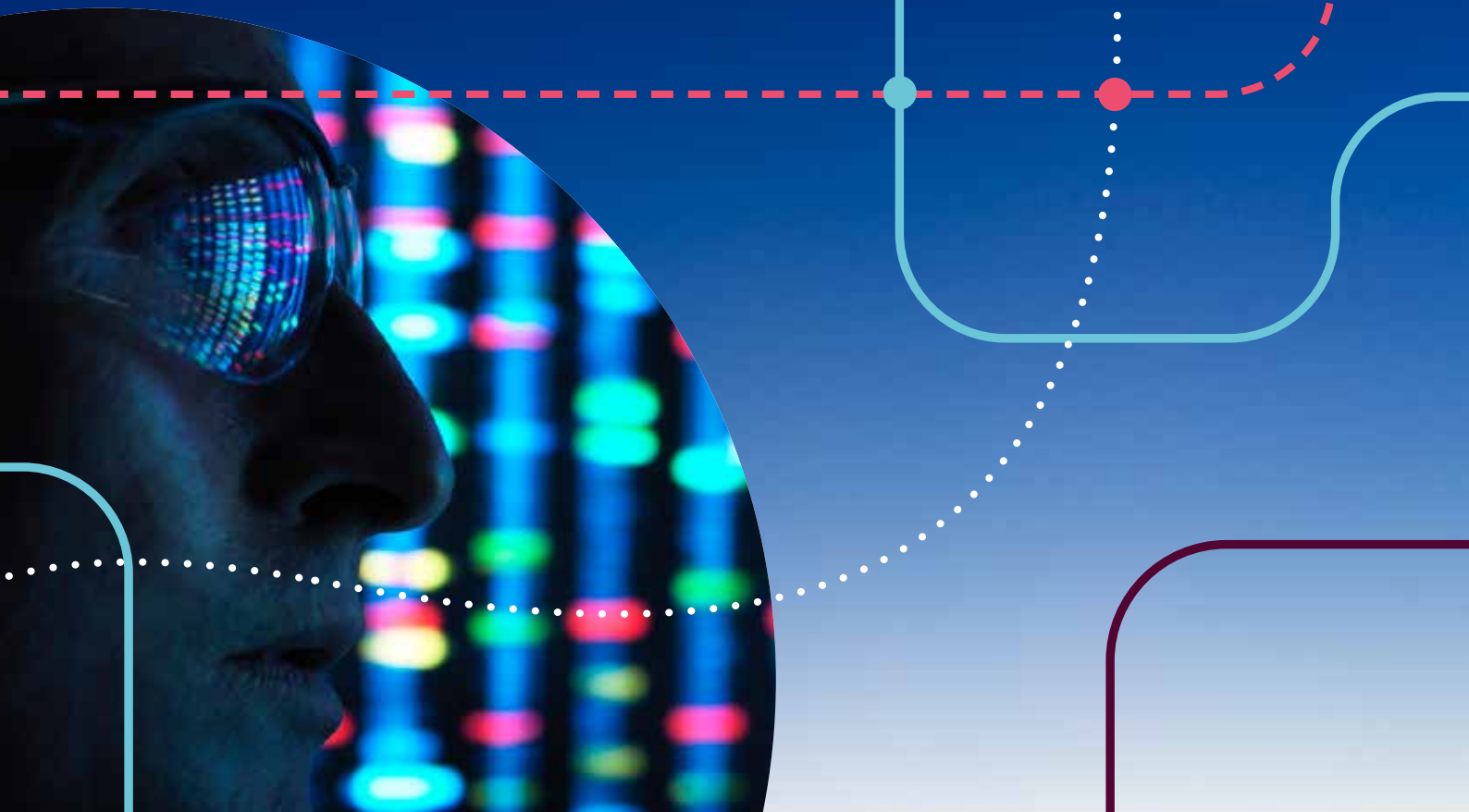
White Paper

Citeline Pharma Intelligence

30th Anniversary of Pharma R&D Annual Review

Pharma R&D
Annual Review 2022
Navigating the Landscape

Discover more at:
pages.pharmaintelligence.informa.com/rdreview



Introduction

Welcome to Pharmaprojects' 2022 review of trends in pharmaceutical R&D. For 30 years now, I've been taking an annual look at the evolution of pharma R&D, and in this article I'll examine the state of play at the start of 2022.

