

Pharmaceutical Innovation and Invention Index 2023

WHITEPAPER
Celebrating the Most Innovative and
Inventive Companies in Pharma

IDEA Pharma Introduction

When we published the 11th annual Pharmaceutical Innovation and Invention Index in 2022, the world was still in the grip of COVID-19. The 12th Index – unsurprisingly – carries residue from that global event, with the financial gains of vaccines still driving performance for Pfizer (tops the Innovation Index for the second year running), and Moderna (makes it into the top 10 for the first time). After just three new companies joined the top 10 in 2022, BMS, Eli Lilly, Boehringer Ingelheim, Gilead, GSK, and Moderna all claimed spots in 2023, replacing Regeneron, Sanofi, Merck, Takeda, Beigene, and BioNTech. For these new entrants, the approval of first-in-class medications (BMS, Eli Lilly, Boehringer Ingelheim), other drug and indication approvals, and rises in revenue secured their spots.

Gilead and GSK are noteworthy climbers into the top 10, but their rise is less stratospheric than those of BI and Eli Lilly, climbing more than 20 and a dozen places respectively. For Eli Lilly, its highest ever revenue has come at the cost of the greatest R&D spend-to-revenue ratio of the top 10 in the Innovation Index; for Boehringer Ingelheim, 2022 brought four breakthrough therapy designations and four fast-track designations, but with commercial performance still largely driven by older products.

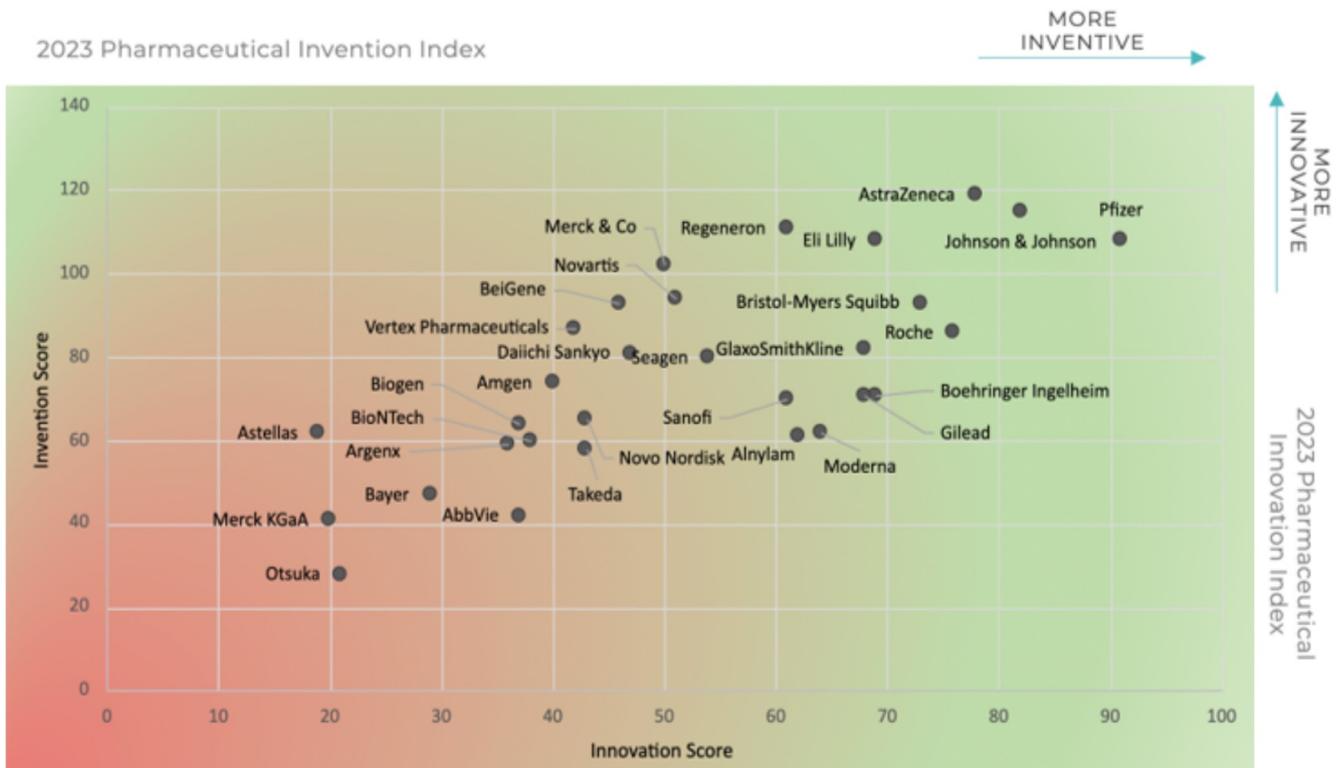
Two notable newcomers to the top 10 of the Invention Index are Regeneron and Vertex: for Regeneron, Dupixent continues to innovate through novel indications, while the Libtayo approval aims to take a slice of the lung cancer market; for Vertex, successes in cystic fibrosis and renal disease have driven the company's inclusion.

This year's data shed light on the difference between success in R&D financial and operational efficiency versus ultimate financial return. Although Novartis had the lowest R&D cost per approval over the last five years – and amassed 12 approvals last year – approvals in the last five years account for less than 10% of their revenue. Contrast this with Pfizer, who had the second lowest R&D cost per approval – and nine approvals last year – but where more than 60% of its revenue has been gained from approvals in the last five years. This is a reminder that leaner R&D alone is not a good index of company performance: Pfizer's success has coupled efficient R&D spend with a more successful recent pipeline, where patent cliffs are a more distant concern.

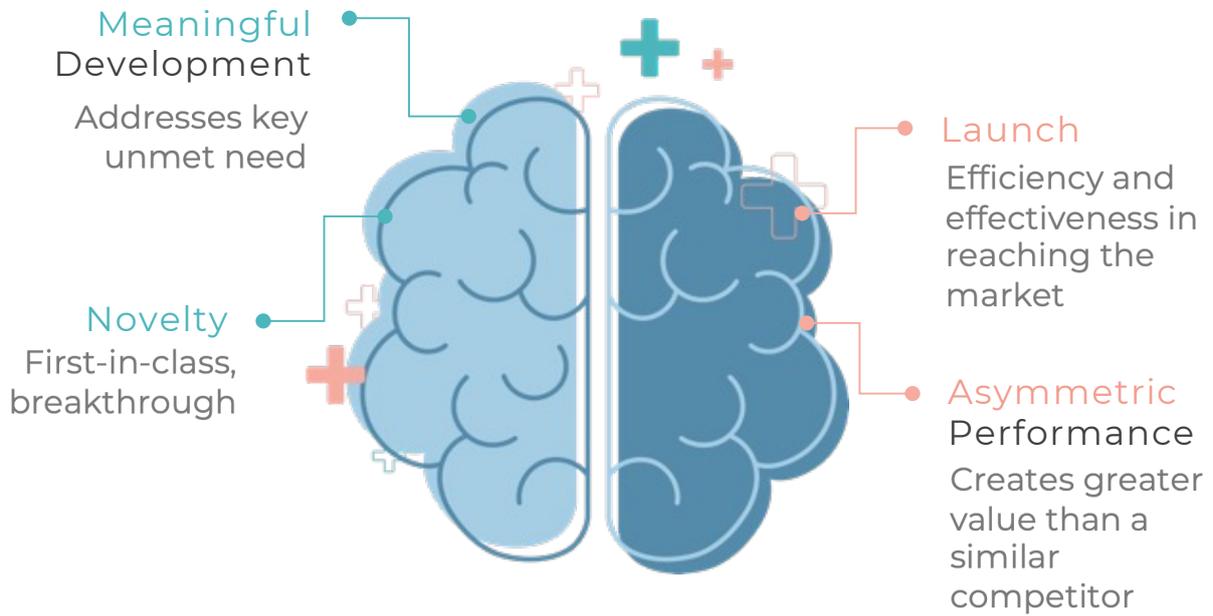
After a torrid year for biotech funding, Spring 2023 has started to see a more acquisitive market, with larger companies hunting for assets and companies to bolster their pipelines, eager to spend their reserves at a time of relative low cost for their targets. The 13th Invention and Innovation indices in 2024 may be lucky for some, as we start to see the impact of these deals on company performance.

