



Pharma R&D Annual Review 2024 Supplement:

New Active Substances
Launched During 2023

Following on from our 2024 review of trends in the current pharmaceutical R&D pipeline (visit [here](#) to download the report for free), this supplement looks at the industry's success stories of 2023 — the drugs launched onto the market for the first time during the year. Our survey focuses exclusively on new active substances (NASs): new chemical or biological entities for which the active ingredient had received no prior approval for human use. This would also include vaccines with novel antigenic components.

As such, this list represents a subset of all the first launches that Pharmaprojects reported during 2023 and excludes an additional 68 first drug launches of reformulated or non-NAS moieties, biosimilars, and imaging agents. So, to continue with our meteorological theme for the Pharma R&D Report this year, this supplement will focus on the drugs that weathered the storm of clinical trials and regulatory approval to emerge, blinking into the sunlight, onto the market during the year just passed.



Weather forecasters have similar issues to pharma industry analysts in terms of successfully predicting the future beyond what is immediately apparent. Once a drug has been approved, in most (but not all) cases, it will move onto the market as sure as a predicted warm front will move through. But, much like entirely accurate weather forecasts cannot really be guaranteed beyond about five days ahead in many parts of the world, as one moves further away chronologically from a projected launch date, the predictability of a positive outcome becomes shrouded by clouds. Not all drugs that are filed for approval will pass muster. Many will fail in Phase III, and by the time you get back to Phase I, the probability of successful marketing diminishes to around 1% — about as likely as successfully forecasting the weather conditions for this day next year. So, let's collectively look out of the window and celebrate the rays of sunshine that bathed the pharma industry during 2023. For every fine day, there were plenty which turned unsettled.

Of course, there are sunny days and then there are sunny days. Pharma doesn't want fine but chilly conditions, it wants to bask in the warmth of a hot drug launch. The sun shone brightest during 2023 on Merck & Co.'s anticancer superstar Keytruda (pembrolizumab), which reportedly posted around \$12 billion in sales, outpacing AbbVie and Eisai's Humira (adalimumab) with \$7.5 billion and Novo

Nordisk's Ozempic (semaglutide) with \$6.7 billion, the latter being supercharged by its second life as the weight loss product Wegovy. Not every launch results in such a heatwave, though. Consider the fate of the high-profile Alzheimer's drug Aduhelm (aducanumab), whose initial approval was controversial to say the least. After not finding favor with US payers and being quickly superseded by the similar but marginally superior Leqembi (lecanemab-irmb), Aduhelm was withdrawn from the market at the start of 2024, having only produced a light drizzle of sales. It seems that this drug's house of cards was rapidly blown over by a few gusts of wind.

What pharma is looking for are not just high-selling drugs enjoying their moment in the sun, but those that will address longer-term issues and actually improve lives. Just as it is scientific innovation that will (hopefully) solve the climate change issue, it is drugs with novel ways of treating disease that are the pot of gold at the end of the rainbow for the industry. Thus, as usual, in this report we'll look not just at statistical trends in the numbers of NASs, but also zero in on the molecules that are still as rare as rains in the desert: those that made it to market with a novel mechanism. They certainly cause the pharma landscape to bloom, and can genuinely change patients' lives. But first, let's look to the skies and survey the entirety of 2023's new active substance launches.





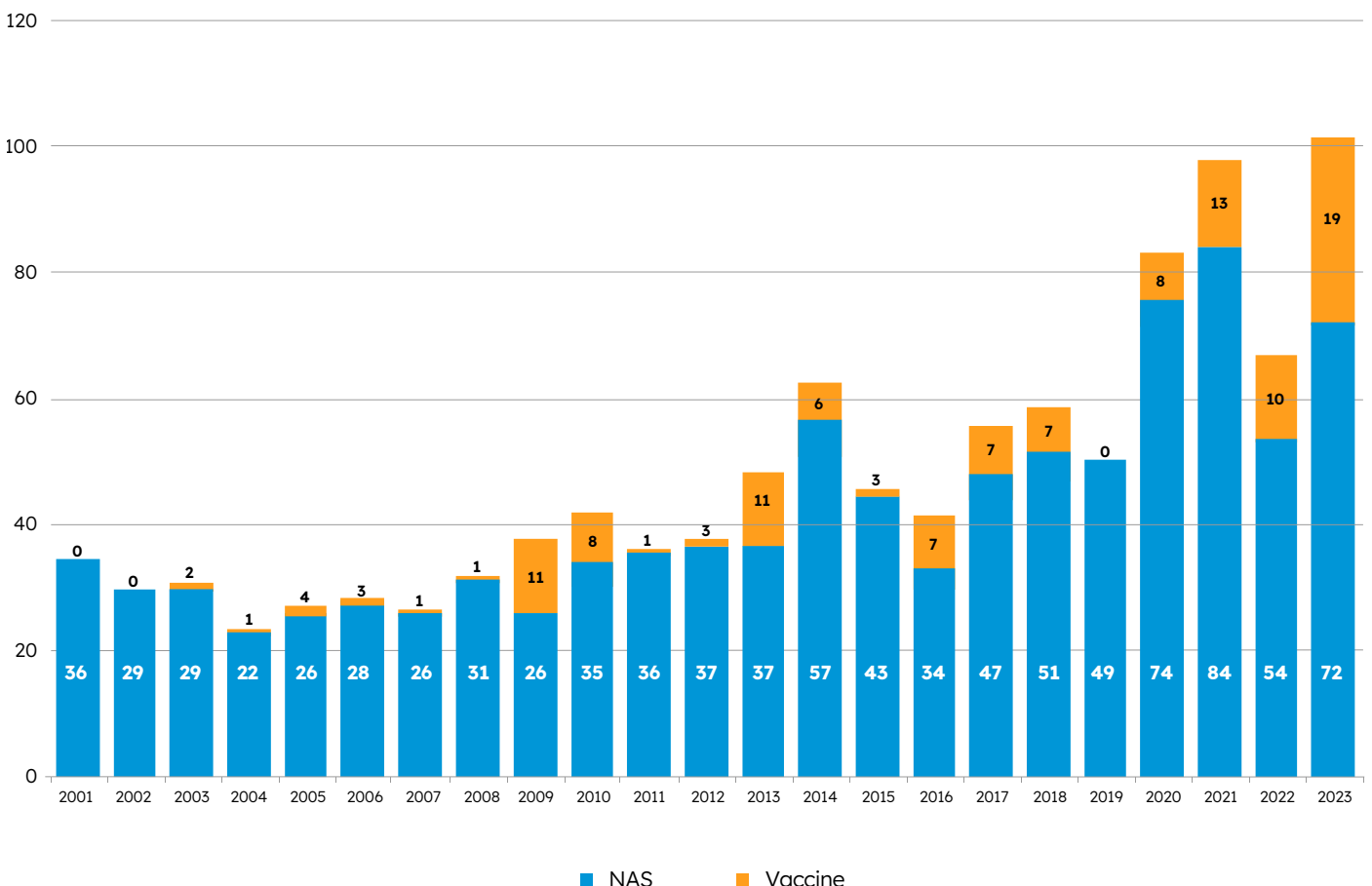
91 New Active Substance Launches

2023 was pharma's second-hottest year ever

When all 10 of the hottest years on Earth have been recorded from 2010 onwards, even the most ardent climate change skeptics might have to concede that something is afoot. Indeed, 2023 was the hottest year yet, eclipsing even 2016, which previously held the record. Heat has been building recently too in pharma in terms of the number of NAS introductions (although, unlike with climate, for the drug industry it's the hotter the better). The year to beat for novel drug launches is 2021. So, how did 2023 fare?

While not beating the record, 2023 came extremely close. As Figure 1 illustrates, 2023 saw 91 NASs across 90 products (one product was a fixed-dose combination containing two NASs) making their market debuts. As such, it fell just six short of 2021's record haul, and made 2023 the second-best year ever in terms of the number of NAS launches. This was also 17 more than 2022 produced, a significant boost, although it's worth noting that the numbers were supercharged by a record number of novel vaccines: 19 in total. For non-vaccine NAS launches, 2023's 72 is the third-highest ever total, behind 2021's 84 and 2020's 74. This represents a very satisfying result for the industry.

Figure 1: Number of NAS launches by year, 2001–23



Source: Pharmaprojects®, March 2024

Segmenting NAS launches by calendar year is a somewhat arbitrary way of counting NAS success, since a few just missing the end of one year and spilling over into the next might depress the first year's figures while boosting the second's. To mitigate the effect of this "calendar bias," we also judge whether the weather is improving by examining rolling averages across five-year periods. By this measure, we see clear global warming of NAS numbers. The mean for the latest five-year period of 2019–23 stands at 78.6, up considerably from 66.4 for the equivalent period last year. As if to reinforce how much the sun is shining for the industry recently, this compares very positively to earlier five-year bands: the mean for 2014–18 was 54.4 (up from 43.6 for the equivalent period (2018–2022) last year); 2009–13 was 41.0 (33.0); and 2004–08 was 28.6 (26.2).

This shows a very clear upward trend for the industry of bringing more new drugs to the market, which is what we would hope to see given that the size of the overall pipeline has been rising inexorably (see main report). It would seem the industry climate for drug development is indeed warming in a most favorable way.





The 2023 NAS Statistics

Trade winds fan the fires in China

It's time now to open the curtains and look up at the complete list of new drugs that entered the pharma firmament during 2023, which you can see in Table 1. Compiling this list is a Herculean effort for the Pharmaprojects team, who every year climb this particular mountain to take in the clean, crisp air. The reason for this is that while first approvals are widely publicized by companies which normally shout about getting their drugs greenlit from the rooftops, confirmation of actual launch, marketing, or availability to patients has less visibility than a foggy day in London. Some drugs become available almost instantaneously on approval, whereas others must wait for reimbursement decisions, sales forces to be assembled, or even (such as with some vaccines) the season to change. It also can be somewhat moot when exactly a drug is considered launched as such.

So, (rain)hats off to the Pharmaprojects team for conducting a large amount of additional research to come up with what we consider to be the definitive list of 2023's NAS introductions.

Table 1 shows the new drugs arranged alphabetically by INN or equivalent, along with the brand name, the companies involved, the diseases which the drugs are approved for, the drugs' mechanisms of action, where the launches first occurred, and determinations of novelty and rare disease/orphan drug status. We also give a determination of month of launch, although this may be approximate for the aforementioned reasons. And just like we can analyze the weather via multiple metrics such as hours of sunshine, temperature, humidity, precipitation, and wind speed, we will analyze our NAS list by each of these measures, too.



