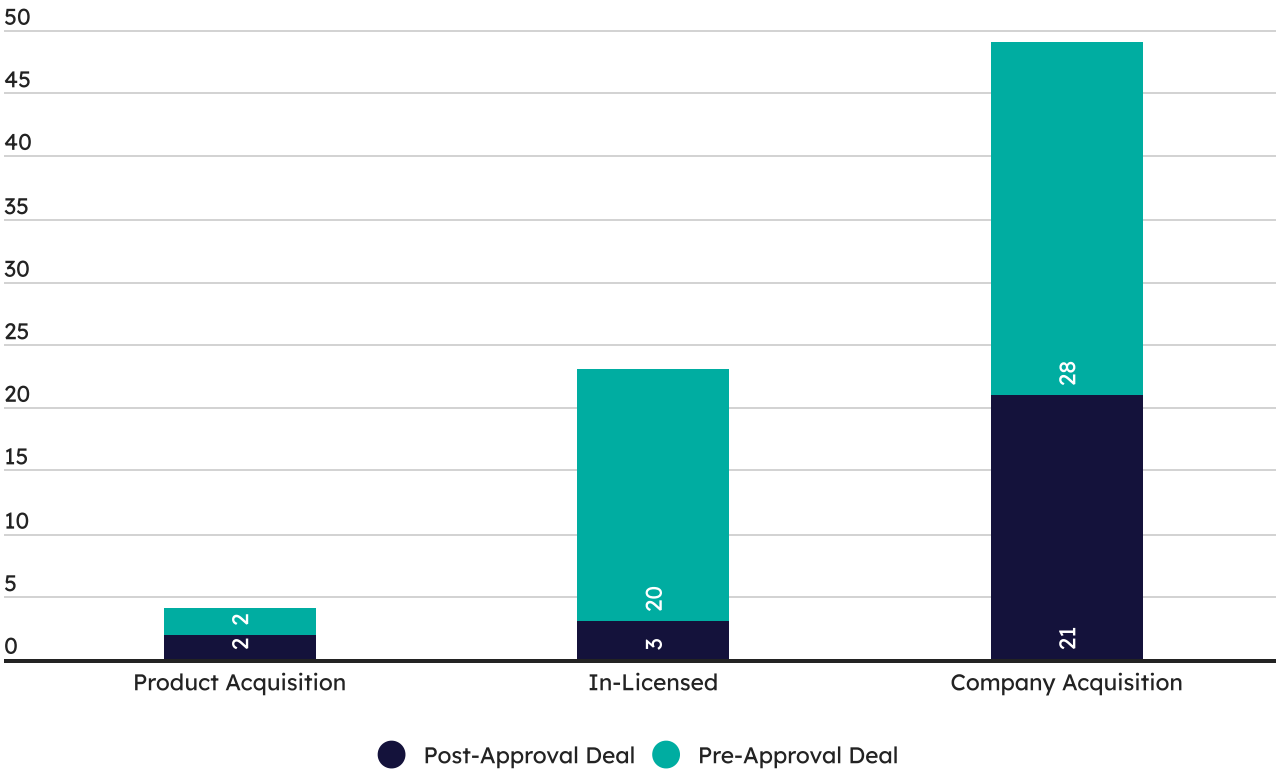
Boehringer Ingelheim first put Ofev (nintedanib) into clinical trials in 2005, having discovered the tyrosine kinase inhibitor internally. Approved for idiopathic pulmonary fibrosis in 2014, it became a blockbuster in 2017. Boehringer has never cut a deal for the product.

Splashing The Cash

There are three main strategies for getting hold of a current or future blockbuster that was originated elsewhere – licensing, buying the product, or buying the whole company.
A company acquisition is the most popular. In the past decade, 49 companies with a product earning blockbuster sales, or still in clinical trials but forecast to be a blockbuster, have been bought out. And buyers are comfortable with a certain amount of risk. Twenty-eight companies took action while the potential billion-dollar seller was still in clinical trials, while only 21 companies reduced their risk by obtaining it post-approval.

Licensing deals are much more likely to occur for clinical stage blockbusters-in-waiting than approved products. Spotting the promise of a drug and signing up rights at an early clinical stage can be a highly lucrative strategy; if things go wrong, milestone and royalty payments need never be made.