Alexander Gray
Chief Medical Officer

2023 Pharmaceutical Invention Index



Invention vs. Innovation



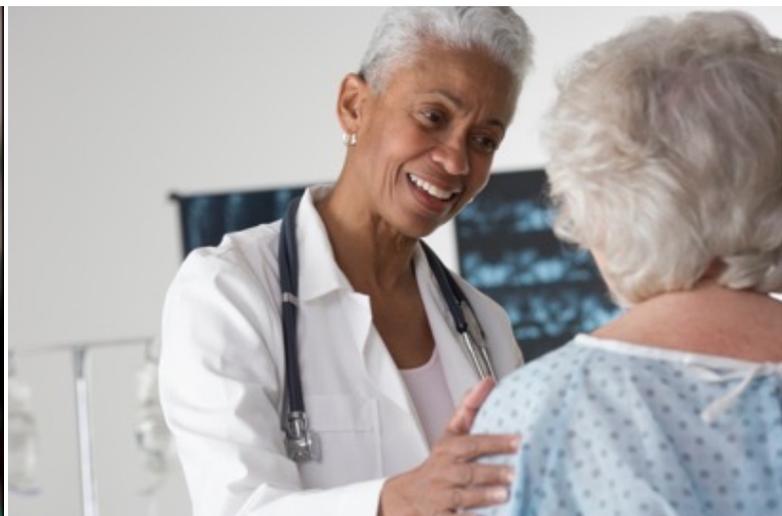
“If you gave the same idea to two different companies in early phase, would they be equally successful...?”

PHARMACEUTICAL INVENTION INDEX

Invention: Bringing ideas or technologies together in a novel way to create something that did not exist before.

PHARMACEUTICAL INNOVATION INDEX

Innovation: Return on invention; creation of meaningful value from invention.



Pharmaceutical Innovation Index 2023 Top 10

The Pharmaceutical Innovation Index seeks to answer the provocative question, ‘If two pharma companies were given the same molecule in early phase, which of the two would be better in developing and launching it?’ The Innovation Index ranks companies utilizing a range of clinical, regulatory, and commercial metrics, ranging from the corporate level down to individual product decisions and outcomes.

This 12th annual Index provides a systematic and objective assessment of how well the top 30 companies perform in bringing new medicines to market and commercializing them successfully.

2023	COMPANY	CHANGE	2022
1	Pfizer	—	1
2	Johnson & Johnson	+2	4
3	AstraZeneca	-1	2
4	Roche	+5	9
5	Bristol-Myers Squibb	+6	11
=6	Boehringer Ingelheim	+21	27
=6	Eli Lilly	+13	19
=8	Gilead	+7	15
=8	GlaxoSmithKline	+7	15
10	Moderna	+7	17

Note: Boehringer Ingelheim & Eli Lilly and Gilead & GlaxoSmithKline are tied in the ranking, in their respective placings.

Companies included in the full Innovation and Invention Index for the first time in 2023: Alnylam and Argenx.

Pharmaceutical Invention Index 2023 Top 10

Released for the first time in 2019 and now in its fifth year, the Pharmaceutical Invention Index examines pipeline invention and novelty by taking a focused look at the breadth and depth of novel agents currently being developed within the top 30 pharma pipelines. The Invention Index provides a more forward-looking view of who is developing medicines that matter, embracing science and innovations in R&D.

2023	COMPANY	CHANGE	2022
1	AstraZeneca	—	1
2	Johnson & Johnson	+2	4
3	Regeneron	+10	13
=4	Eli Lilly	-2	2
=4	Pfizer	+1	5
6	Merck & Co	+4	10
=7	Novartis	-1	6
=7	BeiGene	—	7
=7	Bristol-Myers Squibb	-4	3
10	Vertex Pharmaceuticals	+5	15

Note: Pfizer & Eli Lilly and Novartis, BeiGene & Bristol-Myers Squibb are tied in the ranking, in their respective places.

Companies included in the full Innovation and Invention Index for the first time in 2023: Alnylam and Argenx.

Top Performers Across Both Innovation and Invention Rankings:



PFIZER

1: Innovation

=4: Invention

For the second year in a row, Pfizer has claimed the top spot in the Innovation Index while also improving a spot to claim the tied number 4 ranking in the Invention Index. Riding high from its extraordinary 2021, Pfizer continued to deliver medicines to patients at a breakneck speed (the fastest in the industry) and at a high success rate in 2022.

In 2022, the upward trajectory continued as Pfizer saw revenues exceed \$100 billion for the first time in company history. Impressively, \$61 billion of the company's sales was derived from products launched in just the last three years, the most of any pharma company ever assessed in the subset of the PIII known as the 'Freshness Index'.

As was the case in 2021, the key driver of Pfizer's growth came from the company's COVID-19 products, Comirnaty (tozinameran) and Paxlovid (nirmatrelvir/ritonavir). While Comirnaty continued to be the company's top performer, generating nearly \$38 billion in sales, it was the addition of the COVID-fighting antiviral, Paxlovid (granted emergency use authorization in December 2021) that propelled the company to its new height, generating \$18.9 billion in sales this past year. For context, AbbVie's arthritis and psoriasis treatment Humira, the world's best-selling drug for over a decade, managed \$21.2 billion in 2022 sales.

Pfizer once again showed off its adaptability and agility, leveraging its mRNA platform to swiftly create an updated vaccine for the Omicron BA.4 and BA.5 subvariants. In under a year from the variant's detection, the company had a new bivalent vaccine booster authorized by both the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA), a true testament to the company's innovation in action.

In addition to its record-breaking COVID-19 portfolio, Pfizer attained eight additional regulatory nods in 2022, including two for novel medicines. The two novel medicines being Vydura (rimegepant), the first medicine approved for both acute and prophylactic treatment of migraine in the European Union (EMA), and Cibinqo (abrocitinib) to treat adults with moderate-to-severe, refractory atopic dermatitis (FDA).