Table 1: New active substance launches, 2023

GENERIC DRUG NAME	TRADE NAME	COMPANY	Drug Disease	Mechanism Of Action	Drug Country	Month of Launch	First-in-Class?	Rare Disease?	Orphan Drug Status?
adebrelimab	Ariely	Jiangsu Hengrui Pharmaceuticals	Small cell lung cancer	PD-L1 antagonist	China	April	N	Y	N
anaprazole sodium	An Jiu Wei	Sihuan Pharmaceutical	Duodenal ulcer	H+ K+ transporting ATPase inhibitor	China	August	N	N	N
apadamtase alfa/ cinxadamtase alfa****	Adzynma	Takeda	Thrombotic thrombocytopenic purpura	Metalloproteinase ADAMTS13 stimulant	USA	November	Y	Y	Y
avacincaptad pegol sodium	Izervay	Astellas Pharma	Dry age-related macular degeneration	Complement factor C5 inhibitor	USA	September	N	N	N
befortinib mesylate	Semena	Betta Pharmaceuticals/ InventisBio	Non-small cell lung cancer	EGFR kinase inhibitor	China	June	N	N	N
beremagene geperpavec	Vyjuvek	Krystal Biotech	Epidermolysis bullosa	COL7A1 stimulant	USA	November	Y	Y	Y
bexagliflozin	Brenzavvy	TheracosBio	Type 2 diabetes	SGLT2 inhibitor	USA	July	N	N	N
cantharidin	Ycanth	Verrica Pharmaceuticals	Molluscum contagiosum virus infection	Unidentified pharmacological activity	USA	August	N	N	N
capivasertib	Truqap	AstraZeneca	Breast cancer	Protein kinase B inhibitor/ Ribosomal S6 kinase inhibitor	USA	December	Y****	N	N
carenoprazan hydrochloride	Beiwen	Jiangsu Carephar Pharmaceutical/Shanghai Fosun Pharmaceutical (Group)	Duodenal ulcer/reflux oesophagitis	Potassium-competitive acid antagonist	China	February	N	N	N
cipaglucosidase alfa* + miglustat	Opfolda	Amicus Therapeutics	Pompe's disease	Alpha glucosidase stimulant	Croatia, Germany, Netherlands, Slovakia, UK	June	N	Y	Y
COVID-19 vaccine, Bharat Biotech-2	iNCOVACC	Bharat Biotech	Novel coronavirus infection prophylaxis	Immunostimulant	India	January	N	N	N
COVID-19 vaccine, Clover Biopharmaceuticals		Clover Biopharmaceuticals	Novel coronavirus infection prophylaxis	Surface glycoprotein (SARS- CoV-2) antagonist/Toll-like receptor 9 agonist	China	February	N	N	N
COVID-19 vaccine, CSPC Pharmaceutical	Duentai	CSPC Pharmaceutical	Novel coronavirus infection prophylaxis	Immunostimulant	China	June	N	N	N
COVID-19 vaccine, Genova Biopharmaceuticals	Gemcovac	Emcure Pharmaceuticals/ Genova Biopharmaceuticals	Novel coronavirus infection prophylaxis	Immunostimulant	India	June	N	N	N
COVID-19 vaccine, HIPRA	Bimervax	Laboratorios Hipra	Novel coronavirus infection prophylaxis	Immunostimulant	Austria, Belgium, Croatia, Finland, Ireland, Slovakia, Spain, Sweden	May	N	N	N
COVID-19 vaccine, Sinocelltech	An Nuo Neng 2	Sinocelltech	Novel coronavirus infection prophylaxis	Immunostimulant	China	February	N	N	N
COVID-19 vaccine, Sinocelltech-1	An Nuo Neng 4	Sinocelltech	Novel coronavirus infection prophylaxis	Immunostimulant	China	May	N	N	N

 Source: [Pharmaprojects®](https://www.pharmaprojects.com/), March 2024

****Both drugs are NASs here **** Both mechanisms are novel here * cipaglucosidase alfa is the NAS here

GENERIC DRUG NAME	TRADE NAME	COMPANY	Drug Disease	Mechanism Of Action	Drug Country	Month of Launch	First-in-Class?	Rare Disease?	Orphan Drug Status?
COVID-19 vaccine, Sinocelltech-2		Sinocelltech	Novel coronavirus infection prophylaxis	Immunostimulant	China	December	N	N	N
delandistrogene moxeparovec	Elevidys	Roche/Sarepta Therapeutics	Duchenne's muscular dystrophy	Dystrophin stimulant	USA	November	N	Y	Y
durlobactam** + sulbactam	Xacduro	Entasis Therapeutics/Innoviva	Acinetobacter baumannii infection	Lactamase-A/C/D inhibitor***	USA	September	Y	N	N
efanesoctocog alfa	Altuviiio	Sanofi	Haemophilia A	Factor VIII stimulant	USA	April	N	Y	Y
efbemalenograstim alfa	Yilishu	Sino Biopharmaceutical/Yifan Pharmaceutical	Radio/chemotherapy-induced neutropaenia	Granulocyte colony stimulating factor agonist	China	June	N	N	N
elacestrant	Orserdu	Eisai/Menarini	Breast cancer	Selective estrogen receptor downregulator	USA	February	N	N	N
elivaldogene autotemcel	Skysona	Bluebird Bio	Adrenoleukodystrophy	ABC transporter stimulant	USA	August	Y	Y	Y
elranatamab	Elrexio	Pfizer	Myeloma	CD3 agonist	USA	August	N	Y	Y
enavogliflozin	Envlo	Daewoong Pharmaceutical	Type 2 diabetes	Sodium/glucose cotransporter 2 inhibitor	South Korea	February	N	N	N
enterovirus 71 vaccine, ADImmune	An To Fu Enterovirus 71 Vaccine	Enimmune/ADImmune	Enterovirus 71 infection prophylaxis	Immunostimulant	Taiwan, China	August	N	N	N
epcoritamab	Epkinly	Genmab	Follicular/diffuse large B-cell lymphoma	CD3 agonist	Japan	October	N	Y	Y
equecabtagene autoleucel	Fucaso	Innovent Biologics	Myeloma	T cell stimulant	China	July	N	Y	Y
etranacogene dezaparovec	Hemgenix	CSL Limited	Haemophilia B	Factor IX stimulant	USA	February	N	Y	Y
etrasimod	Velsipity	Pfizer	Ulcerative colitis	Sphingosine 1-phosphate receptor agonist	USA	December	N	N	N
fezolinetant	Veozah	Astellas Pharma	Menopausal symptoms	Neurokinin 3 receptor antagonist	USA	May	Y	N	N
futibatinib	Lytgobi	Otsuka Holdings	Biliary cancer	FGF receptor 1/2/3/4 tyrosine kinase inhibitor	USA	March	N	Y	Y
glofitamab	Columvi	Roche	Diffuse large B-cell lymphoma	CD3 agonist	USA	June	N	Y	Y
gumarontinib	Haiyitan	Haihe Biopharma	Non-small cell lung cancer	MET tyrosine kinase inhibitor	China	March	N	N	Y
herpes zoster vaccine, Changchun BCHT Biotechnology	Ganwei	Changchun BCHT Biotechnology	Varicella zoster virus infection prophylaxis	Immunostimulant	China	April	N	N	N
HPV vaccine, quadrivalent, Serum Institute of India	Cervavac	Serum Institute of India	Human papilloma virus infection prophylaxis	Immunostimulant	India	January	N	N	N

Source: [Pharmaprojects®](#), March 2024

** durlobactam is the novel NAS here ***Lactamase D inhibitor is the novel mechanism here

GENERIC DRUG NAME	TRADE NAME	COMPANY	Drug Disease	Mechanism Of Action	Drug Country	Month of Launch	First-in-Class?	Rare Disease?	Orphan Drug Status?
inaticabtagene autoleucl		CASI Pharmaceuticals/ Juventas Cell Therapy	Acute lymphocytic leukaemia	T cell stimulant	China	December	N	N	N
influenza vaccine, quadrivalent, live-attenuated, seasonal, Serum Institute of India	Nasovac-S4	Serum Institute of India	Influenza infection prophylaxis	Immunostimulant	India	October	N	N	N
interferon-like protein, Genova Biotech	Novaferon	Genova Biotech	Hepatitis-B virus infection	Angiogenesis inhibitor/ Apoptosis stimulant	China	May	N	N	N
iptacopan	Fabhalta	Novartis	Paroxysmal nocturnal haemoglobinuria	Complement factor B inhibitor	USA	December	Y	Y	Y
iruplinkib	Qixinke	Qilu Pharmaceutical	Non-small cell lung cancer	ROS tyrosine kinase inhibitor/ Anaplastic lymphoma kinase inhibitor	China	July	N	N	N
lebrikizumab	Ebglyss	Almirall/Eli Lilly	Atopic eczema	Interleukin 13 antagonist	Germany	December	N	N	N
lecanemab-irmb	Leqembi	BioArctic Neuroscience/ Biogen/Eisai	Alzheimer's disease	Beta amyloid protein antagonist	USA	January	N	N	N
leniolisib	Joeanja	Novartis/Pharming	Activated PI3Kdelta syndrome	PI3 kinase delta inhibitor	USA	April	N	Y	Y
leritrelvir	Le Ruiling	Guangdong Zhongsheng Pharma	Novel coronavirus infection	SARS 3 cysteine-like protease inhibitor	China	June	N	N	N
lotilaner	Xdemvy	Tarsus Pharmaceuticals	Blepharitis	Chloride channel antagonist	USA	August	N	N	N
meningococcal vaccine, Pfizer	Penbraya	Pfizer	Meningococcal infection prophylaxis	Immunostimulant	USA	December	N	N	N
mirikizumab	Omvo	Eli Lilly	Ulcerative colitis	Interleukin 23 antagonist	Japan	June	N	N	N
momelotinib	Ojjaara	GlaxoSmithKline	Myelofibrosis	Activin receptor-like kinase 2 inhibitor Janus kinase 1 inhibitor Janus kinase 2 inhibitor	USA	September	Y	Y	Y
motixafortide	Aphexda	BioLineRx	Stem cell mobilization	CXC chemokine receptor 4 antagonist	USA	September	N	N	Y
nadofaragene firadenovec	Adstiladrin	Ferring/FKD Therapeutics	Bladder cancer	Interferon alpha 2b agonist	USA	October	N	N	N
naloxumab	Jinlilai	CSPC Pharmaceutical	Giant cell tumour of bone	RANKL antagonist	China	September	N	Y	N
nirogacestat	Ogsiveo	SpringWorks Therapeutics	Aggressive fibromatosis/Soft tissue sarcoma	Secretase gamma inhibitor	USA	November	Y	Y	Y
nirsevimab	Beyfortus	AstraZeneca/Sanofi	Respiratory syncytial virus infection prophylaxis	Immunostimulant	USA	November	N	N	N