We'll assess industry trends by examining the pipeline by company, therapeutic area, disease, target, and drug type, using data from Pharma Intelligence's Pharmaprojects, part of the Citeline suite of products, which has been tracking global drug development since 1980. This report will be followed up by our annual supplement reviewing the New Active Substance launches for the year just passed. But here, we will be packing our suitcases and heading to the airport to embark on a journey which circumnavigates the pharma world, travelling through both familiar territories and off the beaten track, to discover the direction of travel of the industry as it resets its compass following a turbulent couple of years, which have been quite a journey to say the least.

Regular readers of this report (which has been running since 1993 so is presented here in its thirtieth edition) will know that in recent years, I've threaded a different theme through each edition, to highlight points, to draw analogies, and to add a little local colour into what could otherwise be a rather lengthy voyage through the dreary suburbs of statistics, charts, and tables. Themes selected so far have included astronomy, movies, the natural world, music, food and drink, and, last year, science fiction. Last autumn, as, in the UK at least, everything seemed to be pretty much back to normal COVID-wise, I selected travel for the theme of the 2022 report, expecting that this year would be the one in which everything returned to standard and, accordingly, we would all jet off on multiple holidays, making up for the lack of travel opportunities we have had to endure since the start of 2020. Sadly, at the time of writing, it looks like I was a little premature, as the world is currently being engulfed by the biggest wave of disease thus far, thanks to the highly infectious Omicron variant. However, I'm hopeful that, by the time you read this, the wave will have largely broken, and that with most people triple-jabbed or recently infected (or, as in my case, both), the virus will have no place left to go, and we will at last be moving from the pandemic to the endemic stage of this cruel disease. So, I'm still optimistic that this year will be the one where foreign vacations come back with a bang. Therefore, like a good eco-tourist, I'm sticking to the prescribed path.

Our modern jet-set lifestyle and the incredible interconnectedness of the contemporary world are often cited as major reasons why SARS-CoV-2 could spread so rapidly worldwide and is why most countries closed their borders at some point as a result, stymying many a planned fortnight in Marbella. While this is undoubtedly true, it's worth noting that this isn't such a modern phenomenon as you might think. Spanish flu managed to wreak havoc across the entire world perfectly successfully without supersonic planes crammed with holidaymakers making intercontinental trips in just a few hours. Its progress was most likely exacerbated by large-scale troop movements at the end of the First World War, and while these were on a minute scale compared with today's (or, more accurately, pre-2020's) level of international migration, it still managed to sweep across the globe in less than a year. Even in mediaeval times, there was sufficient global trade and travel to export a disease such as bubonic plague around the world efficiently. Of course, with the benefit of hindsight, the responses in some countries to COVID were sluggish, even to the point of a fiddling while Rome burned in some cases. But the reality is that any sufficiently infectious zoonosis, unless contained immediately at the point of origin, is going to go global at a mile a minute, and this really isn't anything new.

Tourism and travel for the masses though is indeed a wonder of the modern age. Until the 1960s, international trips were really only the province of the wealthy, and indeed, as a child, my family never ventured beyond the shores of the UK. My parents' generation just didn't have that option, with my mum never having boarded a plane to this day, and my dad only having done so as part of his conscripted National Service to Egypt. All that changed when cheaper airline travel arrived in the seventies and going abroad for a summer holiday became de rigueur. My generation (I'm 57) thus have had a completely different experience of the world. According to one of those interactive maps that pops up on Facebook from time to time, I've visited 43 countries so far, with journeys to all corners of the globe and trips to every continent (not counting Antarctica). I feel truly fortunate to be living in an age where opportunities to experience so many far-off cultures and habitats first-hand exist for many of us. In fact, having that taken away temporarily was one of the hardest things to endure during the past two years of the pandemic. What was once a privilege now seems like a right.

I've been lucky to undertake some of that international travel as part of my job, partly because pharma is the epitome of a global industry. This may be one of the reasons why the public has traditionally regarded it with distrust (faceless multinational corporations etc), but it's also the reason why it could mobilize on such an extraordinary scale in response to COVID. One of the fascinating, previously under the radar, aspects of pharma R&D which the pandemic cast new light on was the global supply chain. It became evident that it's not enough to just develop a vaccine: having all of its constituent parts for manufacturing of the vaccine antigen and its delivery vector, which in themselves, probably come from many different international sources, is just the start. You then need glass vials, cold storage, transport, needles, PPE, and trained vaccinators. Plus, you need infrastructure – something often found wanting outside of the richer, developed countries. Getting the vaccines to people all over the world has been putting together a jigsaw where the constituent pieces are scattered across the globe. And, as has often been stated with respect to vaccination, no-one is safe until everyone is safe. The rise of Omicron is testament to that.