Pfizer was also busy putting its hard-earned cash to work with four acquisitions: Arena Pharmaceuticals, Biohaven Pharmaceuticals, Global Blood Therapeutics, and ReViral, which should further strengthen its pipeline and portfolio of products for years to come.

JOHNSON & JOHNSON

2: Innovation

2: Invention

After an up and down few years innovation-wise, Johnson & Johnson (J&J) comes in at number 2 in each index in 2023, settling further into the top five in the 2023 Innovation Index while also continuing its annual climb in the Invention Index.

Though J&J had a slight revenue increase (\$52.1 to \$52.6 billion) and decreased R&D spend by over \$3 billion, the company saw almost a \$5 billion decrease in net income. The revenue generated was spearheaded by \$9.7 billion and \$7.9 billion in sales from Stelara (ustekinumab) and Darzalex Faspro (daratumumab / hyaluronidase-fihj), respectively.

Despite the negative growth in earnings, the company scored highly in major part due to two regulatory approvals for multiple myeloma treatments: Carvykti (ciltacabtagene autoleucel), a BCMA-targeted CAR T-cell therapy, and Tecvayli (teclistamab), a bispecific T-cell engaging antibody (BiTE). Both treatments are indicated in relapsed/refractory multiple myeloma, with Tecvayli breaking new ground as the first BiTE approved for multiple myeloma. Given that BiTEs are expected to eat into the market share of CAR T-cell therapies in later lines, J&J has ensured a strong foothold across all lines of treatment via Tecvayli's first-mover advantage for the foreseeable future. Given only 4.2% of company revenue came from drugs approved within the last three years, these two promising hematologic oncology treatments are a welcome addition to J&J's marketed portfolio.

Talquetamab is another drug to watch in multiple myeloma. This is another BiTE in J&J's pipeline that received FDA Breakthrough Therapy Designation. J&J is currently exploring its therapeutic potential as monotherapy and in combination with Tecvayli. This parallel development of two of the first (expected) BiTEs in multiple myeloma is the type of treatment paradigm-shifting approach that has kept J&J relevant on the Innovation Index in recent years.

On top of new drug approvals in multiple myeloma, J&J progressed several other areas of its pipeline. Stelara, already indicated for Crohn's disease, ulcerative colitis, and psoriasis in adults, added a pediatric indication for moderate-to-severe psoriasis, further expanding the product's utility. Imbruvica (ibrutinib), the company's multi-indicated tyrosine kinase inhibitor, also expanded its label with the FDA's approval of treatment in pediatric chronic graft-versus-host disease. This expansion in marketed labels was also supplemented by a label expansion for Cabenuva (cabotegravir and rilpivirine) which was co-developed with GSK – the first and only long-acting HIV treatment – for use every two months. Also added to J&J's "first-and-only" resumé was a Canadian approval for Rybrevant (amivantamab-vmjw), which is indicated following failure of chemotherapy in patients with non-small cell lung cancer (NSCLC) with EGFR exon 20 insertion mutations.

The breadth of revenue sources within J&J's portfolio is strong. Although the giant has been fueled financially by relatively older (>3 years on market) treatments, the promise of therapy area redefinition by posing later line threats to CAR T-cell therapies in multiple myeloma bodes well for the overall return on invention.

ASTRAZENECA

3: Innovation

1: Invention

AstraZeneca's reappearance as one of the most innovative companies in 2021 was no fluke. The British pharma giant solidified its place in the top three for a second year in a row, coming in at number 3 in the Innovation Index and earning the number 1 spot in this year's Invention Index.

2022 was another year of growth for the company with an approximate \$7 billion increase in revenue from 2021. Over 10% of sales were generated from drugs approved within the last three years, which places the drugmaker in the top half of companies of similar size.

Looking under the hood, the reason for AstraZeneca's success becomes clear. In terms of moving medicines closer to market (a core metric of the Innovation Index), AstraZeneca had one of the higher R&D success rates, at 19%. The company also earned 34 approvals in major markets (US, EU, China, and Japan) and had 29 pipeline progression events. This included the approval of two novel medicines: Imjudo (tremelimumab) for liver cancer and NSCLC, and Beyfortus (nirsevimab) for the prevention of respiratory syncytial virus (RSV) in infants.

Like much of the industry, AstraZeneca's growth in 2022 was led by its oncology products, which had a 15% increase in sales from 2021—more than any other area in the organization—driven by Tagrisso (osimertinib), Enhertu (trastuzumab deruxtecan), Imfinzi (durvalumab), Lynparza (olaparib), and Calquence (acalabrutinib).

Perhaps most impressive though is the state of AstraZeneca's pipeline, with its broad scope, diversity, and potential to impact key unmet needs, leading the company to the top of this year's Invention Index. At the end of 2022, the company boasted 179 pipeline projects, of which 155 were in clinical development. While several large pharma players have similarly broad pipelines, what set AstraZeneca apart was the potential of its products to have an outsized impact in disease areas and populations with high unmet needs.

What will be especially interesting to watch in the future is how the British giant continues to build out its already impressive pipeline. This is because the company has one of the highest levels of investment into AI-enabled drug discovery of any company over the last three years. While it is too early to tell what impact this will have, it highlights AstraZeneca's dedication to maintaining an already stellar pipeline.

ROCHE

4: Innovation

11: Invention

After a dip in the innovation rankings from second in 2021 to ninth in 2022, Roche has regained its spot in the top five, coming in at number 4. While Roche's return on invention was stellar in 2022, its showing in invention did drop three positions to 11th for 2023.

Roche's earnings dropped from \$15.0 billion (\$67.8 billion revenue) the previous year to \$13.4 billion (\$68.4 billion revenue) in 2022, but with new drug approvals coming in oncologic and ophthalmologic indications, Roche continues to play its hand in a wide range of different therapeutic markets.

The main detractor from Roche's invention score in 2022 was its failure to demonstrate efficacy of its AC Immune-discovered candidate anti-amyloid-beta antibody in early Alzheimer's disease.

Two new drug approvals led the way in 2022, as Vabysmo (faricimab-svoa) was approved by the

FDA as the first bispecific antibody to treat an ophthalmic condition, enabling Roche to make significant headway in outcomes of two leading causes of vision loss: neovascular (wet) age-related macular degeneration (AMD) and diabetic macular edema (DME). The other new drug approval giving Roche's innovation ranking a boost was Lunsumio (mosunetuzumab), a CD20xCD3 BiTE. This conditional approval—obtained in both the US and EU—in third-line relapsed or refractory follicular lymphoma puts Roche up against J&J's two late pipeline BiTEs in B-cell malignancies and, potentially, multiple myeloma.

Beyond new drug approvals, Roche also gained ground through the label expansion of Evrysdi (risdiplam) for infants two months or older with spinal muscular atrophy (SMA) and full FDA approval of Polivy (polatuzumab vedotin) along with the R-CHP regimen in first-line DLBCL, marking the company's ability to find market share even in highly-saturated treatment paradigms.