Source: Phmaprojects®, March 2024

GENERIC DRUG NAME	TRADE NAME	COMPANY	Drug Disease	Mechanism Of Action	Drug Country	Month of Launch	First-in-Class?	Rare Disease?	Orphan Drug Status?
omaveloxolone	Skyclarys	Biogen	Friedreich's ataxia	Transcription factor Nrf2 stimulant	USA	June	N	Y	Y
omidubicel	Omisirge	Gamida Cell	Stem cell engraftment	Not applicable	USA	September	N	N	Y
para-toluenesulfonamide	Purocenta	Gongwin Biopharm/Tianjin Chase Sun Jiandakang	Non-small cell lung cancer	Adenosinetriphosphate synthase inhibitor	China	August	N	N	N
palovarotene	Sohonos	Clementia/Ipsen	Fibrodysplasia ossificans progressiva	Retinoic acid gamma receptor agonist	USA	November	N	Y	Y
pegmolesatide	Saint Luolai	Jiangsu Hansoh Pharmaceutical	Renal disease-induced anaemia	Erythropoietin receptor agonist	China	September	N	N	N
pirtobrutinib	Jaypirca	Eli Lilly	Mantle cell lymphoma	Bruton tyrosine kinase inhibitor	USA	January	N	Y	Y
pneumococcal vaccine, SK Chemicals-2	SKYPneumo	SK	Pneumococcal infection prophylaxis	Immunostimulant	South Korea	May	N	N	N
pozelimab	Veopoz	Regeneron	CD55 deficiency with CHAPLE syndrome	C5a inhibitor	USA	August	Y	Y	Y
repotrectinib	Augtyro	Bristol-Myers Squibb	Non-small cell lung cancer	Anaplastic lymphoma kinase inhibitor/ ROS receptor tyrosine kinase inhibitor/ Src inhibitor/TrkA/B/C tyrosine kinase inhibitor	USA	December	N	N	Y
retaglipin	Rizetang	Jiangsu Hengrui Pharmaceuticals	Type 2 diabetes	Dipeptidyl peptidase 4 (DPP IV) inhibitor	China	December	N	N	N
retifanlimab	Zynyz	Incyte	Merkel cell carcinoma	PD-1 antagonist	USA	April	N	Y	Y
rezafungin acetate	Rezzayo	Cidara Therapeutics/Melinta Therapeutics	Candida albicans infection	1,3-Beta-glucan synthase inhibitor	USA	July	N	N	N
ritlecitinib	Litfulo	Pfizer	Alopecia areata	Janus kinase 3 inhibitor	USA	June	N	N	N
rotavirus vaccine, Pharm Aid Ltd	Rota-V-Aid	Pharm Aid	Rotavirus infection prophylaxis	Immunostimulant	Russian Federation	August	N	N	N
rozanolixumab	Rystiggo	UCB	Myasthenia gravis	Fc fragment of IgG receptor and transporter antagonist	USA	July	N	Y	Y
RSV vaccine, GlaxoSmithKline, older adults	Arexvy	GlaxoSmithKline	Respiratory syncytial virus infection prophylaxis	Immunostimulant	USA	August	N	N	N
RSV vaccine, Pfizer	Abrysvo	Pfizer	Respiratory syncytial virus infection prophylaxis	Immunostimulant	USA	August	N	N	N
simnotrelvir	Senuoxin	Simcere Pharmaceutical Group	Novel coronavirus infection	SARS 3 cysteine-like protease inhibitor	China	February	N	N	N
sovateptide	Tyvalzi	Pharmazz/Sun Pharmaceutical Industries	Cerebral ischemia	Endothelin B receptor agonist	India	September	Y	N	N

Source: [Pharmaprojects®](#), March 2024

GENERIC DRUG NAME	TRADE NAME	COMPANY	Drug Disease	Mechanism Of Action	Drug Country	Month of Launch	First-in-Class?	Rare Disease?	Orphan Drug Status?
sparsentan	Filspari	Traverse Therapeutics	Berger's disease	Endothelin A receptor antagonist	USA	August	N	Y	Y
sunvozertinib	Schweizer	Dizal (Jiangsu) Pharmaceutical	Non-small cell lung cancer	EGFR kinase inhibitor	China	August	N	N	N
tabelecleucel	Ebvallo	Pierre Fabre	Post transplant lymphoproliferative disorder	T cell stimulant	Croatia, Netherlands, Slovakia	April	N	Y	Y
tafolecimab	Sintbilo	Innovent Biologics	Heterozygous familial hypercholesterolaemia/ Mixed dyslipidemia	PCSK9 inhibitor	China	August	N	N	N
talquetamab	Talvey	Johnson & Johnson	Myeloma	CD3 agonist	USA	December	Y	Y	Y
tofersen	Qalsody	Biogen/Ionis Pharmaceuticals	Amyotrophic lateral sclerosis	Superoxide dismutase-1 inhibitor	USA	July	Y	Y	N
trofinetide	Daybue	Acadia Pharmaceuticals/ Neuren Pharmaceuticals	Rett Syndrome	Insulin-like growth factor 1 agonist	USA	April	N	Y	Y
typhoid conjugate vaccine, Bio Farma	Bio-TCV	Bio Farma	Typhoid infection prophylaxis	Immunostimulant	Indonesia	November	N	N	N
typhoid vaccine, SK Chemicals	Skytyphoid	SK	Typhoid infection prophylaxis	Immunostimulant	South Korea	April	N	N	N
ublituximab-xiyy	Briumvi	TG Therapeutics	Relapsing-remitting multiple sclerosis	CD20 antagonist	USA	January	N	N	N
vilobelimab	Gohibic	InflaRx	COVID-19 complications	C5a inhibitor	USA	June	N	N	N
vorolanib	Fumena	AnewPharma/Betta Pharmaceuticals	Renal cancer	Colony stimulating factor 1 receptor antagonist/ Platelet-derived growth factor receptor kinase inhibitor/ VEGFR-1/2/3 tyrosine kinase inhibitor	China	July	N	Y	N
zavegepant	Zavzpret	Pfizer	Migraine	Calcitonin gene-related peptide inhibitor	USA	August	N	N	N
zuberitamab	Anruixi	BioRay Pharmaceutical	Diffuse large B-cell lymphoma	CD20 antagonist	China	May	N	Y	N
zuranolone	Zurzuvae	Biogen/Sage Therapeutics	Postpartum depression	GABA A receptor agonist	USA	December	N	N	N

Source: Pharmaprojects®, March 2024

Many of our readers will be most keen to see for which companies the sun shone brightest, and which were left chasing rainbows. So, we kick off our analysis by examining which pharma firms delivered the most new drugs during the past year. Table 2 lists all the companies that launched more than one NAS during the year, and where they fell in our chart of companies by pipeline size, on the basis that the best performance could be considered the most drugs delivered from the smallest pipeline. It also includes, for the remaining top 10 pharma by pipeline size, those that didn't manage to bring two or more drugs to the market.

Therefore, if there is one company that must be feeling as right as rain this year, it must be Pfizer. With involvement in six NASs, it heads the table with the most introductions by a company in a single year in many a moon. What's more, it scattered its showers of success across a range of therapeutic areas, producing two vaccines (Penbraya for meningococcal infection and Abrysvo for respiratory syncytial virus), along with one drug apiece for cancer (Elrexio [elranatamab]), alimentary (Velsipity [etrasimod]), dermatological (Litfulo [ritilecitinib]), and neurological (Zavzpret [zavegepant]) conditions. Arguably, Pfizer contributed the most to, and made the most from, the COVID-19 pandemic, so it seems to be riding the wave of its success there. Admittedly, it has the second-largest pipeline, but it fared considerably better than the company with the largest, Roche, which only contributed two NASs.

It was also a very successful year for the much smaller Biogen, only 40th by pipeline size, but second in our table, having delivered four NASs to market. In contrast to Pfizer, the Cambridge, MA-based firm enjoyed all its success in a single therapeutic area, neurological diseases. It produced new drugs for a variety of conditions within that group, however, covering Alzheimer's disease, Friedreich's ataxia, amyotrophic lateral sclerosis (ALS), and postpartum depression (PPD). Also, unlike Pfizer, which went it alone in all cases, Biogen preferred to be a collaborative partner in three out of four of its successful ventures.

The company with the best NAS launch to pipeline size ratio was Chinese company SinoCellTech, although, since all its three debutantes were different kinds of vaccines for COVID-19, perhaps these should more properly be considered as three flavors of a single item. The only other company that delivered three

NASs was another of the big pharma club, Eli Lilly.

Further down the table, there were no fewer than 12 companies delivering two NASs, including a few perhaps less familiar names. Betta Pharmaceuticals is one of the many Chinese-headquartered companies featuring here, but heads the list of double deliverers as it has the smallest pipeline. It produced two anticancer drugs, Semena (befotertinib mesylate) and Fumena (vorolanib) for non-small cell lung and breast cancer, respectively, both with collaborators. It is joined by fellow Chinese firms Innovent Biologics, CSPC Pharmaceutical, and Jiangsu Hengrui. The latter made headlines last year by topping our list as it delivered four novel NASs to the market, but this year has fared less well. Propping up the table are three of the top 10 companies by pipeline size that had a less successful year for new drug launches, with Johnson & Johnson and Bristol Myers Squibb only managing one apiece, and Merck & Co. out of luck completely.

Table 2: Top company NAS launch performance, 2023

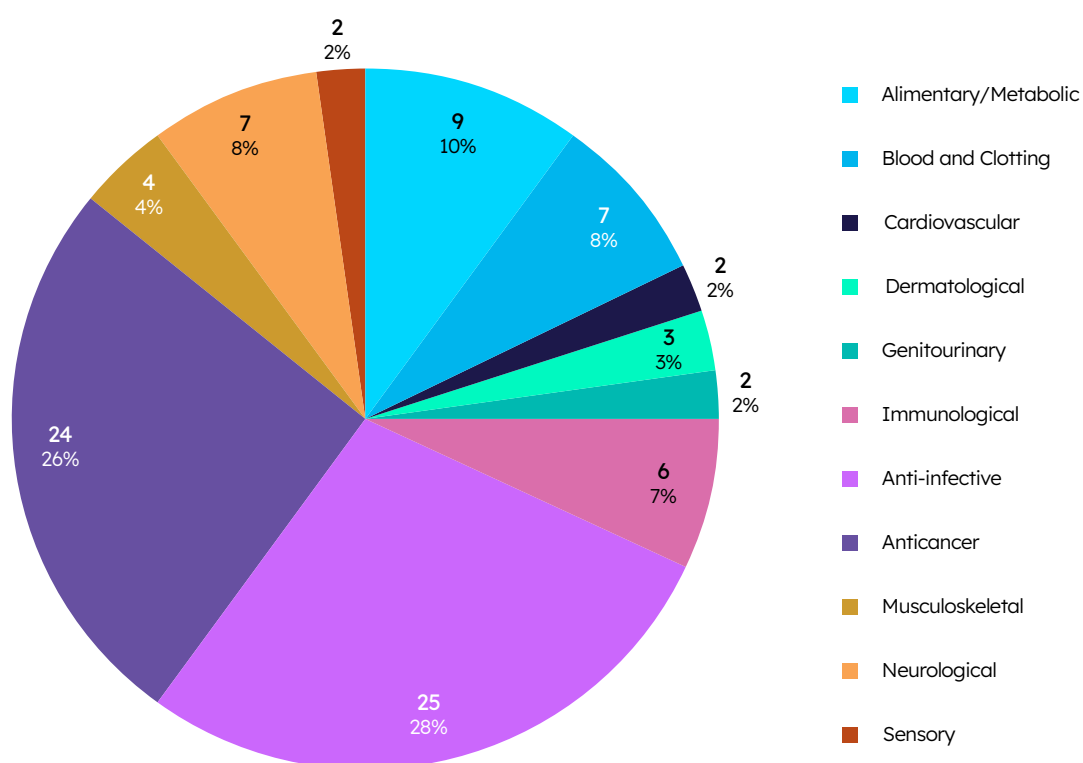
COMPANY	NUMBER OF NASs	POSITION IN PIPELINE CHART
Pfizer	6	2
Biogen	4	40
SinoCellTech	3	218
Eli Lilly	3	4
Betta Pharmaceuticals	2	81
SK	2	41
Innovent Biologics	2	32
CSPC Pharmaceutical	2	24
Astellas	2	22
Eisai	2	20
GlaxoSmithKline	2	11
Sanofi	2	10
Jiangsu Hengrui	2	8
Novartis	2	6
AstraZeneca	2	3
Roche	2	1
Johnson & Johnson	1	7
Bristol Myers Squibb	1	5
Merck & Co.	0	9

Source: Pharmaprojects®, March 2024

Overall, this year's top 10 companies were involved in 21 of the 91 NASs first launched, or 23.1%, slightly down from the 24.3% seen last year. It's interesting to see how many drugs were delivered solely by smaller concerns, indicating that partnering with big pharma is not an essential.