Travel also seems like a good theme as the R&D process itself is very much like a journey. At the start of drug development, the destination must be decided on and then the logistics of the trip must be determined. Having done your planning, the preclinical phase is like gathering

everything together before embarking on your travels: getting your candidate and checking its efficacy, toxicity, and delivery is a bit like getting your passport, tickets, and foreign currency together and packing your suitcase before you leave the house. Then, you're ready for take-off. After arriving at your destination, you're getting the lie of the land, working out how things work in this new territory – a bit like Phase I trials. Having settled in, you're willing to become a little more adventurous, taking in the sights as you move into Phase II. And by Phase III of your holiday, you're growing in confidence and starting to try out a few phrases in the local lingo. Reaching the filing stage, you're beginning to feel like a native and contemplating retiring to this little piece of paradise. All that's left to complete the perfect vacation is to successfully launch yourself back home (no mean feat in the era of pre-departure COVID tests!).

Just like a holiday of course, there are lots of things which can go wrong at any stage of pharma R&D along the way. Many compounds never make it out of preclinical, akin to being refused boarding to your plane as you forgot to renew your passport. Arriving at your destination in human studies, things don't always pan out – the hotel often doesn't look like the pictures in the brochure. Even as your drug passes through the latter stages of its journey, something unexpected can go wrong – you can get lost after turning off the beaten track, or even have to cut your expedition short after one too many sangrias sees you spending a night in the local police cell. Modern travel, like drug development, is rarely devoid of stress, and is composed of many moving parts, which all need to align like the stars guiding an ancient mariner if you're to successfully complete your voyage.

As with travel, information is key if one is to effectively negotiate pharma R&D. For a vacation, you need the most up-to-date information, including timetables and maps. And you need to know how your resort has changed since your last visit. This is what this report intends to do. Using analogies from, and references to, the world of travel and tourism along the way, the Pharma R&D Report will act like the guidebook you purchase before you plan your trip – the Rough Guide to Pharma R&D if you like. We'll document how the land of drug development is changing, highlight some of the local points of interest which no-one can afford to miss, and also direct you to some of the more surprising and interesting secluded out-of-the-way places which you may not have discovered without using the local knowledge of our experts. So, hitch a ride with me and strap yourself in – I'll be your tour guide. It's time to journey into the centre of the R&D pipeline.

> "A journey of a thousand miles begins with a single step."
>
> **Lao Tzu**

Checked-In and Ready for Take-Off: Total Pipeline Size

Pharma breaking the sound barrier as it zooms past 20K

As we wake up and excitedly make our departure on the first day of our trip, let's get this show on the road by taking a bird's eye view of the scope of the territory we'll be exploring, by looking at the total number of drugs currently in the pipeline. As usual, it's worth starting off with a definition of what we mean by pipeline, since all of the analyses in this report will be focusing on this set of drugs. By pipeline, we mean that we are counting all drugs in development by pharmaceutical companies, from those at the preclinical stage, through the various stages of clinical testing and regulatory approval, and up to and including launch. Launched drugs are still counted, but only if they are still in development for additional indications or markets. Drugs whose development has had the brakes put on, or whose development is complete, are not included. All data were collected on 4 January 2022.