Bristol Myers Squibb™

BRISTOL-MYERS SQUIBB

5: Innovation

=7: Invention

Bristol-Myers Squibb (BMS) gains six places in the innovation rankings in 2023, but at the same time loses six in the invention rankings, ending up at number 5 and =7 respectively. Despite only 2.7% of its \$46.2 billion revenue coming from drugs approved in the last three years, BMS did attain three new drug approvals this past year, providing some optimism for the freshness of its revenue going forward.

Opdualag (nivolumab/relatlimab), BMS' follow-on combination of best-selling PD-1 inhibitor Opdivo (nivolumab) and the LAG-3 inhibitor relatlimab in unresectable or metastatic melanoma, became the first LAG-3 targeting agent to achieve FDA approval, marking the biggest innovation of the year for BMS. After bagging \$58 million in sales from the treatment in the second quarter of 2022, the company has high hopes that this first mover advantage will propel Opdualag to become the new standard of care in melanoma, providing durability to the company's immuno-oncology portfolio.

Another key new approval for BMS in 2022 was that of Camzyos (mavacamten), making it the first and only FDA-approved allosteric and reversible cardiac myosin inhibitor targeting the underlying pathophysiology of obstructive hypertrophic cardiomyopathy (HCM). The readout of the EXPLORER-HCM trial confirmed that the first-in-class treatment is suitable for treating the root of HCM, further raising the bar for treatment of patients with high unmet need with class II-III symptomatic disease. The other new drug approval for BMS was also a first in class, with Sotyktu (deucravacitinib) becoming the first allosteric tyrosine kinase 2 (TYK2) inhibitor approved in psoriasis treatment.

The three first-in-class approvals bode well for BMS in terms of innovation, but less identifiable activity in the company's early pipeline brought it back to =7 in invention. That said, the sheer size of its pipeline (3.8x portfolio) should keep it firmly in contention for the foreseeable future.

BOEHRINGER INGELHEIM	=6: Innovation	15: Invention
----------------------	----------------	---------------

Boehringer Ingelheim (BI)* exploded from 27th on last year's Innovation Index all the way to tied number 6 for 2023, due in part to its landing the first ever FDA approval to treat generalized pustular psoriasis (GPP). This new approval along with the company's successful array of marketed treatments led the way to its estimated \$7 billion increase in revenue. Revenue growth was driven by established products in the Jardiance (empagliflozin) family as well as Ofev (nintedanib), as the company's medicines reached a record 30 million people this past year.

Spevigo (spesolimab), BI's latest approved therapy, is an interleukin-36 blocker. The approval marks a substantial innovation in the treatment of GPP, where off-label therapies have been previously used. Having been authorized by the FDA, the drug is currently under review by the EMA for this indication.

*Financial performance data are based on estimates, as Boehringer Ingelheim is a private company

Another milestone for BI in 2022 was the expansion of the indication for Jardiance to treat adults with chronic heart failure. This builds upon the company's approved indications in both the US and EU in type 2 diabetes and is a testament to the company's strong demonstrated capability of maximizing the commercial value of marketed assets. Jardiance also had a strong clinical showing outside the approval in chronic heart failure, as the EMPRISE real-world study of more than half a million diabetic patients showed a 50% reduction in the risk of heart failure compared with DPP-4 inhibitors and by 30% compared with GLP-1 agonists, two mechanisms of immediate competition in the space.

This progress of getting a key therapy to market and positive clinical readouts in populations of interest are what propelled BI to a 21-spot boost in the Innovation Index.



ELI LILLY	=6: Innovation	=4: Invention
-----------	----------------	---------------

After a heavy fall from first in the 2021 index to nineteenth last year, Eli Lilly has reclaimed its mojo, jumping back into the fray to land at tied number 6 on the 2023 Innovation Index. Eli Lilly's pipeline also looked very healthy this year, earning it the tied number 4 spot in the Invention Index.

Lilly recorded revenue of \$28.5 billion in 2022, the highest in the company's history (founded in 1876). New growth in 2022 was driven by its new breast cancer medicine Verzenio (abemaciclib), and the launch of Mounjaro (tirzepatide) to control blood sugar in type II diabetes. Looking ahead, Mounjaro could easily become Lilly's top product as it seeks to compete with Novo Nordisk's GLP-1 drug blockbuster Wegovy/Ozempic (semaglutide).

In 2022, Lilly also demonstrated its continuing effort to innovate on digital solutions for clinical practice.

The company introduced the first fully connected and personalized platform for diabetes care (Tempo). If successful, it could become a case study to emulate given pharma's historically poor track record when combining digital with its traditional pharmacologic business.

A clue as to why the company continues to rank so well in this index can be gleaned by looking at its dedication, year after year, to investing in R&D. Lilly's R&D-to-revenue ratio in 2022 was 25.2%, the highest among the top ten companies in this year's PIII. Over the years, the company has been one of the best in the industry when it comes to reinvesting dollars back into R&D (as a percentage of revenue).

GILEAD

=8: Innovation

=16: Invention

Gilead jumped seven places earning the company tied number 8 in this year's Innovation Index, while the pipeline continued to stagnate leaving it stuck in 16th spot in the Invention Index.

Gilead reported that 2022 was the first year its base company grew since 2015, when it reached its peak in HCV product sales. Much of this growth was driven by the company's core HIV portfolio, particularly from blockbuster Biktarvy (bictegravir, emtricitabine and tenofovir alafenamide), which showed a 20% increase in sales, year-on-year (YOY).

Impressively, and in line with the rest of the industry, Gilead's oncology sales increased at the most dramatic rate of 71% YOY. This was largely driven by Trodelvy and the company's cell therapy portfolio (Kite).

Though a very positive year, it was not necessarily a smooth journey for Gilead, which had to navigate a Complete Response Letter (CRL) for Sunlenca (lenacapavir), related to concerns around vial storage, and a partial clinical hold (now reversed) on its \$4.9 billion oncology bet, magrolimab, related to adverse event concerns.

Ultimately, the company overcame both challenges, with Sunlenca gaining approval as a first-in-class capsid inhibitor for use in HIV-1 and getting the FDA green light to restart recruitment on all magrolimab trials.

Despite a solid performance on the Innovation Index, Gilead's Invention Index score lagged. This is due in part to the lower-than-average number of pipeline products Gilead has compared with its peer companies of a similar size. That being said, the Gilead pipeline makes up in quality what it lacks in quantity, which very likely helped it from slipping lower in the index.

GSK

GLAXOSMITHKLINE

=8: Innovation

12: Invention

After a year's hiatus, GSK re-entered this year's top ten, with jumps in both the Invention and Innovation Indices. The latter largely driven by successes in GSK's vaccine franchise. Priorix received FDA approval against measles, mumps and rubella in children, while its RSV vaccine hit the mark in the phase 3 trial in older adults, laying the foundations for regulatory submission in the second half of the year.