Externally Sourced Blockbusters Approved 2014-2023



Note: "Pre-approval deal" does not include assets that were preclinical when the deal was struck

Source: Evaluate Pharma

Development Versus Dealmaking: How To Obtain A Blockbuster

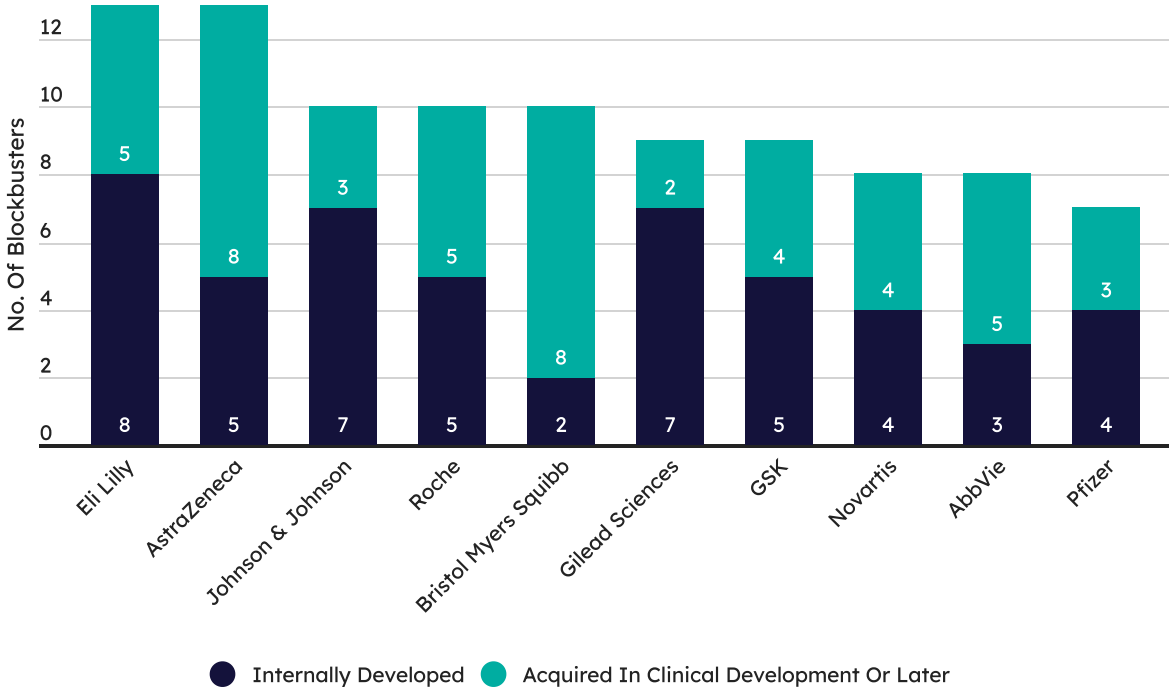
Who You Gonna Call?

If the effort to develop or otherwise obtain blockbusters over the past 10 years is a competition, the joint winners are Lilly and AstraZeneca. Each has gained approval in that time for 13 assets with actual or forecast blockbuster sales. But Lilly managed to originate eight, whereas only two of AstraZeneca's were discovered by that company (AstraZeneca bought in a further two and in-licensed another while they were still preclinical).

And Lilly's blockbusters are bringing in more, driven by the obesity surge. Mounjaro (tirzepatide), is forecast to be Lilly's best seller in 2028 with sales of $12.1bn. AstraZeneca's biggest drug that year will be its lung cancer therapy Tagrisso (osimertinib), with sales of $7.8bn.

Looked at a different way, though, perhaps AstraZeneca's achievement is the greater. The UK group is punching above its weight in terms of market cap, since its valuation of $205bn is less than a third of Lilly's worth. And even more impressively, the cumulative figure for actual and forecast sales of AstraZeneca's 13 blockbusters from 2014 to 2028 comes to $306bn. The equivalent number for Lilly is $283bn.

Companies With The Most Blockbusters Approved, 2014-2023



Note: "Internally Developed" includes assets acquired or licensed while still preclinical

Source: Evaluate Pharma

Of these top 10 companies, the best at originating its own products, in percentage terms, is Gilead Sciences, Inc.. Seven of its nine blockbusters were invented in-house, for a 78% hit rate.

Bristol Myers Squibb Company is at the other end of the scale, having bought in all but two of its 10 money-spinners. Its $74bn acquisition of Celgene Corporation netted it four of them, but a better value deal was its 2009 takeout of Medarex for the much lower sum of $2.4bn, through which it gained the checkpoint inhibitors Yervoy (ipilimumab) and Opdivo (nivolumab). Sales of the latter are forecast to peak in 2027 at $13bn, showing that, done right, deals can be an excellent way of entering the blockbuster hall of fame.