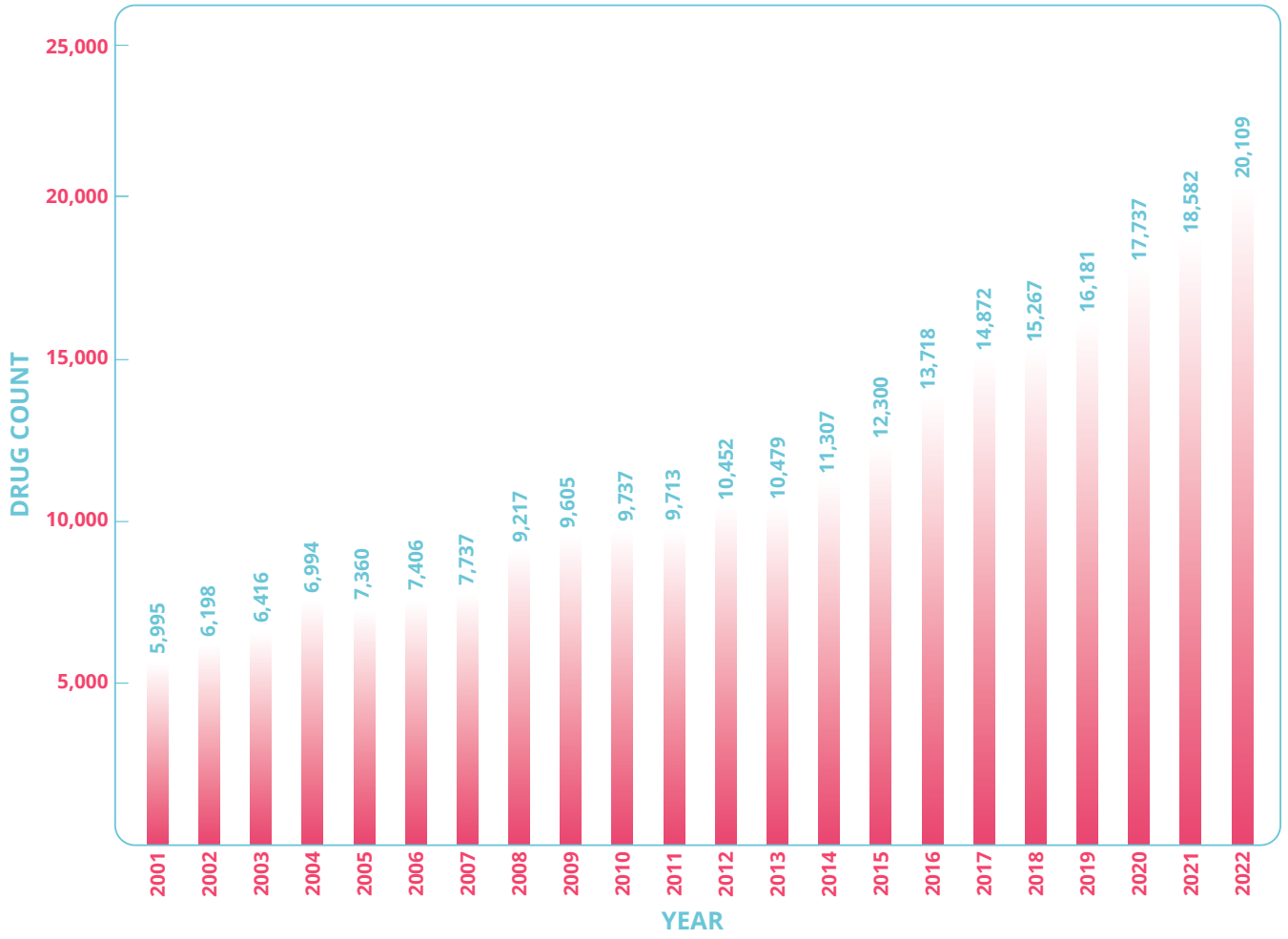
Like planning a holiday to a country with an unstable regime, it hasn't been so easy to predict what we would find on landing in 2022. COVID-19 undoubtedly had a disrupting effect, coming as it did two years ago apparently from nowhere. It was certainly a case of all-hands-on-deck as pharma made a titanic effort to avoid the COVID iceberg, but did the pandemic rock the boat and cause everyone to man the lifeboats, or are we now pursuing plain sailing as we chart towards calmer waters? If you're interested in a broad-brush answer to this question, perhaps a look at the total number of drugs currently in R&D would float your boat.

Well, Figure 1 appears to show that the industry is cruising, and it is full steam ahead. Hitting 20,109 pipeline drugs, pharma appears to have the wind in its sails, if you'll excuse the mildly mangled metaphor. This represents an expansion rate of 8.22% over 2021's number – a growth rate coming in close to twice the 4.76% seen over the previous 12 months. It's not as big as 2020's 9.62% but, given that 2019 and 2018's figures were 5.99% and 2.66%, respectively, it's at the upper end of the figures seen over the past five years, and considerably above the five-year average of 6.25%. It also takes the pipeline size beyond the magical 20,000 number for the first time.

This means that there are 1,527 more drugs in development than there were this time last year, whereas last year the uplift was only of 845 drugs. As we'll see later, new additions of COVID-related agents came in at a much lower rate during the past 12 months, so they don't account for this big increase. It seems that pharma is, however, sailing along at some speed, buoyed by the prevailing winds resulting from the crisis.