Which therapeutic areas are providing the diversity of a lush rainforest, and which are experiencing drought conditions? As Figure 2 shows, anti-infectives returned to pole position in 2023, accounting for 25, or 28%, of new releases, although considering that 19 of these were vaccines, it was actually not a great year for anti-infective drugs. Nevertheless, strictly speaking, this therapeutic area pushed 2022's leader anticancers into second place, with 24 (26%). Considering that 40.1% of the overall pipeline is devoted to oncology, this is a disappointing haul, suggesting that this area remains a high-risk one for R&D. Coming in third with nine NASs was alimentary/metabolics, while neurologicals had a much better year than of late, getting seven products over the line, tying with the blood & clotting category. There were slimmer pickings elsewhere, but all the major therapeutic areas were represented, with the notable exception of respiratory.

Figure 2: 2023 NAS launches by therapeutic group



Source: Pharmaprojects®, March 2024



The proportion of drug NASs categorized as biotechnology drugs remained at roughly half, with 44 out of the 91 molecules being produced by such techniques. This is a bigger proportion than biotech takes up in the pipeline, indicating that such targeted therapies have perhaps a better chance of success. Monoclonal antibodies accounted for 17 of these, but, surprisingly, there were no pure bispecific or multispecific antibody debutantes this time around, nor any antibody-drug conjugates. There were, however, four bispecific cell engagers. Over in the cell therapy arena, there were two new CAR-T therapeutics, plus two using stem cells and one based on T cells. It was a great year for gene therapy overall, with seven of the year's NASs involving some kind of genetic manipulation (including the two CAR-Ts, which are genetically modified *ex vivo*). In the RNA field, there was one new antisense drug, one new aptamer, and three of the year's novel COVID-19 vaccines that employed the renowned mRNA technology. The remaining biotech-derived NASs were spread among various kinds of recombinant protein therapeutics.

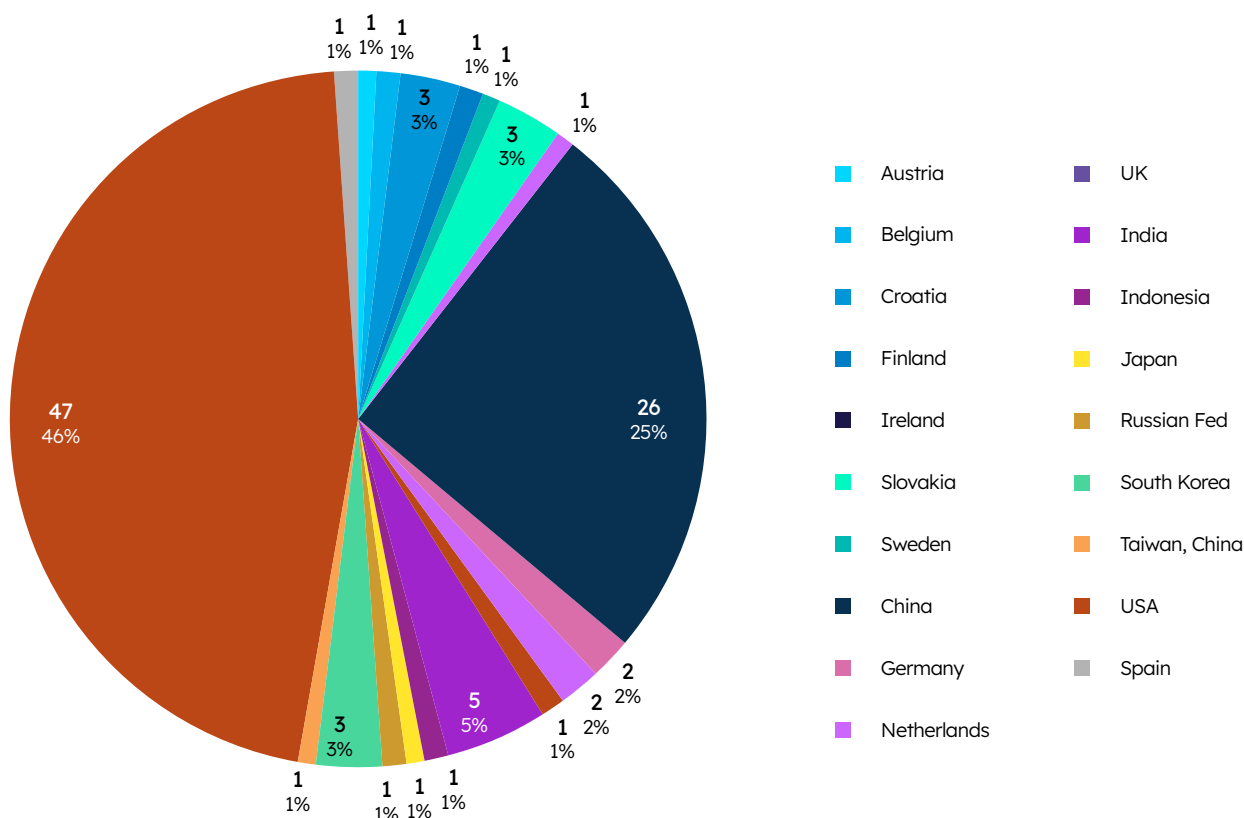
Our planet, due to its tilt, enjoys seasons in many parts, although the degree to which these vary depends on latitude. While equatorial regions vary less temperature-wise throughout the year, and are more likely to have their seasons divided along dry/rainy lines, the more temperate parts of the globe tend to parse their years into winter/spring/summer/autumn. Thus, as I write this in early March, there's a chill wind in London, while a colleague I spoke with yesterday in Sydney was complaining about extreme heat.

This could be flipped in a few months (although to be fair, it never gets that cold in Sydney). I think the place I've been to in the world where I've experienced the greatest range of temperatures has been Montreal. One July, I sweltered in a sticky 42°C (108°F), while in winter I endured a night dipping to -25°C (-13°F). That's some difference. The point I'm making is that, way before man understood that the Earth takes 365-odd days to orbit the sun, it was the weather that gave us the concept of a year, and that not all parts of the globe are equal in their experience.



Similarly, not all countries in the world share the same experience of NAS introductions, with some countries finding the industry prefers their climates to others. Where the golden sunlight fell across the world is summarized in Figure 3. Note that some drugs that might have been simultaneously launched in more than one market will have been counted more than once.

Figure 3: 2023 NAS launches by country/region



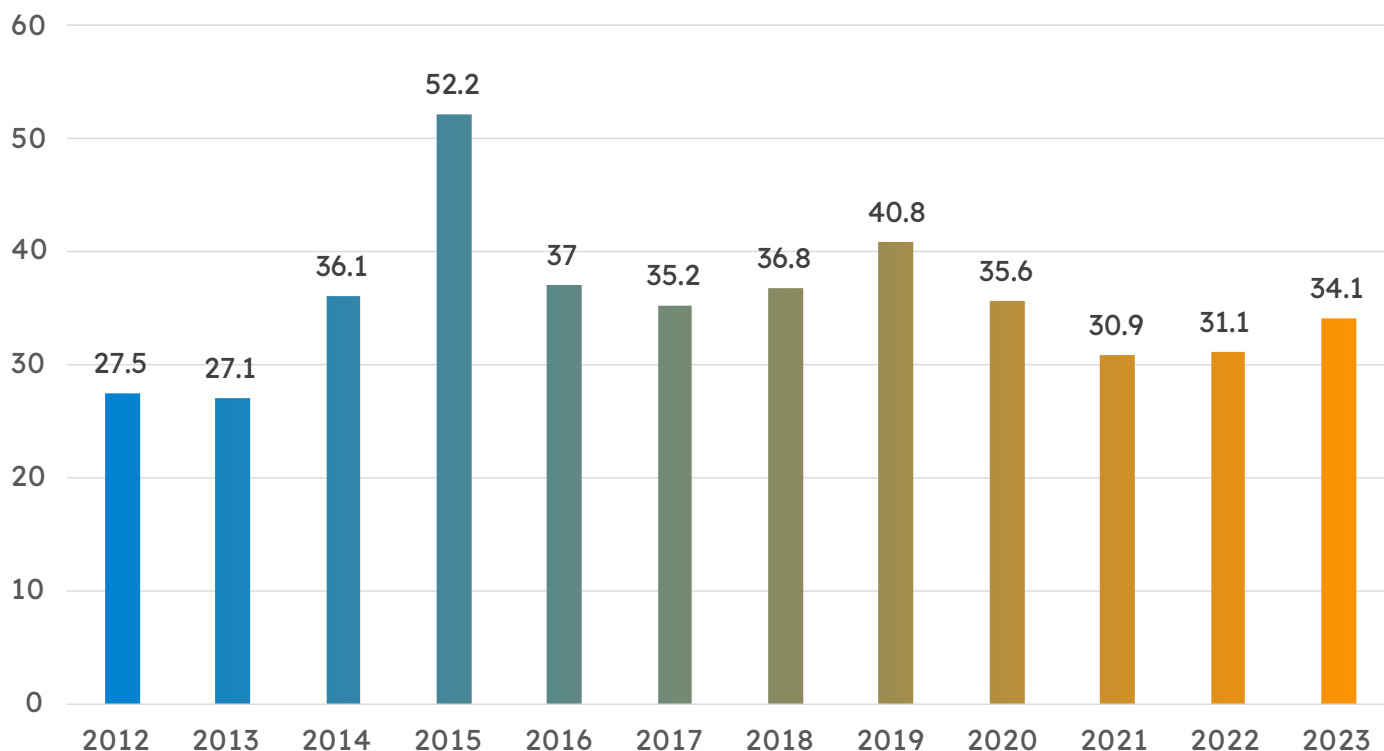
Source: Pharmaprojects®, March 2024

The US, still the biggest pharma market in the world, has always had favored nation status here. If anything, it maintained its hold in 2023, with 46% of debuts taking place there, up significantly from 32% last year and returning to the level seen in 2021. China, however, continues to advance, largely due to the emergence of its own world-class pharma industry. It enjoyed 25% of all NAS first launches last year, up from 21.6% the year before — all from homegrown fare. Contrast this to Japan, which we called out last year for hosting 14 of the NAS introductions; well, this year, that number has fallen right back to two, so 2022 is left looking highly anomalous. It was even beaten by fellow Asian countries India and South Korea, and by EU minnows Slovakia and Croatia. Increasingly, the tempest seems to be between clashing air masses from the two superpowers, the US and China.