GSK's other stronghold, its HIV franchise, also had triumphs in 2022. Its HIV drug Cabenuva (cabotegravir and rilpivirine), which was co-developed with J&J, received FDA approval for two-month dosing, marking an easier dosing schedule than the one-month dosing previously approved on the label. Cabenuva remains the first and only long-acting treatment indicated in virally-suppressed HIV-1 patients.

Overall, 2022 was a "landmark" year for GSK. The successful spin-off of its consumer healthcare, which was initially met with a lukewarm reception, meant GSK could focus solely on drugs and vaccines. The UK pharma favorite ended the year reporting an increase in sales and a significant jump in net income (£15.6 billion vs. £5 billion in 2021). GSK has high hopes for 2023, with bullish sales and revenue targets off the back of its 2022 success.

MODERNA

10: Innovation

=20: Invention

Rising seven spots in the Innovation Index, Moderna has found the top 10 in 2023 in large part due to its solidification of regulatory approval for Spikevax, its 2-dose messenger RNA (mRNA) vaccine, which was previously only approved under an emergency use authorization in the US and EU. It goes unsaid that this vaccine, along with its direct competitor Comirnaty, was innovative in both a situational and commercial sense. Moderna's catapult up the innovation rankings these last two years comes as no surprise to anyone.

Perhaps as impressive as clinically developing and commercializing the first mRNA-based vaccine at record pace, is the subsequent efforts of Moderna to further globalize access to Spikevax with agreements with the US and EU authorities. All of this is in addition to expanding the company's commercial footprint via four Asia-Pacific-based subsidiaries and the announcement of plans to expand into six additional European countries to support the delivery of mRNA vaccines and therapeutics.

In terms of pipeline, Moderna maintained steady pace towards market in other key diseases of focus. One notable positive readout came for the company's investigational cancer vaccine, which is being co-developed with Merck, which met its primary efficacy endpoint in the Phase 2b KEYNOTE-942 trial in combination with Keytruda (pembrolizumab).

Though much of Moderna's 2022 success is attributable to regulatory nods for Spikevax boosters and mix-and-match, the continued work to apply mRNA technology in other indications shows that the company has a keen ability to innovate and leverage its technology in other disease spaces as well.

New Entries to the Index



ALNYLAM

11: Innovation

=22: Invention

Alnylam's success in 2022 can be primarily attributed to two high-revenue products: Onpattro (patisiran), used to treat nerve damage caused by hereditary transthyretin-mediated amyloidosis, and its follow-on therapy, Amvuttra (vutrisiran).

Specifically, 2022 global net product revenues for Onpattro and Amvuttra were approximately \$558 million and \$94 million, respectively, representing 37% total transthyretin amyloidosis annual growth for Alnylam compared with 2021 alone.

These developments are likely to lead to a showdown with Pfizer's blockbuster Vyndaqel (tafamidis) franchise, within an increasingly competitive rare disease field.

In 2022, Alnylam's Oxlumo (lumasiran) also achieved the first FDA approval for the treatment of primary hyperoxaluria type 1 (PH1), by lowering oxalate in urine.



ARGENX

26: Innovation

25: Invention

In 2022, Argenx's subcutaneous formulation of the active ingredient in Vyvgart (efgartigimod alfa-fcab) hit the primary endpoint in a phase 3 trial, clearing the biotech to file for FDA approval of a product it expects to become the most popular version of the autoimmune drug.

Vyvgart is currently the first-and-only approved neonatal Fc receptor blocker in the US, Japan, and the EU. Argenx is planning for multi-dimensional expansion to reach more patients with Vyvgart through additional regulatory approvals for generalized myasthenia gravis (gMG), the launch of SC efgartigimod for gMG, and new autoimmune indications with the Vyvgart regulatory submission for immune thrombocytopenia in Japan.

Vyvgart generated global net revenues of \$173 million in the fourth quarter of 2022 and \$401 million in the full year of 2022.

Argenx also advanced a robust portfolio of innovative clinical programs in 2022, including ARGX-117 (C2 inhibitor) and ARGX-119 (muscle-specific kinase [MuSK] agonist). Both programs have the potential to be first-in-class opportunities for multiple severe autoimmune indications.

Firms That Faced Notable Setbacks



MERCK & CO	16: Innovation	6: Invention
------------	----------------	--------------

Merck & Co fell steeply in this year’s Innovation Index but performed strongly in the Invention Index, perhaps signaling only a short break from the top 10.

While Keytruda (pembrolizumab) retained its crown as the world’s second best-selling non-COVID drug, there were a few setbacks as the company tries to get as much value as possible out of the drug. The PD-1 inhibitor failed to meet its primary endpoint in a late-stage trial for unresected locally advanced head and neck squamous cell carcinoma. Similarly disappointing results came in a Phase 3 trial in metastatic castration-resistant prostate cancer, as it showed that Keytruda in combination with chemotherapy did not hit its primary endpoints compared with chemotherapy alone.

Although the drop in the Innovation Index was chiefly due to clinical failures of Keytruda, the company also hit some drawbacks in its joint development and commercialization partnership with AstraZeneca for Lynparza (olaparib) when the oncology blockbuster had its Phase 3 trial in colorectal cancer halted due to futility.

Despite the setbacks, Merck & Co has promising activity in its pipeline. After a relatively uneventful 2021, it received many Fast Track and a few Breakthrough Therapy Designations, contributing to a solid Invention Index score, and putting the company in a strong position for robust performance next year.



TAKEDA	19: Innovation	26: Invention
--------	----------------	---------------

After last year’s spectacular 21-spot jump into the top 10, the Japanese drug maker plummeted in both Innovation and Invention Indices, coming in at tied 19th and 26th, respectively.

Takeda had some clinical misses in 2022, with maribavir failing to meet its primary endpoint in a Phase 3 study, while a Phase 2 study of the company’s investigational oral orexin agonist TAK-994 was suspended. Takeda’s ranking was also dragged down by a poor showing on the Freshness Index, with a lower percentage of its drug revenue coming from approvals in the last five years, as well as a lack of novel drug approvals, both of which were contributing factors to its success last year.

Takeda’s reinvestment into R&D appeared to be on the lower side this year, which also contributed to its dip in the Invention Index.

However, after a flurry of acquisitions at the end of 2022/ early 2023 (Nimbus Therapeutics and the rights to commercialize Hutchmed’s experimental oncology drug fruquintinib), Takeda, being no stranger to big jumps in the ranking, could be gearing up for a comeback next year.

PIII Innovation Methodology

HYPOTHESIS:

If two companies each had the same NCE at the same stage of development (end of Phase I), which company would do the best job of commercializing the product?

CONSTRAINTS:

This hypothesis cannot be measured directly, therefore, a surrogate measure is required.

Each measure of the index must be measured universally across ALL pharmaceutical companies under consideration in a comparable manner and be publicly accessible.