In fact, 6,343 new drugs were added to the Pharmaprojects database during 2021 – considerably more than the 5,544 added during 2020 and leaving the 4,730 added the year before that in its wake. Undoubtedly there is some effect here of better detection of new drugs thanks to our ever-improving editorial methods, but this is surely only part of the story. It really does feel this year that, rather than being hampered by the pandemic, the industry has been turbocharged by it. And this may be an underestimate of its growth rate. This time last year, around 4% of active drugs had not been updated for more than 12 months, whereas this year, we have reduced that figure down to 0.5%. The end result of the

FIGURE 1:
Total R&D pipeline size, by year, 2001–22



Source: Pharmaprojects®, January 2022

review which we conduct for many drugs that haven't been updated for over a year is a move of that drug to the 'No Development Reported' (NDR) status, thus taking it out of the Active data set. So, improved scrutiny of drugs for which little new information has been released can lead to more being marked as Inactive, thus actually lowering this year's Active total. Without this improved scrutiny, we could be looking at double-digit growth for the total pipeline size.

The speedboat of pharma is indeed generating considerable churn in the R&D ocean. As well as the 6.3K new drugs added, over the course of the year a total of 221 drug discontinuations were confirmed and a further 4,658 were moved out of the Active data set as a result of being marked as NDR – actually similar figures to those seen in 2020. Fortunately, any suppression in the overall pipeline size brought about by improved editorial practice has a systematic effect, so comparisons within each analysis will remain perfectly valid.

Still, nearly six and a half thousand new R&D candidates joining the pipeline in a single year is quite extraordinary. How do these drugs break down by therapeutic area? No fewer than 38.8% of them have an anticancer focus, with neurologicals coming in second at 14.7%, and

anti-infectives, where most of the COVID-related entities reside, only coming in third with 12.0% of new drugs. Interestingly, this is well below the 17.5% of new drugs which are focused on one or more rare disease – of which more later.

Does its rapidly expanding waistline imply that everything is all ship shape and Bristol fashion in the world of pharma? As always, we caveat the excitement at a bigger-than-ever pipeline with the warning that the vast majority of these drugs are still prelaunch, so are costs with risks attached, rather than successful revenue-generators curing patients. Has pharma followed on from a record-breaking year in 2020 when, despite the best efforts of the pandemic to derail it, it had its most successful year ever, delivering 82 New Active Substances (NASs) to the market? While we'll be dealing with the finalized list of 2021's drug debuts in the follow-up supplement to this report, early indications are that it was another very successful year, with over 80 confirmed NAS launches already, and this figure is set to rise. It does indeed seem then, that the pharmaceutical industry is continuing to chart the right course through the choppy COVID-infested waters.

"The world is a book and those who do not travel read only one page."