The righthand-most columns of Table 1 give an indication of whether our NASs were launched for rare diseases, and whether these developments were encouraged by concomitant orphan drug designations. A rare disease is defined as one with a prevalence of less than one in every 2,000 people in the EU, or affecting fewer than 200,000 people in the US (equivalent to around one in every 1,600 people). In 2023, 32 of the 91 NASs were developed and launched to treat a rare disease, up slightly in terms of number from 30 in 2022, but providing a rather lower percentage (35.2% vs. 40.5%). Despite this, the percentage of NASs that made it onto the market with the helpful incentive of orphan drug status rose slightly, as evidenced in Figure 4.

Figure 4: Percentage of NAS launches with an orphan drug designation, 2012–23



Note: 2016–22 figures refer only to drugs with orphan drug status for their marketed indication in their marketed country.
Source: [Pharmaprojects®](#), March 2024

But it’s the other yes/no column to the right that always excites our readership the most: whether a new drug can be considered novel. It’s to these drugs which we’ll turn our attention in the next section of this report.





The Novel NASs of 2023

Is the well of innovation drying up?

It's human nature to be excited by things that are new, different, or interesting. A moderately cloudy day with light winds and a bit of drizzle is unlikely to make the evening news. But give us something extraordinary, such as hail the size of baseballs or snowdrifts as big as houses, and suddenly our interest is piqued. It's the same in pharma: new drugs are all well and good, but what about those which are first in class and exhibit something genuinely novel? In other words, where did the lightning bolts of innovation strike in the drug industry in 2023?

There are many definitions of innovative, but for our purposes here we define a drug as novel if it is a drug reaching the market which employs a mechanism of action that has not been seen on a marketed drug before. And it is here that the skies

for the 2023 NAS report begin to darken somewhat. By this measure, only 14 of the 91 in this year's crop can be classified as first in class. This is a much poorer showing than 2022's 20 out of 74, both numerically and percentage-wise, where it comes in at 15.4% vs. 26.7%. It seems a year that produces both quantity and quality (in terms of novelty) is as rare as ball lightning. Whether the well of innovation is genuinely drying up is unclear at this point; it might just be a single disappointing year of sparse rainfall rather than pharma innovation being genuinely under the weather.

Drops of innovation did fall across a range of therapeutic areas, though, with anticancers and blood & clotting being the main beneficiaries this time around, with four novel NASs apiece. Elsewhere, neurologicals was the only other therapeutic area to deliver novelty on more than one front, with two innovative debutantes. One each came from the cardiovascular, dermatological, genitourinary, and anti-infective arenas. We're going to look at the 14 novel NASs here in a bit more detail.





Ogsiveo (nirogacestat) hit the market in the US in November for the treatment of patients with desmoid tumors, also known as aggressive fibromatosis. As the first launched gamma secretase inhibitor, Ogsiveo will provide relief to its patients by not only shrinking tumors, but also by significantly improving pain, which is the most debilitating symptom reported by people living with the condition. SpringWorks Therapeutics, a company focused on rare diseases and cancer, hopes this approval will open the floodgates to future launches of Ogsiveo for indications like soft tissue sarcoma, multiple myeloma, and ovarian granulosa cell tumors, for which it is already in Phase II or Phase III trials, so that it can provide a greater benefit to patients in the US and around the world.

In 2022, the NAS landscape was fertile ground for novel oncology therapies, with six first-in-class therapies entering the market, making it the leading therapeutic area. However, the ground has since dried out somewhat, with only four in 2023. Even with a lower number of novel anticancer therapies, the three small molecules and one antibody in this year's set will hope to make a significant difference to the patients who will be taking them.

We will start with Ojjaara (momelotinib), which was launched in September in the US for the treatment of myelofibrosis in patients with anemia, for which it is the first and only treatment to date. GSK's small molecule inhibits Janus kinase (JAK) 1 and 2, like other approved therapies for myelofibrosis, but Ojjaara separates itself from the pack through its additional inhibition of activin A receptor, type I (ACVR1). JAK inhibitors are commonly used to reduce spleen size and alleviate constitutional symptoms associated with myelofibrosis; however, many patients also develop anemia. Ojjaara addresses this complication through ACVR1 antagonism, which leads to downregulation of hepcidin expression and increased availability of iron for erythropoiesis, reducing the anemia. However, leading up to Ojjaara's approval, the drug had a bit of a checkered past; it changed hands multiple times over the past decade and experienced a three-month delay in the decision from the US Food and Drug Administration (FDA) in 2023. Nonetheless, it has finally made it to market, and the cloudy outlook for patients with myelofibrosis has improved with a forecast of more anemia-free, sunny days in the future.

Joining the battle against breast cancer, the most common malignancy in the world, is AstraZeneca's Truqap (capivasertib), which hit its first market, the US, last year. Specifically, Truqap is indicated for use in combination with Faslodex (fulvestrant), a selective estrogen receptor downregulator, for hormone receptor (HR)-positive, HER2-negative locally advanced or metastatic breast cancer with one or more biomarker alterations (PIK3CA, AKT1, or PTEN). Truqap is truly one of a kind through its adenosine triphosphate (ATP)-competitive inhibition of all three AKT isoforms (AKT1/2/3). Breast cancer cells encountering the drug will not only have to deal with Truqap-induced interruption of their oncogenic signaling, but they are also affected by the downregulation of their estrogen receptors. This provides something of a perfect storm against those cells. The drug was filed for this indication in the EU too, and potential follow-on indications under clinical study include prostate cancer and non-Hodgkin's lymphoma.



To round out the novel NAS oncology launches for 2023, we have the lone biologic therapy: Talvey (talquetamab). Talvey, a Johnson & Johnson asset, is a bispecific monoclonal antibody targeting G-protein-coupled receptor family C group 5 member D (GPRC5D) and the epsilon chain of CD3, for the treatment of relapsed or refractory multiple myeloma. GPRC5D is a commonly expressed protein on myeloma cells, and CD3 is found on T cells. Once Talvey engages both cells, the T cell is able to secrete perforins and granzyme to lyse the target cell. While bispecific T-cell-engaging antibodies are not a novel concept, the targeting of GPRC5D makes Talvey a first-in-class therapy. There are currently eight total approved T-cell engagers, including Talvey, split across five targets: CD20, CD19, BCMA, premelanosome protein, and GPRC5D. With the cell engager pipeline constantly growing, we can expect to see more novel drugs and their mechanisms included in future renditions of these reports. There appears to be something in the wind here.

Moving on to the four novel NASs in the blood & clotting area, we find Fabhalta (iptacopan), which was launched in the US by Novartis for the treatment of paroxysmal nocturnal hemoglobinuria (PNH). PNH is a rare blood disorder whereby red blood cells prematurely break down, causing effects characterized by somatic symptoms, hemolytic anemia, and hemoglobinuria. Fabhalta is the first oral Factor B inhibitor that acts proximally in the alternative complement pathway and regulates the cleavage of C3 and amplification of the terminal pathway. Novartis's launch of Fabhalta is set to be a breath of fresh air for patients as it improves hemoglobin levels and helps them to avoid blood transfusions and to reduce reported fatigue.

Also focusing on the complement system, Veopoz (pozelimab) is a monoclonal antibody that targets complement factor C5 to inhibit terminal complement overactivation. Developed by Regeneron, Veopoz brightens the outlook as the first and only treatment indicated specifically for complement hyperactivation, angioathic thrombosis, and CHAPLE disease, also known as CD55-deficient protein-losing enteropathy, a genetic disorder that affects a scattered patch of fewer than 10 patients identified in the US and 100 worldwide. In this ultra-rare disease, mutations of the complement regulator CD55 gene result in the complement system attacking the body's own cells.

Symptoms of CHAPLE include malnutrition, edema, and severe thrombotic vascular occlusions. Unsurprisingly, this is one of the nine novel NASs in this year's list which are set to benefit from having been granted orphan drug status.

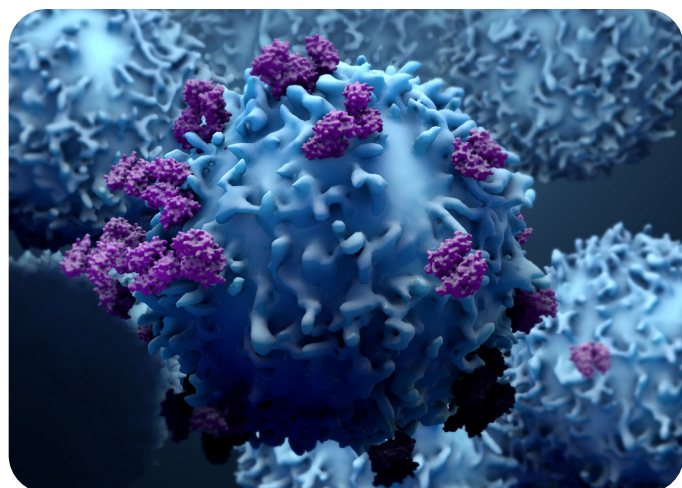
The final novel product in the blood & clotting area is the only one of all our new drugs which actually contains two — albeit closely related — NASs. Takeda's Adzynma is a combination of apadamtase alfa and cinxadamtase alfa, which differ only by a single amino acid, with the former's glutamine being swapped out in the latter for an arginine. But for the purposes of this report, since neither has been used before, we are considering them as separate NASs. Adzynma was launched in the US in 2023 as the first and only recombinant ADAMTS13 enzyme replacement therapy for the treatment of congenital thrombotic thrombocytopenic purpura (cTTP), an ultra-rare, chronic blood clotting disorder caused by inherited mutations in the ADAMTS13 gene. This gene codes for the ADAMTS13 enzyme, which is responsible for regulating blood clotting. If left untreated, cTTP leads to the formation of blood clots in small vessels throughout the body. Adzynma was previously granted orphan drug designation by the FDA, as well as fast track and rare pediatric disease designation. Indeed, Adzynma is the sunshine on a rainy day that cTTP patients have so patiently been waiting for, offering a treatment option that did not previously exist for this debilitating and severe condition.



In the field of neurology, we have seen two new fronts of drug development come to fruition, bringing brighter prospects for the treatment of ALS and adrenoleukodystrophy. The sun shone brightly on sufferers of cerebral adrenoleukodystrophy in August 2023 as we saw the first launch ever of a drug for this disease in the form of Skysona (elivaldogene autotemcel). Adrenoleukodystrophy is a rare hereditary disorder that damages the myelin sheath on neurons and adrenal cells in the adrenal gland, and is caused by mutations in the ABCD1 gene. Skysona is a gene therapy, developed by bluebird bio, comprising autologous CD34+ hematopoietic stem cells transduced with a lentiviral vector that encodes the mutated ABCD1 gene with cDNA, allowing a functional copy of adrenoleukodystrophy protein to be produced. The drug stabilizes the disease; however, it does not affect other disease manifestations such as adrenal insufficiency. Despite this drawback, Skysona is a bright start in the journey to cure adrenoleukodystrophy completely.

Biogen brings in the second novel neurological in the form of Qalsody (tofersen). This is an antisense oligonucleotide that treats familial ALS. ALS is characterized by the progressive degeneration of nerve cells in the central nervous system, causing difficulty in voluntary control of limbs and, eventually, trouble breathing. Qalsody works by targeting the production of superoxide dismutase 1 (SOD1), an enzyme that is thought to be the second most common cause of ALS, by binding to SOD1's mRNA and promoting degradation of the toxic SOD1 protein. Qalsody was given accelerated approval based on its ability to reduce neurofilament light chain in the blood of ALS patients, a biomarker that indicates the level of nerve cell damage.