The Pharmaceutical Innovation Index consists of the following key metrics:

1. 'Freshness Index' – percentage of company sales generated by products launched in the last three and five years (a measure of a company's ability to "refresh" its portfolio in the face of patent loss, providing a comprehensive portfolio)
2. Regulatory designations and approvals
3. Financial performance related to (but not limited to):
 - a) Revenue growth (1-year, as well as 5-year change)
 - b) R&D spend (1-year, as well as 5-year change)
4. In addition, IDEA Pharma monitors company websites, annual reports, and industry sites to identify key events related to (but not limited to):
 - a) Label expansions of currently approved branded products
 - b) Progression of assets to next phase
 - c) Study successes/failures
 - d) Return vs. investment
 - e) Contracts with major payor organizations, expanded access to different markets
 - f) Changes in R&D strategy, research collaborations, etc.
 - g) Company restructuring to capitalize on areas of strength, optimization of portfolios/franchises
 - h) Innovative commercialization or sales strategies
 - i) Mergers and acquisitions which would increase a company's ability to generate commercial success

Each of the above are collated by IDEA Pharma and scored. The combination of these scores is subsequently used to calculate an overall company score and provide an ordinal ranking.

PIII Invention Methodology

HYPOTHESIS:

An index designed to objectively examine pipeline invention and measure pipeline novelty.

CONSTRAINTS:

Third-party pharma company data inputs (source: GlobalData) are used to feed each of the key metrics. Our best assumption is the data are comprehensive, and up to date.

The Pharmaceutical Invention Index consists of five key metrics:

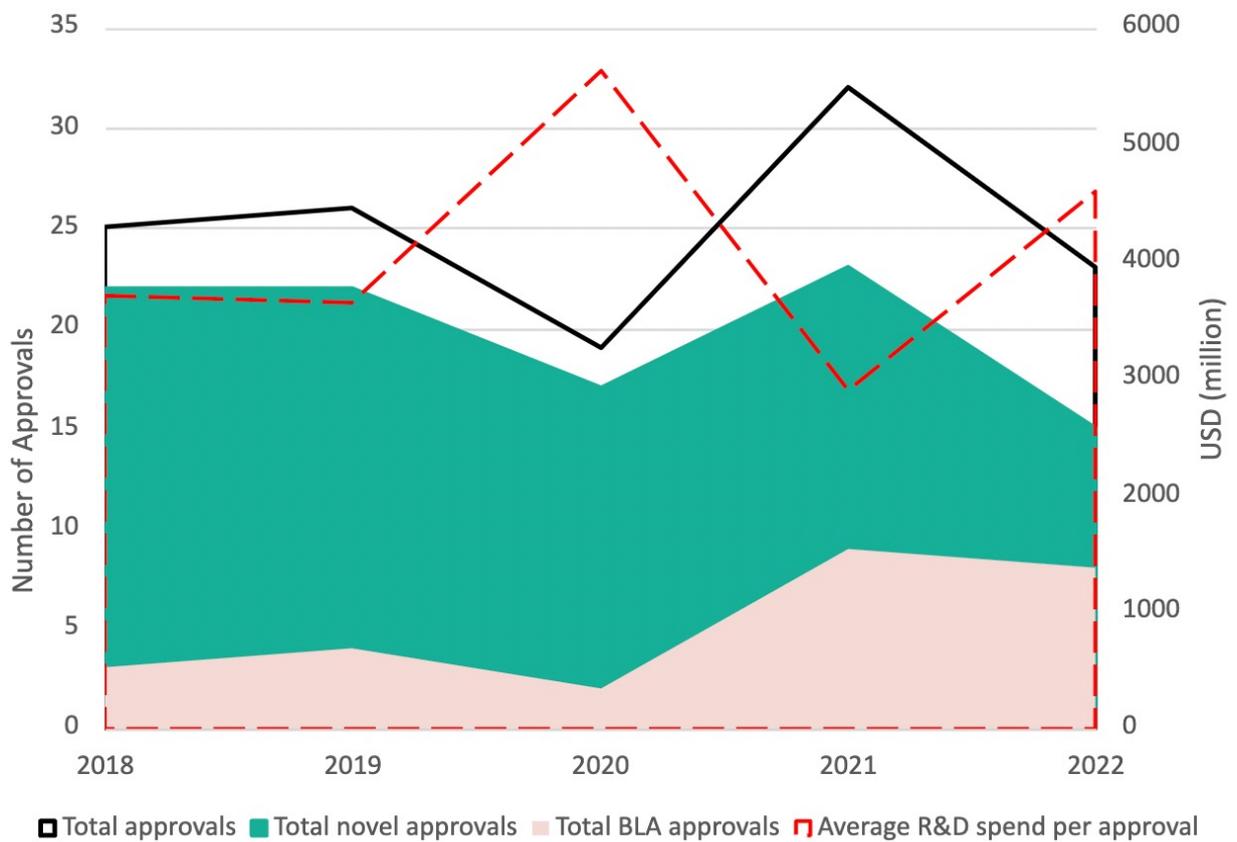
1. The proportion of pipeline to marketed drugs
2. The number of trials investigating novel agents
3. The proportion of 'novel' regulatory designations
4. An assessment of the company's R&D investment
5. The number and scale of key events related to novel pipeline agents

Data from GlobalData are used to objectively evaluate each company and produce an independent category score for each of the top 30 companies. Additionally, key company events are monitored, and stories related to novel pipeline agents are carefully reviewed for each company. Companies are scored on the basis of the number of events as well as the potential scale of pipeline impact. The combination of these scores is subsequently used to calculate an overall company score and provide an ordinal ranking.