Saint Augustine

Arrival: The 2022 Pipeline by Phase

Early development surges as pharma gets its place in the sun

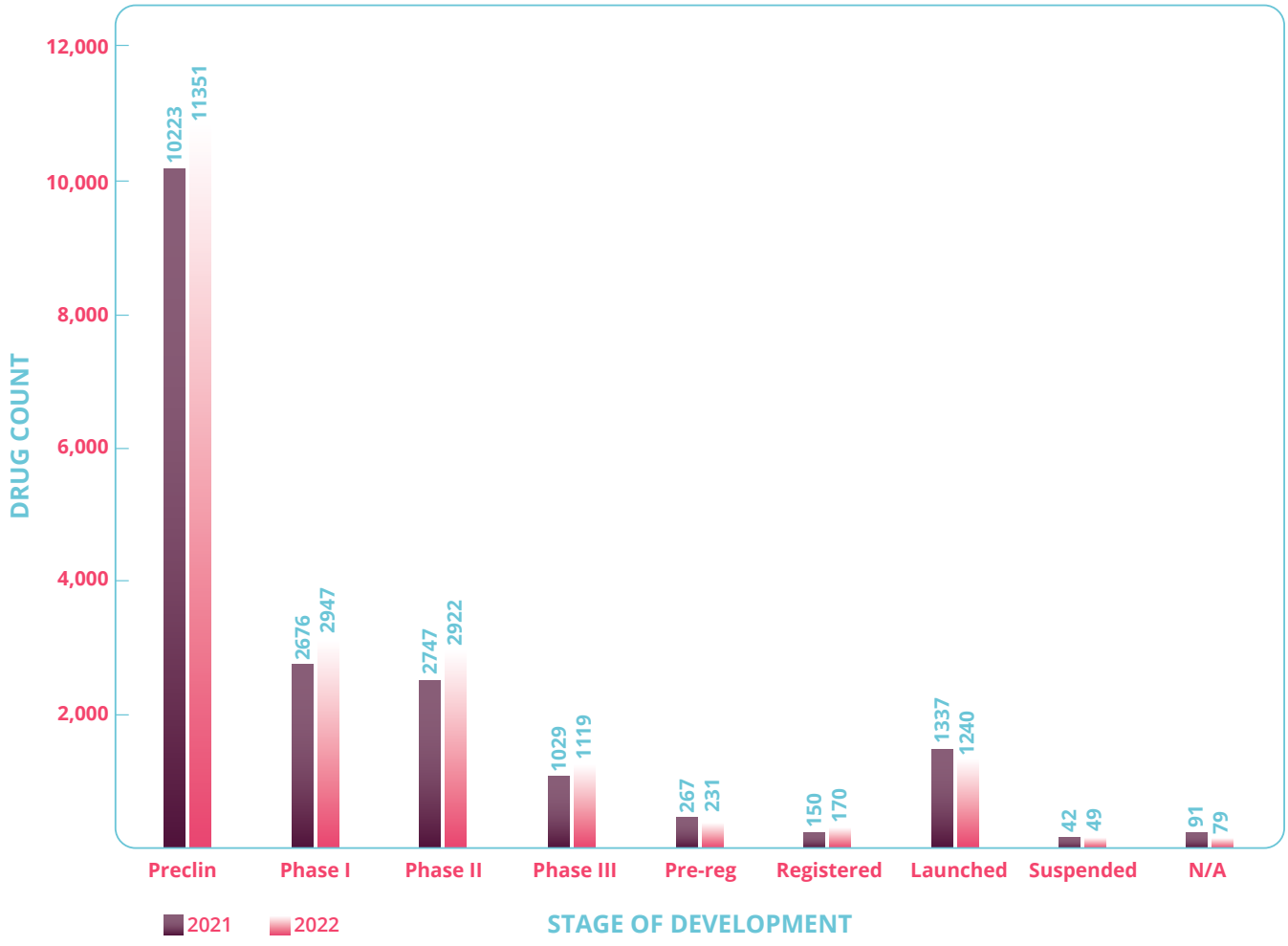
The pharmaceutical industry, like the travel industry, is always looking for something new. Another thing they have in common is a propensity for making lists and league tables. Depending on which travel magazine or website/blog you read, the hot new tourist destinations for 2022, as travel reopens, are Greenland (and its exciting sounding Disko Bay), Rwanda, and Turkmenistan, as well as the cities of Auckland, New Zealand (which seemed to feature in a few polls); Gyeongju, South Korea; and Oslo, Norway. These all sound like intriguing and innovative destinations to me, as someone who loves to try somewhere new.

Innovation and newness are also key to pharma, and perhaps unsurprisingly, the growth in the pipeline is concentrated at the more cutting-edge end of the development cycle. We can see this clearly if we break down the 20,109 drugs in the pipeline by their current global statuses – the most advanced stage of development each drug has reached in any country, for any disease, and by any company. This is what Figure 2 does.

You can see that the lion's share of pipeline expansion occurred in drugs which were still at the preclinical stage, with a growth rate here of a phenomenal 11.0%. Remember, all of these drugs have been confirmed by our analysts to be genuine development candidates authenticated as still being taken forward within the past 12 months – we don't just scrape the internet and add in any compound we come across. This is a considerable uptick on the rate of expansion in the preclinical pipeline witnessed in 2020, which was only 6.0%. An additional 1,128 drugs are in preclinical development compared with this time last year, although it's worth noting that it's at this phase that a lot of the churn noted earlier will have taken place, so there are not just more overall, but many more different ones this year compared to last. These drugs of course have a long way to go, but as the saying goes, "to travel hopefully can be better than to arrive".

The number of drugs in Phase I clinical trials also seems to have stepped up a gear. With 2,947 drugs at the Phase I stage at the start of 2022, pharma has definitely been putting its foot on the gas here. This represents a growth rate of 10.1%, outpacing the overall expansion in the pipeline and overtaking the 6.4% seen last year.