Our sole novel NAS in the cardiovascular bucket this time also has neurological overtones, treating as it does acute cerebral ischemic stroke. Tyvalzi (sovateltide), developed by Pharmazz, is notable in that it is a novel NAS that was first launched in an unusual country, India. It is the first endothelin B receptor agonist to hit the market, and promotes neurovascular remodeling by forming new neurons (neurogenesis) and blood vessels (angiogenesis). It can help to improve the quality of life of stroke patients, and has the advantage that it can be administered intravenously up to 24 hours after the onset of symptoms, compared to current treatment options which limit patients to a narrower time window of four to five hours. Acute cerebral ischemic stroke is a condition in which there is impaired blood flow to the brain that can result in brain damage, permanent disability, or even death. Strategically, Pharmazz partnered with India's leading pharma company, Sun Pharmaceutical, which was granted rights to commercialize Tyvalzi in India in return for Pharmazz being entitled to up-front and milestone payments, including royalties.



Moving to genitourinary/women's health, Veozah (fezolinetant) is a first-in-class, oral neurokinin 3 (NK3) receptor antagonist to treat moderate-to-severe menopause-related vasomotor symptoms (VMS), developed by Astellas Pharma and launched in the US. Veozah is the first non-hormonal therapy approved to treat VMS due to menopause, which is most often characterized by hot flashes and night sweats and is an area of huge unmet need that has long lacked innovation. Traditionally, treatment has been heavily focused on hormone replacement therapy (HRT), but HRT's benefit-risk profile for use for such symptoms remains uncertain. Instead, Veozah works very differently by binding to and blocking the activities of the NK3 receptor, which plays a role in the brain's regulation of body temperature and causes the hot flashes associated with menopause. Veozah was caught in somewhat of a whirlwind prior to its approval after FDA delays due to an extended review period. However, Veozah has certainly weathered the storm and is described by Astellas as an eventual blockbuster, offering a new treatment alternative to address women's health needs that have long been underserved.

There was only one new drug for dermatological diseases, which is particularly of note in that it is the first ever topical gene therapy to reach the market. Vyjuvek (beremagene geperpavec) is a gene therapy that has been developed by Krystal Biotech for the treatment of the rare disease dystrophic epidermolysis bullosa in both its dominant and recessive forms. Epidermolysis bullosa is caused by a loss of function of COL7A1, which encodes collagen VII (COL7), the loss of which destabilizes the upper dermal layers, making them so fragile that tearing and blistering can occur from the slightest friction. Vyjuvek works by delivering functional copies of COL7A1 to restore the function of COL7, which is a major component for the anchoring of dermal

layers. The drug is applied directly in a gel suspension and is delivered to dermal layers by a viral vector that utilizes herpes simplex virus-1 (HSV-1); this drug is also the first to utilize HSV-1 as a vector in such a way. It is hoped that a successful rollout will cause the development of topical gene therapies to snowball in the coming years.

Finally, we have a novel anti-infective drug. Due to the development of drug resistance, Acinetobacter infections have become a leading cause of death, posing a global threat to patients on ventilators in hospitals and nursing homes. Innoviva has provided a ray of sunshine here with its combination of the established beta-lactam antibacterial sulbactam with the new molecule durlobactam in the product Xacduro. Xacduro, initially developed by Entasis Therapeutics prior to Innoviva's 2022 acquisition of the company, is novel because it inhibits lactamase D as well as other lactamase types. The increasing resistance of Acinetobacter baumannii has reduced sulbactam's usefulness in treating infections, but studies have shown that the combination with durlobactam restores sulbactam's activity. Xacduro has been approved for use in patients 18 years of age and older for the treatment of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia caused by susceptible isolates of Acinetobacter baumannii-calcoaceticus complex.

There may have been only been a handful of fine, sunny days of novelty across 2023, but that doesn't quite tell the whole story. There's a second tranche of NASs which, although they might not be novel by our strict definition of delivering a new mechanism to market, have brought other firsts, advanced patient care, or are otherwise worthy of note. Let's look at a different kind of blue sky thinking.





Other notable NASs

Brightening skies for previously untreatable diseases, but squally showers threaten to spoil the CNS picnic

Our chapter on other notable NASs is like one of those days that is a mixture of sunshine and showers. There are some definite bright spots, as drugs have reached the market for some diseases which had previously not had any options for pharmaceutical intervention. At the same time, there are some drugs which debuted into the sunshine, only to have to scurry for shelter as some unexpected deluges threatened to rain on their parades. As with the weather, despite all the forecasts, there is some inherent unpredictability in launching a new drug. Let's start with a case in point in Alzheimer's disease.

Eisai and Biogen's Leqembi may have been only the second anti-amyloid treatment for Alzheimer's disease when initially approved by the FDA in January 2023, but it became the first to secure full approval from the FDA later in the year in July, and thus the first to be granted reimbursement from the US Centers for Medicare & Medicaid Services. Given the high unmet need in Alzheimer's disease and pent-up demand for disease-modifying treatments, Leqembi could grow into a big-selling blockbuster, but its launch trajectory has been slow. The challenging diagnosis, administration, and reimbursement environment have diminished expectations for a splashy launch, even after the US government agreed to cover the treatment's costs. Eisai is leading the commercial effort, but Biogen will add sales representatives to the field during 2024 in both US and ex-US markets. Leqembi is launched in Japan and has been approved in China, with an approval decision expected in Europe during the first half of 2024. Of course, the same companies' previous effort, Aduhelm, whose initial approval was always controversial, did not find favor with payers or prescribers, and was in fact withdrawn completely early in 2024 as attention switched to Leqembi. But, as yet, there is no guarantee of success for this newer drug.

There is a similarly unsettled outlook for Roche and Sarepta's gene therapy for Duchenne muscular dystrophy, Elevidys (delandistrogene

moxeparvovec). It is still awaiting further regulatory decisions after it first won an accelerated US FDA approval in June to treat ambulatory patients aged four to five years old with a confirmed Duchenne gene mutation. The go-ahead was based on Phase II studies, but in late October its Phase III EMBARK confirmatory trial in all patients with Duchenne muscular dystrophy missed its primary endpoint. However, despite being restricted to a small number of Duchenne patients, the gene therapy has enjoyed a strong launch: its full-year sales reached \$200 million. Elevidys's high up-front price of \$3.2 million makes it one of the world's most expensive treatments, and some analysts are forecasting blockbuster sales for 2024, which would make it one of the most successful gene therapy launches to date. An FDA label expansion for the wider Duchenne cohort would take the product to new heights, but first the regulator needs to be convinced. Sarepta maintains that the EMBARK study was confounded by the limitations of the North Star Ambulatory Assessment test at 52 weeks post-treatment, on which EMBARK's primary endpoint was based, and argues that all the secondary endpoints in the study, including a key time-to-rise measure, showed robust significance. Assuming the FDA grants an expedited review lasting six months, a final decision would come by August 2024, although the company believes the pressing nature of the need in Duchenne — and the relatively straightforward nature of the data — mean a decision is possible well ahead of that time.

Sage Therapeutics and Biogen's GABA-A receptor positive allosteric modulator zuranolone was launched in the US in December under the brand name Zuruvae following FDA approval as the first oral product specifically indicated for PPD. Although it has had only a few months on the market, early sales have been promising, Sage has said, but expectations for the product have been cautious as the launch of Sage's first drug for PPD, Zulresso (brexanolone), in 2019 never really got off the ground. Zulresso has

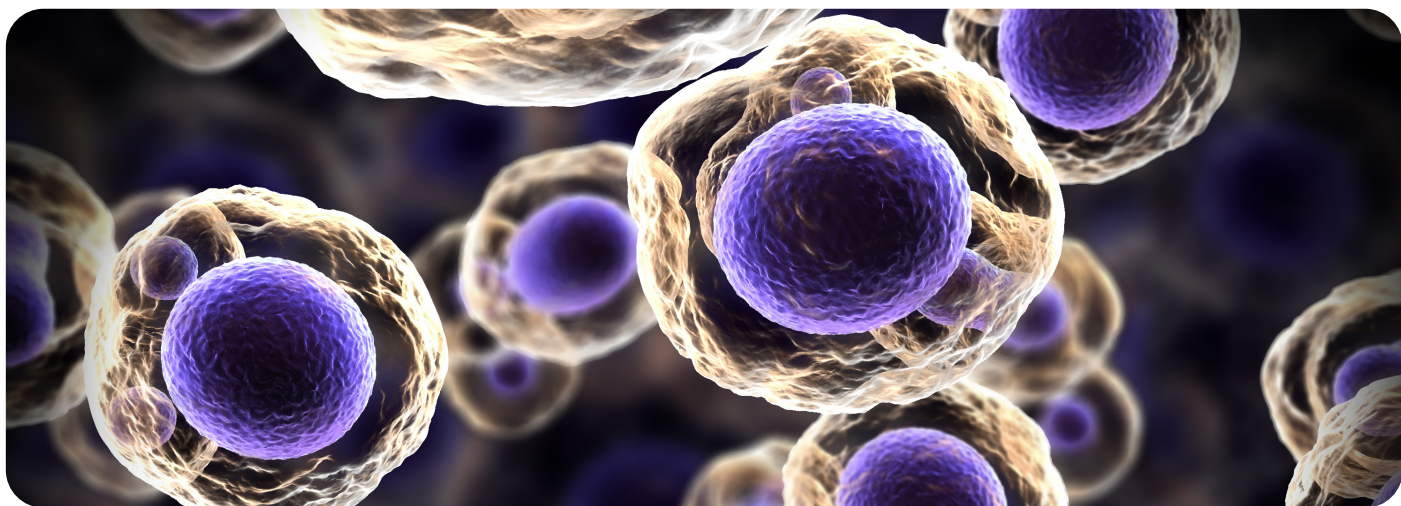
particularly challenging commercial dynamics in that it is administered intravenously over 60 hours and requires constant inpatient monitoring. Zurzuvae, by contrast, is given orally over a 14-day course of treatment, but it does carry warnings on the risk of CNS depressive effects, including somnolence, confusion, and driving impairment. Sage and Biogen had hoped to receive approval of the drug for major depressive disorder in addition to PPD, but the FDA has requested another trial before granting the broader approval.

A CNS drug which definitely got off to a good start, though, was Acadia Pharmaceuticals' Daybue (trofinetide) for the rare neurological disorder Rett syndrome. Early sales impressed so much that the company acquired the global rights to the drug and another promising neurological disorder candidate from partner Neuren Pharmaceuticals. The synthetic analog of the amino terminal tripeptide of insulin-like growth factor 1 became the first drug therapy for Rett syndrome when the FDA approved it in March for patients aged two years and upwards. Its launch comfortably exceeded analyst consensus forecasts, with blockbuster sales possible, and the product has little in the way of competition in the pipeline.