Drug Approvals vs. R&D Expenditure

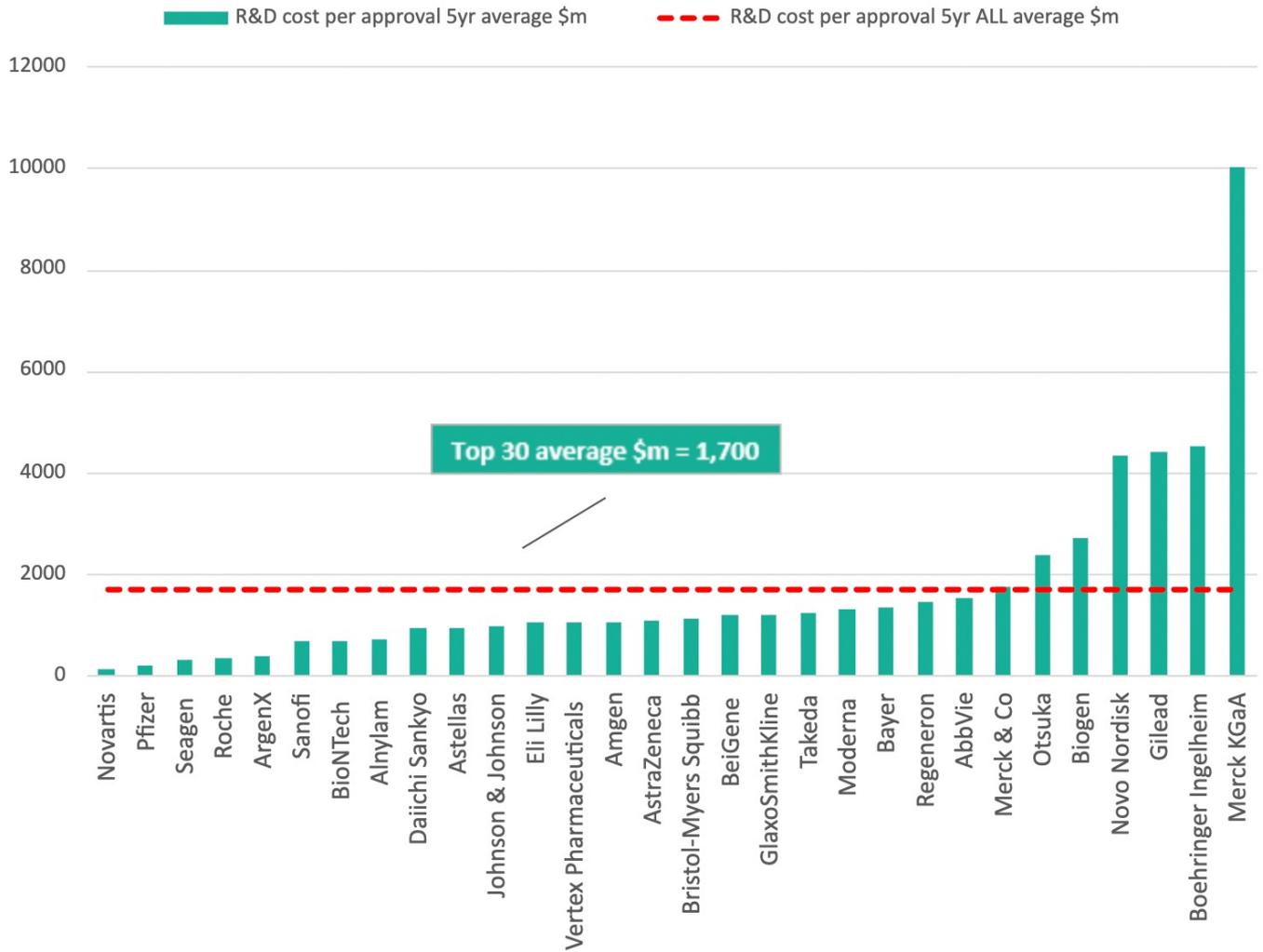
Top 30 Pharma 2018–2022

The average R&D spend per approval was at a 5-year low in 2021, but has started to rise again during the past year.