FIGURE 2:
Pipeline by development phase, 2022 versus 2021

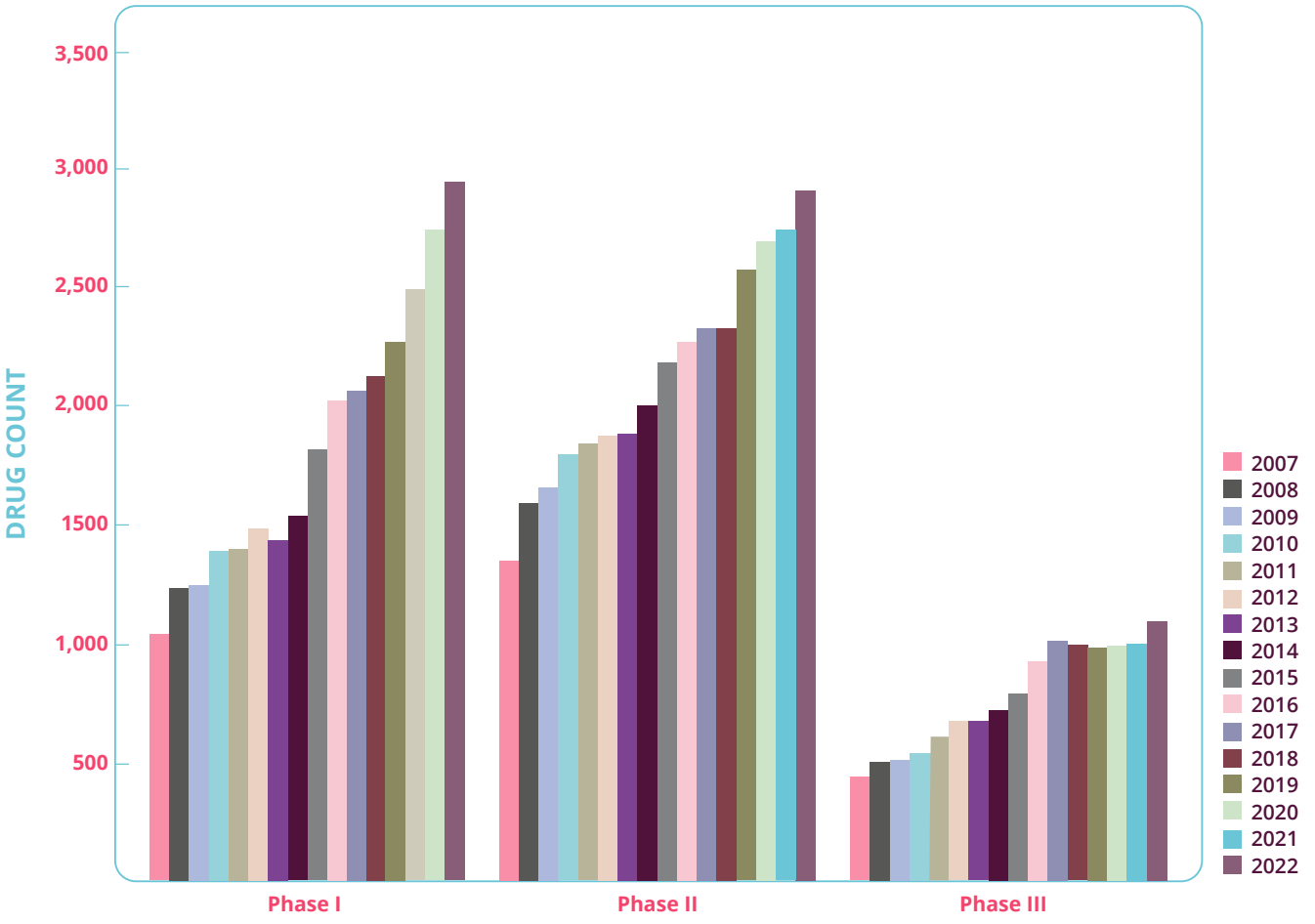


Source: Pharmaprojects®, January 2022
N/A: not applicable and is applied to companion diagnostics prelaunch

And whereas, at Phase II and Phase III were a paltry 2.0% and 0.9%, respectively, last year, this year pharma has been burning rubber here too, recording much more rewarding accelerations of 6.4% and 8.7%, respectively. Note that these data are a snapshot in time: the fact that there are roughly the same numbers of drugs in Phase II as there are in Phase I in no way means that virtually all drugs undergoing Phase I then progress serenely to Phase II. In fact, there is considerable attrition between the two Phases, but as Phase II development generally takes much longer, drugs 'pile up' at the Phase II stage. It's a bit like how a traffic jam builds up when the motorway goes down from three lanes to two.

For Phase III in particular, this represents something of a recovery after pharma suffered a bit of a breakdown in recent years, or at the very least was crawling along in the slow lane. This can be seen more clearly in Figure 3, which looks a little further back in time to see how trends in the numbers of drugs in clinical trials have changed over the past 15 years. You can clearly see that the numbers at Phase III have been idling in neutral in recent years, but that this year, they seem to have been hotwired into action somewhat. Similarly, it's clear that pharma is flooring the gas pedal more across the other clinical stages. While the numbers of drugs in Phase I and Phase II has always increased, the 2021–22 period really does see the industry tearing along in the fast lane, overtaking previous years and leaving them for dust.