It was a case of it never rains but it pours in management of the infant viral infection respiratory syncytial virus (RSV). Though none falls under the heading of first in class, three new products for RSV burst onto the scene in 2023, creating a blockbuster market in the disease, which has only ever previously been served by the old antibody product Synagis (palivizumab). After several decades of research, the first vaccines to protect adults against RSV were approved by the FDA in May: GSK's Arexvy

and Pfizer's Abrysvo. And both hit the ground running. The UK major took an early commercial lead, to which it has clung since, with Arexvy generating sales of £1.2 billion (\$1.53 billion) in 2023, while Abrysvo contributed \$890 million to Pfizer's coffers. The two could soon be joined by Moderna's RSV vaccine mRNA-1345. It was filed with the FDA in July 2023, with a green light expected by April 2024, and the company claims its clinical data support a best-in-class profile, with its ready-to-use prefilled syringes offering a more attractive option to pharmacists and clinicians. Then, there was AstraZeneca and Sanofi's Beyfortus (nirsevimab), a next-generation antibody treatment to prevent RSV in infants. The product also flew off the shelves following its launch in November to the extent that the firms had to plug a US shortage by providing 230,000 doses that were originally intended for the Southern Hemisphere.





Tarsus Pharmaceuticals also has a chance of reaching blockbuster sales with its Xdemvy (lotilaner ophthalmic solution) 0.25% for Demodex blepharitis, given the high prevalence of the eyelid condition and the efficacy the drug demonstrated in pivotal trials. The one-time veterinary antiparasitic agent was launched in humans in the US last August, making it the first treatment to directly target the *Demodex folliculorum* mites that are the root cause of the disease. Xdemvy is a potent, non-competitive antagonist of insect and arachnid GABA-Cl channels and has high lipophilicity, allowing for its effective uptake in the oily sebum of hair follicles in the eyelid margins where the mites live. Demodex blepharitis affects about 25 million Americans, and although Tarsus is planning to start with a fraction of those, it still sees this as a \$1 billion opportunity. Moreover, Tarsus is now pursuing a pipeline-in-a-pill strategy for the product, developing it in various formulations for Lyme disease, rosacea, and meibomian gland dysfunction.

Pharming's Joenja (leniolisib) for activated phosphoinositide 3-kinase delta syndrome (APDS), a rare genetic disorder that impairs the immune system, was another first-for-disease launch last year. People with the progressive primary immunodeficiency, which is estimated to affect one to two people per million, are susceptible to swollen lymph nodes or an enlarged spleen, as well as autoimmunity and inflammatory symptoms, and may also be at higher risk for blood cancers. Until the thumbs-up for Joenja, treatment options were limited to antibiotics for infections and immunoglobulin replacement therapy. It's another example of how the pharma industry's deluge of new drugs had many bright spots among them.





The Forecast

Successful year sees the pharma industry outlook set fair

Our two-part almanac of how the pharma industry is faring at the start of 2024 is drawing to a close. We've seen that the climate for the industry is generally set fair, with a growing pipeline, a broad therapeutic focus, and a healthy crop of new drugs. There are, however, a few wispy clouds on the horizon, such as the high Phase II failure rate, and a year when innovation was perhaps a little disappointing. As we set sail across the relatively calm waters of 2024, it's time to look forward. Will progress continue serenely, or can we expect storms to blow up and make our journey somewhat more tempestuous?

Looking back to the global events I was highlighting last year, the past 12 months, like the weather in most parts, have been decidedly mixed. It would seem that the energy crisis is over for now, COVID-19 has settled into the background, and inflation in many Western economies is retreating to more acceptable levels. That being said, some countries (for example, the UK) have teetered into recession, the war grinds on miserably in Ukraine, and we have added the horrendous Israel-Gaza conflict into the mix. While the pharma industry has a warmer jacket than many other industries to protect it from the elements, it is by no means immune. But, retaining our focus specifically on pharma, what can we expect to see in the year ahead?



Firstly, let's put our forecasting hat on and speculate which new drugs we might be featuring in next year's NAS report. Every year, my colleague Alexandra Shimmings, executive editor, commercial R&D for Scrip, puts a metaphorical finger in the air to see which way the wind is blowing and selects a few drugs of interest that she expects to receive their first approvals and launches in the current calendar year. Her predictions for 2024 appear in Table 3.

Table 3: Selected important approvals/first launches expected in 2024

PRODUCT	COMPANY(IES)	MECHANISMS/INDICATIONS
Casgevy (exagamglogene autotemcel)	Vertex/CRISPR Therapeutics	Sickle cell disease and beta thalassemia
datopotamab deruxtecan	AstraZeneca/Daiichi Sankyo	TROP2-directed ADC for NSCLC
donanemab	Eli Lilly	Beta amyloid protein antagonist for Alzheimer's disease
KarXT (trospium chloride + xanomeline)	Karuna Therapeutics/ Bristol Myers Squibb	M1/M4-muscarinic agonist for schizophrenia
mRNA-1010 (influenza vaccine, Moderna Therapeutics , mRNA, quadrivalent)	Moderna	mRNA-based flu vaccine
mRNA-1345 (respiratory syncytial virus vaccine, Moderna Therapeutics)	Moderna	RSV vaccine for older adults
patritumab deruxtecan	Merck & Co.	HER3-targeting ADC for NSCLC
resmetirom	Madrigal Pharmaceuticals	THR agonist for NASH with liver fibrosis
seladelpar	CymaBay Therapeutics/ Gilead Sciences	Selective peroxisome proliferator-activated receptor (PPAR) delta agonist
sotatercept	Merck & Co.	Activin receptor 2a regulator for pulmonary arterial hypertension
Wainua (eplontersen)	Ionis Pharmaceuticals/ AstraZeneca	Hereditary transthyretin-mediated amyloidosis with polyneuropathy

Source: [Pharmaprojects/Scrip®](#), March 2024

Let's look in a bit more detail at some of the bright spots we're expecting through 2024. Vertex and CRISPR Therapeutics' Casgevy (exagamglogene autotemcel) — the world's first CRISPR/Cas9-based gene therapy — is expected to be launched this year following its approval for the treatment of patients over the age of 12 years with sickle cell disease and transfusion-dependent beta thalassemia. The go-ahead came initially in the UK last November, followed by the US and EU. Casgevy is a one-time *ex vivo* gene therapy and uses CRISPR/Cas9's "genetic scissors" to



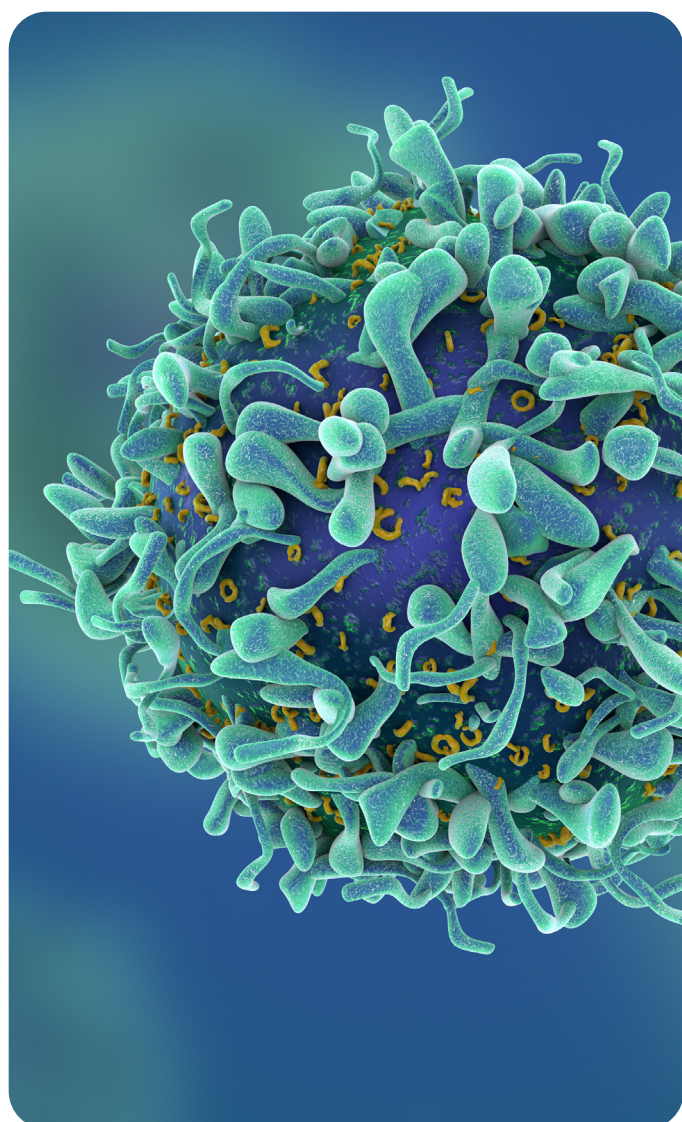
permanently cut out or suppress the BCL11A genomic variant, helping to restore normal red blood cell production in patients with both conditions. The expectation is that it could provide a lifelong cure for many patients, though long-term follow-up is needed. For CRISPR Therapeutics — which was co-founded in 2013 by Emmanuelle Charpentier, the co-discoverer and developer of CRISPR gene editing — the launch will provide its first product revenue stream and help fund its pipeline of *ex vivo* and *in vivo* CRISPR-edited therapies.

One product that will definitely feature in next year's NAS supplement, as it was already launched in January 2024, is Ionis Pharmaceuticals' Wainua (eplontersen). Ionis, which partnered with AstraZeneca, received approval in December 2023 from the FDA for the drug for the treatment of adults with hereditary transthyretin-mediated amyloidosis (ATTR) with polyneuropathy. The transthyretin (TTR)-directed antisense oligonucleotide drug is an important addition to AstraZeneca's cardiovascular portfolio, and it is the first drug that Ionis will help commercialize. Wainua is self-administered as a once-monthly subcutaneous injection, offering a potential advantage over Alnylam Pharmaceuticals' Amvuttra (vutrisiran), a TTR-directed small interfering RNA (siRNA) administered subcutaneously every three months in a doctor's office, and which was approved in 2022.

Wainua also is being developed for ATTR cardiomyopathy, but Phase III data are not expected until 2025. Expansion into ATTR cardiomyopathy would be a substantially larger

indication for both drugs. The market is currently dominated by Pfizer's transthyretin stabilizer Vyndamax/Vyndaqel (tafamidis), which generated \$3.32 billion in 2023.

Despite a number of delays at the FDA, approval is still expected this year for Eli Lilly's donanemab in the stormy area of Alzheimer's disease. Eli Lilly will now have to wait until after an FDA advisory committee meeting due in the second quarter of 2024 to discuss the Phase III TRAILBLAZER-ALZ 2 trial results for the anti-amyloid antibody in early Alzheimer's disease. The surprise decision is thought to be due to the agency's need for advice on how to label the drug for optimal use in the real world as opposed to the clinical trial setting. Experts believe the agency may be looking for input given the innovative trial design that Eli Lilly used for both whom to enroll and when to stop treatment. The drug is expected to eventually get the go-ahead, when it will become the second anti-amyloid antibody with full approval after Biogen and Eisai's Leqembi.



The first product for non-alcoholic steatohepatitis (NASH, also known as metabolic dysfunction-associated steatohepatitis [MASH]) has been approved, marking the first success after a string of R&D failures in the liver disease indication. Madrigal Pharmaceuticals' thyroid hormone receptor beta (THR β) agonist candidate resmetirom also looks to have around a two-year head start on any potential rivals. Launch, which will be Madrigal's first, will give the company the opportunity to forge a new market nearly four years after Intercept Pharmaceuticals' obeticholic acid failed to break through in mid-2020. Now that the dam has been breached, many more candidates are coming through the pipeline to fulfill this underserved market.