Development Or Dealmaking? The Top 20 Blockbusters

Drug	Company	Strategy	Stage at which it changed hands
Keytruda	Merck & Co.	Internally developed	Preclinical*
Ozempic	Novo Nordisk	Internally developed	-
Biktarvy	Gilead Sciences	Internally developed	-
Dupixent	Sanofi	Internally developed	Preclinical*
Opdivo	Bristol Myers Squibb	Acquired in clinical development or later	Phase I
Darzalex	Johnson & Johnson	Acquired in clinical development or later	Phase II
Trikafta	Vertex Pharmaceuticals	Internally developed	-
Jardiance	Boehringer Ingelheim	Acquired in clinical development or later	Phase III
Skyrizi	AbbVie	Acquired in clinical development or later	Phase III
Trulicity	Eli Lilly	Internally developed	-
Ocrevus	Roche	Acquired in clinical development or later	Phase III
Farxiga	AstraZeneca	Acquired in clinical development or later	Marketed
Tagrisso	AstraZeneca	Internally developed	-
Entyvio	Takeda	Acquired in clinical development or later	Phase II
Mounjaro	Eli Lilly	Internally developed	-
Wegovy	Novo Nordisk	Internally developed	-
Tecentriq	Roche	Internally developed	Preclinical*
Rinvoq	AbbVie	Internally developed	-
Verzenio	Eli Lilly	Internally developed	-
Enhertu**	Daichi Sankyo	Internally developed	-
Enhertu**	AstraZeneca	Internally developed	Preclinical*

**Drugs which changed hands at the preclinical stage are defined as internally developed for the purposes of this analysis. **Enhertu was originated by Daiichi and licensed to AstraZeneca; since it brings in blockbuster sales for both, this analysis counts it twice.*

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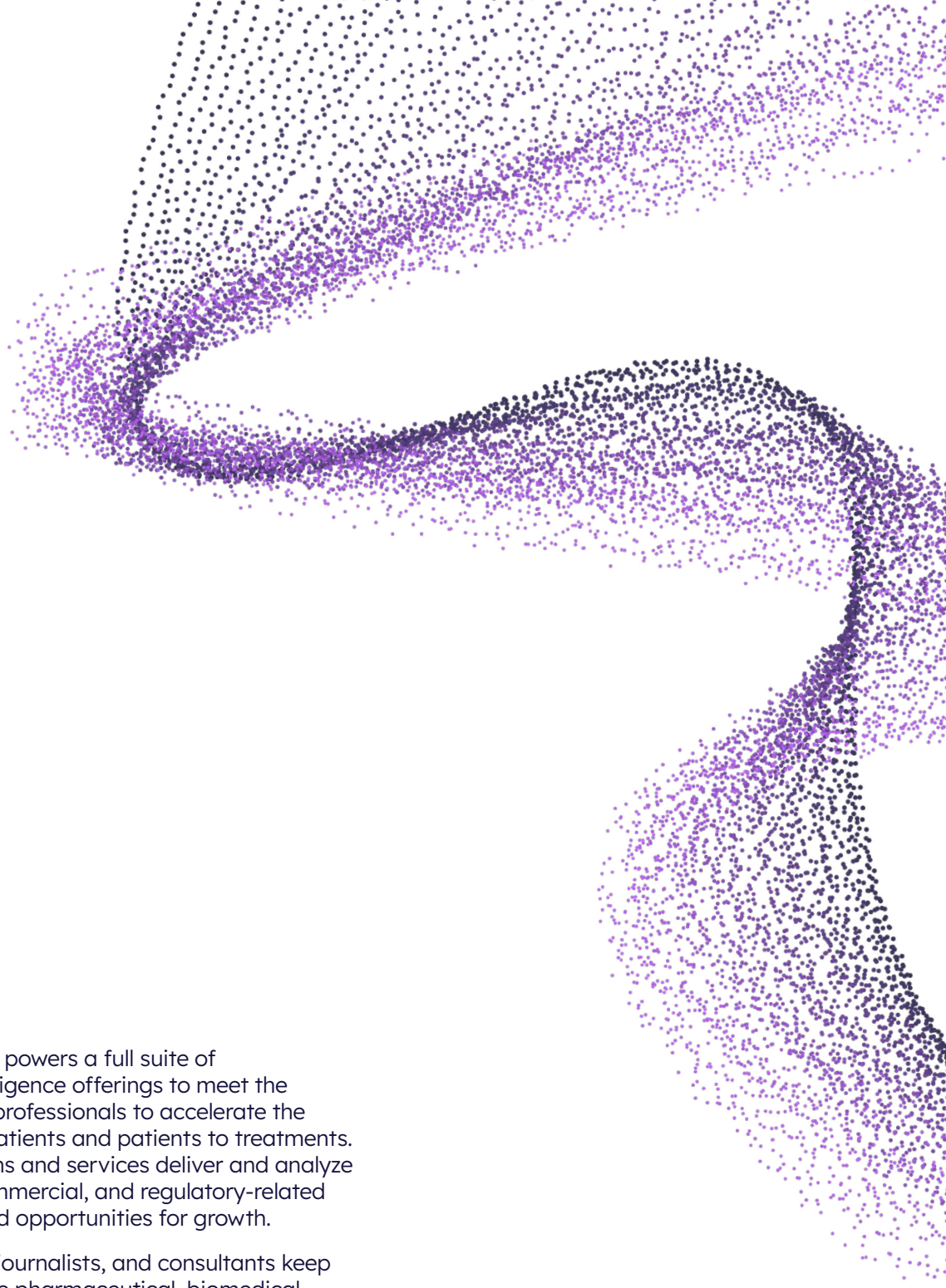

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