5yr Average R&D Spend Per Approval

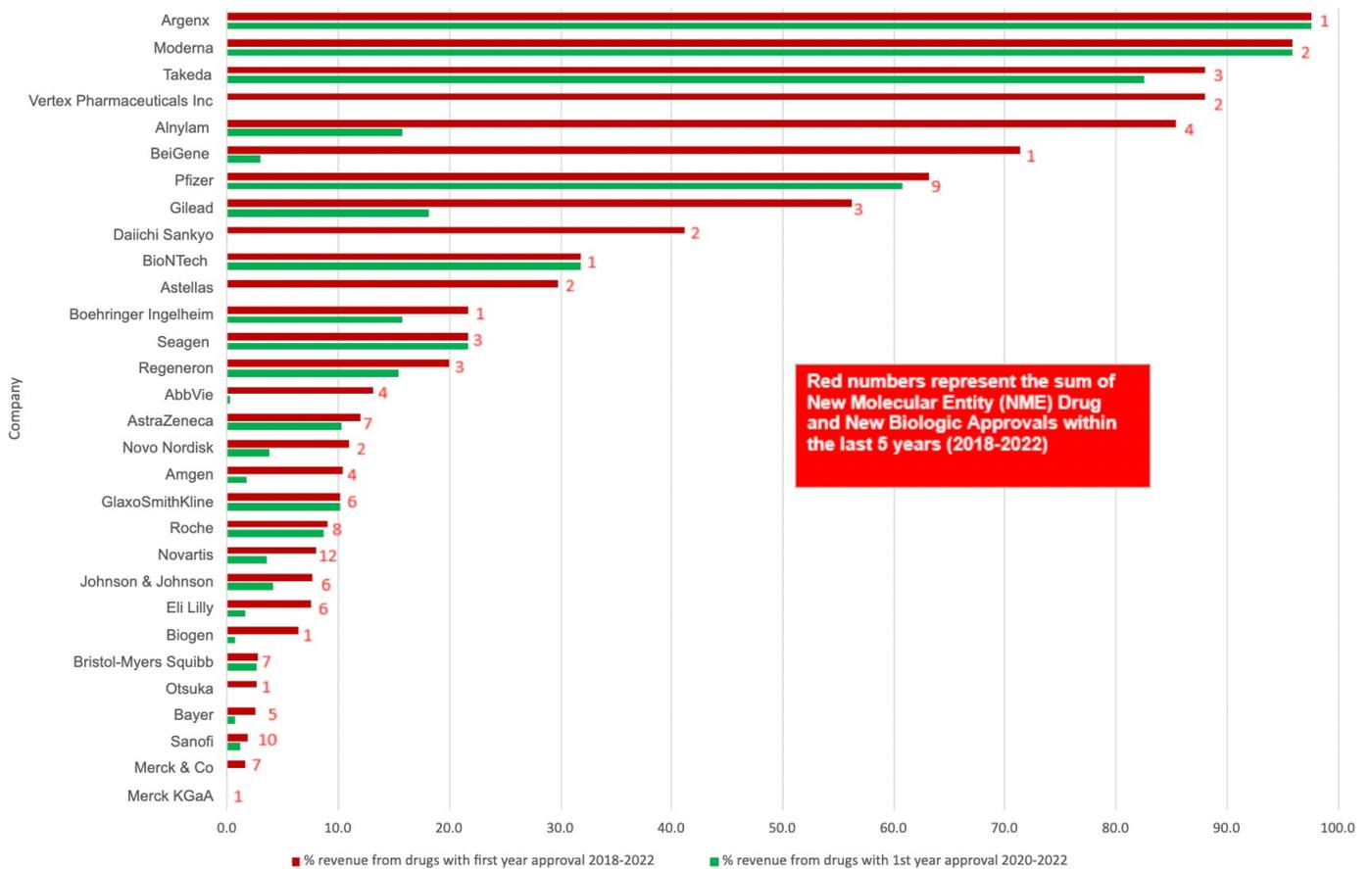
2018-2022



Freshness Index

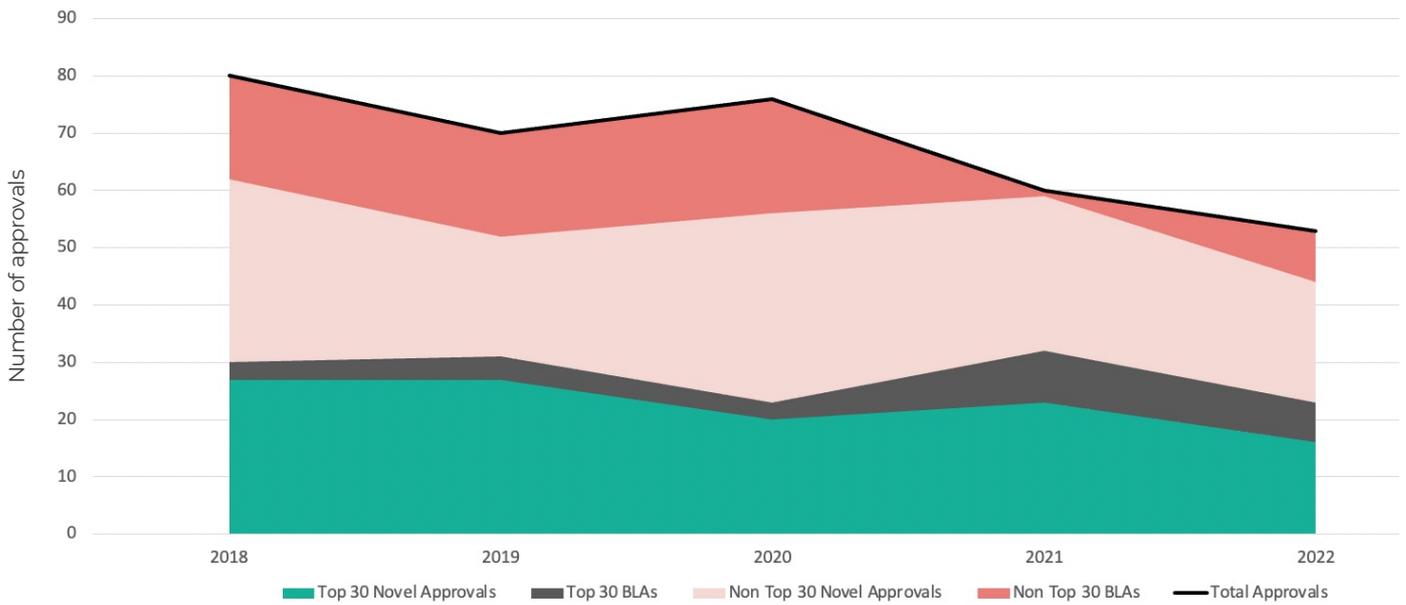
The Freshness Index shows percentage of company sales generated by products launched in the last three and five years (a measure of a company's ability to "refresh" its portfolio in the face of patent loss, providing a comprehensive portfolio).

3 and 5 year freshness index / No of US approvals



Top 30 vs. Non-top 30 Approvals

2018–2022



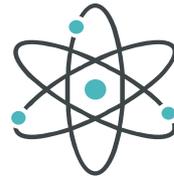
Approximately half of the total approvals come from the Top 30 companies investigated in the Pharmaceutical Innovation and Invention Index

Did You Know?

FOR THE TOP 30 PHARMACEUTICAL COMPANIES IN 2022...

~\$904bn

GLOBAL REVENUE
TOTALED



15 Novel

& 8 BIOLOGIC DRUGS
APPROVED

~\$162bn

GLOBAL R&D
EXPENDITURE
TOTALED,
REPRESENTING



~\$4.6 BILLION

AVERAGE COST OF LAUNCHING
A NEW DRUG

1200

PHI Trials

955

PHII Trials

271

PHIII Trials

19

Pre-Registrational
Trials

~1,300 DRUGS ARE IN DEVELOPMENT IN OVER 2,500 CLINICAL STUDIES

463 REGULATORY DESIGNATIONS:



257

Orphan Drugs



88

Fast Tracks



29

Priority Reviews



3

Accelerated
Assessments



49

Breakthrough
Therapies



37

Other (e.g.
Sakigake
Designation,
PRIME)

Index 2023

#1

Pfizer

First in Innovation

+21

Boehringer
Ingelheim

Most Improved

Innovation: Return on
invention; creation of
meaningful value from
invention

Company	Rank	Change from 2022
Pfizer	1	—
Johnson & Johnson	2	+2
AstraZeneca	3	-1
Roche	4	+5
Bristol-Myers Squibb	5	+6
Boehringer Ingelheim	=6	+21
Eli Lilly	=6	+13
Gilead	=8	+7
GlaxoSmithKline	=8	+7
Moderna	10	+7
Alnylam	11	NEW
Regeneron	=12	-9
Sanofi	=12	-2
Seagen	14	+4
Novartis	15	+4
Merck & Co	16	-12
Daiichi Sankyo	17	+5
BeiGene	18	-12
Novo Nordisk	=19	+4
Takeda	=19	-12
Vertex Pharmaceutical	21	-9
Amgen	22	-9
BioNTech	23	-15
AbbVie	=24	-11
Biogen	=24	+4
Argenx	26	NEW
Bayer	27	-2
Otsuka	28	+4
Merck KGaA	29	+2
Astellas	30	-4



Index 2023

#1

AstraZeneca
First in Invention

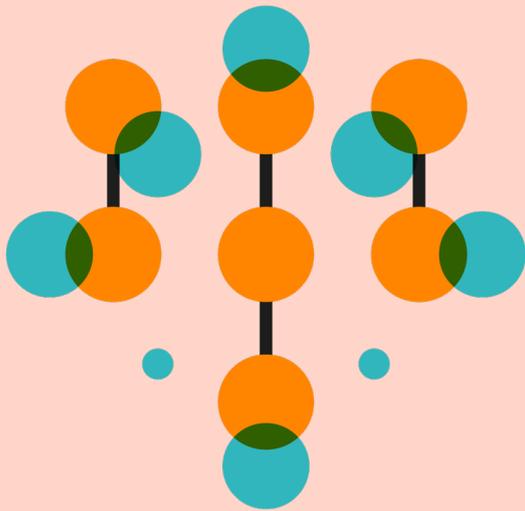
+13

GlaxoSmithKline
Novo Nordisk
Most Improved

Invention: bringing ideas or technologies together in a novel way to create something that did not exist before

Company	Rank	Change from 2022
AstraZeneca	1	—
Johnson & Johnson	2	+2
Regeneron	3	+10
Eli Lilly	=4	-2
Pfizer	=4	+1
Merck & Co	6	+4
Novartis	=7	-1
BeiGene	=7	—
Bristol-Myers Squibb	=7	-4
Vertex Pharmaceutical	10	+5
Roche	11	-3
GlaxoSmithKline	12	+13
Daiichi Sankyo	=13	+12
Seagen	=13	+10
Boehringer Ingelheim	15	-4
Gilead	=16	+1
Sanofi	=16	+4
Novo Nordisk	18	+13
Biogen	19	+2
Astellas	=20	+8
Moderna	=20	-8
Alnylam	=22	NEW
Amgen	=22	-13
BioNTech	=22	-3
Argenx	25	NEW
Takeda	26	-8
Bayer	27	-4
AbbVie	28	-15
Merck KGaA	29	—
Otsuka	30	—





Pharmaceutical Innovation and Invention Index 2023

WHITEPAPER
Celebrating the Most Innovative and
Inventive Companies in Pharma