Another small company hoping to bring its first product to market is CymaBay Therapeutics. Its selective peroxisome proliferator-activated receptor (PPAR) delta agonist seladelpar is under FDA review for a related liver disease indication, primary biliary cholangitis, under a breakthrough therapy designation. Phase III data from its RESPONSE and ENHANCE studies showed that the drug could provide a meaningful improvement over existing therapies for the rare, chronic inflammatory liver disease which is thought to affect about 130,000 patients in the US and 125,000 in Europe. The company is now being bought for \$4.3 billion by Gilead Sciences, which has a very strong liver disease presence with its hepatitis franchises, making CymaBay a good strategic fit.

A similar story is playing out for Karuna Therapeutics, whose schizophrenia treatment KarXT (xanomeline + trospium chloride) could be a major step forward in a therapy area that has lacked progress for decades. It proved an irresistible attraction to Bristol Myers Squibb, which moved to acquire the firm for \$14 billion in December 2023. An FDA decision is expected by Sept. 26, 2024 on the potential first-in-class M1/M4-preferring muscarinic receptor agonist that the companies say is not associated with common side effects of marketed antipsychotics such as weight gain and extrapyramidal symptoms. While trospium chloride has already been brought to the market for use in pollakisuria and overactive bladder, xanomeline would be a NAS in this medicine.

At the other end of the scale, AstraZeneca and Daiichi Sankyo are looking to extend their dominance in the antibody-drug conjugate (ADC) space with the approval of their TROP2-

directed agent datopotamab deruxtecan (Dato-DXd) in non-small cell lung cancer (NSCLC). The product's US filing has been accepted but with a standard rather than accelerated review, meaning that an approval and launch could just squeak in by year end. AstraZeneca's filing is based on prespecified subgroup data in non-squamous disease cases (about 75% of patients) from the TROPION-Lung01 trial in patients with locally advanced or metastatic NSCLC who have been treated with at least one prior therapy; overall survival (OS) data are still awaited. Market expectations for the product have only increased after the OS miss for Gilead Sciences' rival TROP2-targeting ADC Trodelvy (sacituzumab govitecan) in the EVOKE-01 trial in January, although the two studies tested the products in slightly different settings. Dato-DXd has also produced promising data from the TROPION-Breast01 Phase III study in breast cancer.

Another ADC, the HER3-targeting patritumab deruxtecan, is one of many new products that Merck & Co. expects to launch this year to help reduce its dependence on Keytruda (pembrolizumab). Along with the activin signaling inhibitor sotatercept for pulmonary arterial hypertension (PAH), patritumab deruxtecan for metastatic EGFR-mutated NSCLC should begin contributing revenue in the second half of the year. Sotatercept and patritumab deruxtecan both came from Merck's business development initiative. Sotatercept was acquired with the \$11.5 billion purchase of Acceleron Pharma in 2021 and could be the first disease-modifying PAH treatment. Opinion leaders have called the data on the drug "transformative" for the disease. Existing vasodilator PAH therapies work by lowering hypertension in the lung, thereby reducing the right heart strain and failure typical of the disease. Sotatercept, by contrast, is a potential first-in-class activin signaling inhibitor and blocks the proliferation of cells in pulmonary artery walls, the underlying disease mechanism of PAH. Patritumab deruxtecan was in-licensed last year through a \$4 billion up-front deal with Daiichi Sankyo for three ADCs. It achieved positive results last September in the Phase II HERTHENA-Lung01 study in patients with EGFR-mutated, locally advanced or metastatic NSCLC following disease progression with an EGFR tyrosine kinase inhibitor and platinum-based chemotherapy. The candidate has been granted breakthrough therapy designation for this setting and was filed in the US at the end of 2023.

Finally, 2024 is also set to be a pivotal year for Moderna and its mRNA platform, with two likely launches. These are for its flu vaccine candidate mRNA-1010 and RSV vaccine candidate mRNA-1345. The latter will face a particularly competitive environment after GSK's and Pfizer's RSV vaccines got off to such strong starts following their 2023 launches. Moderna has pledged to eventually show superior efficacy to the frontrunners, but could struggle to challenge GSK, which has established a strong early lead.



As any meteorologist will tell you, forecasting is always a risky business, and hindsight is of course a wonderful thing. In the UK, there has been much glee derived over the years from endlessly recycling 1987 footage of hapless weather presenter Michael Fish reassuring viewers that there definitely wasn't a hurricane on the way just hours before a hurricane arrived and uprooted around 15 million trees in southern England. Hopefully our forecast from last year's report of which new drugs would enter the market wasn't quite so wide of the mark, so let's revisit the 10 bright prospects that we highlighted last year.

Well, most of our predictions were pretty accurate, with the aforementioned RSV vaccines, plus elacestrant, etranacogene dezaparvovec, nirsevimab, omaveloxolone, trofinetide, and zavegepant all making it onto 2023's launch list successfully. Another of last year's selections, fecal microbiota, live-jslm, made it to market, but wasn't classified as an NAS. Another, pegcetacoplan, was highlighted for its forthcoming approval in the US for geographic atrophy, which it indeed received in February 2023. But this drug had previously been launched for another indication, paroxysmal nocturnal hemoglobinuria, so this wasn't a first launch. Only one drug featured, Johnson & Johnson and Idorsia Pharmaceuticals' antihypertensive apocritentan, hasn't made it to market yet. It remains awaiting approval in both

the EU and US, with nods expected in the first half of this year. So, on the whole, our forecast proved more accurate than many a weather prediction.

Looking more broadly into 2024, which therapeutic areas do industry experts feel have the most potential to bask in warm sunlight this year? Our sister publication Scrip recently surveyed over 100 biopharma executives to ask them this same question (read the full article [here](#)). The mood was generally optimistic, particularly in the industry's area of greatest focus, cancer.

"In the evolving landscape of cancer treatment, targeted therapies continue to be a transformative technology driving innovation," said Steve Worland, CEO of eFFECTOR Therapeutics. "These therapies are designed to home in on specific molecular or genetic features of cancer cells, disrupting their growth mechanisms while sparing healthy tissues. By homing in on precise disease drivers, targeted therapies hold the potential to maximize treatment efficacy while minimizing side effects, thus improving the overall quality of life for cancer patients."

Other industry spokespeople focused on the hot topic of immuno-oncology. Detlev Biniszkiwicz, chairman of NextPoint Therapeutics and managing director of biotech investment firm MPM BioImpact, was one of a number of experts calling out checkpoint inhibitors for special mention. "Over the last four years, the dominant play in oncology has been PD-1/L1 plus something else," he noted. "We are learning that PD-1/L1 is not the only backbone checkpoint in immuno-oncology (IO) and we are just starting to scratch the surface of understanding resistance mechanisms to standard-of-care treatments. I expect we will continue to see momentum build in the antibody-drug conjugate space as well as a revival of oncology targets such as CD3."

Christopher Haqq, head of R&D and chief medical officer at Elicio Therapeutics, also called out a branch of immuno-oncology in the article. "In 2024, I expect we'll see developments in technologies that increase the potency of T cell-based immunotherapies," he predicted. "I'm particularly excited about cancer vaccines because after years of setbacks in trying to develop vaccines that are safe and can also mount a durable immune response, I believe we're finally making headway."

Another area which is eliciting a lot of interest and was highlighted in Scrip was obesity and cardiometabolic drugs, particularly in light of the spectacular commercial success experienced by Novo Nordisk as it moved its glucagon-like peptide-1 agonist semaglutide into the obesity arena as Wegovy. Michael Shah, a pharmaceutical industry analyst at Bloomberg Intelligence, expects that obesity will remain in the spotlight in 2024, citing one of the class of 2023, Eli Lilly's Zepbound (tirzepatide) as another market driver. Jay Galeota, CEO of Kallyope, suggested that excitement in this area could move beyond GLP-1 agonists, citing increasing interest in other types of incretin-based therapies.

Another commentator, Jay Backstrom, CEO of Scholar Rock, highlighted the drawbacks of the GLP-1 approach. "As GLP-1 therapies for obesity continue to gain traction, the substantial loss of lean muscle mass poses a challenge toward achieving sustainable and healthy weight loss," he said. "Therapies that can preserve muscle mass will be of utmost importance as GLP-1 uptake accelerates and patients undergo longer durations of treatment. In 2024, after decades of long interest, I anticipate our industry will realize the market opportunity for novel muscle-targeted therapies that block myostatin across a spectrum of cardiometabolic disorders and neuromuscular diseases."

Lastly, after decades in the doldrums, there is renewed optimism in the frequently intransigent area of CNS diseases. "The way we saw major advances in oncology in the 2000s and 2010s, I believe we will see major progress in treatments for central nervous system and neurodegenerative diseases in the 2020s," Rachel Lenington, chief operating officer of Athira Pharma, predicted. PureTech Health's CEO Daphne Zohar concurred. "I'm particularly excited about neuroscience where the unmet need is massive and [there are] some exciting new therapeutics in the pipeline," she stated, noting further that "there is a huge unmet need for patients struggling with mental health disorders."

Excitement is also building in exploring further uses of drugs that have only previously been used recreationally, to open new therapeutic avenues. "Traditional treatments for conditions such as major depressive disorder or substance use disorder, including ketamine and serotonergic psychedelics, promote neuroplasticity to help repair damaged neurons

in the brain; however, this can take anywhere from weeks to years," commented Mark Rus, CEO of Delix Therapeutics. "I expect we will continue to see a greater focus on mental health and increased research into novel compounds, such as the neuroplastogens, which are engineered with scientific rigor to produce functional neuroplasticity on a much faster time scale and effectively mitigate harmful effects, and physically repair the brain," he continued. Potential for advances in this difficult area could be literally mind-blowing.

Ongoing progress across the panoply of therapeutic areas seems guaranteed, as sure as the sunshine follows the rain. Things have been warming up nicely for pharma this decade, which has also proven pharma's ability to react quickly to an emerging threat. The outlook seems fine and settled for an industry which continues its fight to save humanity. We just need to sort out climate change now.

I hope you've enjoyed this year's survey of the global weather patterns circulating around the global pharmaceutical industry. Come rain or shine, we'll be back next year to take the industry's temperature once again.



A satellite view of Earth from space, showing the curvature of the planet and various geographical features like continents and oceans. The image is used as a background for the text overlay.

About the Author

Ian Lloyd

Senior Director, Pharmaprojects
& Data Integration

Ian Lloyd is the Senior Director of Pharmaprojects and Data Integration, overseeing the content and analyst services for our drug development solution. He supports clients in their drug pipeline data requirements and inquiries, providing insight into the best search strategies to answer their drug-related business questions and identifying and analyzing trends in pharma R&D. For the past 31 years, he has authored the “Pharma Annual R&D Review” and its new active substances (NAS) launches supplement. This has become a must-have industry report for those seeking to identify the changing fortunes of drug R&D. Ian joined Pharmaprojects in 1987, when it was part of PJB Publications. Prior to joining Citeline’s Pharmaprojects, Ian previously worked in molecular biology as a research assistant at the University of Bristol.

Additional research and reporting by Scrip’s Alexandra Shimmings, and Pharmaprojects analysts Sydney Enokawa, Tollan Bell, Abdirazak Mohamed, Joseph Toebbe, and Arbesa Bela.