FIGURE 3:
Clinical phase trends, 2007–22



Source: Pharmaprojects®, January 2022

These statistics certainly suggest that, rather than meeting its Waterloo in its battle with SARS-CoV-2, the industry was imbued with a new kind of Dunkirk spirit. The wobble in trial activity seen at the beginning of the outbreak was mercifully short-lived.

In terms of industry-sponsored clinical development, in 2020 there was a 12% decrease in confirmed trial starts for diseases other than COVID-19, pushing the number of trial starts for drug development not specifically focused on vaccines or treatments for the new coronavirus back to a level last seen in 2015. However, in 2021 we saw a modest 2% increase in confirmed trial starts compared to the 2020 numbers. "A recovery in trial starts is to be expected given many sponsors have now started to embrace newer ways of both recruiting for and running clinical trials, plus the wide variation in size and type of COVID-related restrictions in different regions over time", comments Andy Benson, Senior Director of Trialtrove, our sister product which tracks individual clinical trials in the same way Pharmaprojects does drugs. "And we can expect the number of confirmed 2021 trial starts to tick up a little more, as delayed reporting of trial activity (particularly for Phase I trials and in some territories) still has an impact when analysing trial data, so that 2% increase could be a few percentage points higher when the dust settles", he continued. It seems that those running clinical development, after sailing close to the wind for a bit, have indeed weathered the COVID storm and are now experiencing something of a following breeze.

"One's destination is never a place, but a new way of seeing things."

Henry Miller

Meet Your Fellow Travelers: Top Companies

Familiar faces on the tour are joined by Chinese newcomers

It's probably a cliché, but travelers are often divided into two types: the adventurous and the safe. Those in the former travelers group always like to go somewhere new, enjoying nothing more than the thrill of heading off-piste, negotiating challenging terrains or unfamiliar languages, and generally pushing the envelope to get that new experience or that rarely seen vista. Then there are those who don't like to be taken too far out of their comfort zones, returning to the same familiar resort year after year, and choosing the egg and chips option from the English menu in the local taverna. I would like to think that I fit firmly into the former camp (although having said that, I have been to Ibiza 15 times!), but I can certainly understand that some have a fondness for their regular haunts and the greater chance of relaxation that familiarity brings.

The latter type of tourist would certainly be feeling at home looking at this year's chart of the top 25 companies by the size of their R&D pipelines (Table 1). There are no unfamiliar faces in the top 15 at all, which comprises exactly the same 15 companies as last year, with very little jostling for new positions either. It's a sixth year with the largest R&D empire for Novartis, although the company's pipeline did contract slightly from 232 to 213 drugs. It also once again originated the most drugs. However, it had a slightly less successful year, only being involved in two first launches, unlike in 2020, when it delivered three. It's still looking over its shoulder at its compatriot Roche, which is runner-up again, but has posted a bigger fall in its pipeline size, putting more road between the two. The remainder of the top five – Takeda, Bristol Myers Squibb, and Pfizer – each reported that their pipeline world was shrinking slightly too.

The biggest climber in terms of places within the top 10 was AstraZeneca, up three places but with only four more drugs, so not really in the conquering Everest scale of ascents. The British company had something of a chequered year, maximizing its feat of being the first to market with a COVID-19 vaccine early in the year, but finding its agent falling out of favour as the mRNA vaccines from Pfizer/BioNTech and Moderna overtook it. Only Sanofi and Eli Lilly out of the top 10 also reported growing numbers of R&D projects, with the latter the sole member of the upper echelon for which the trend can be positively reported as upward.

The stagnant or slightly declining pipeline tallies in the top 10 can at least in part be attributed to very low activity amongst the big hitters in the mergers and acquisitions arena. Novartis acquired Cadent Therapeutics early in the year, while Pfizer hitched its wagon to the star of Trillium Therapeutics, and Lilly chose Protomer Technologies as its fellow traveler. AstraZeneca's modest rise can probably be accounted for by its completion of a traveler more sizeable acquisition, Alexion Pharmaceuticals. However, both Sanofi and Merck & Co bucked the trend by buying six and four firms, respectively: Sanofi thought Kymab, Tidal Therapeutics, Kiadis Pharma, Translate Bio, Kadmon Holdings, and Origimm were just the ticket; while Merck made headway acquiring OncoImmune, Pandion Therapeutics, VelosBio, and, in the year's most significant deal, Acceleron Pharma. But against this backdrop, four of the top 10 (Roche, Takeda, Bristol Myers Squibb, and Johnson & Johnson) paddled their own canoes and stayed out of the M&A game completely – a most unusual state of affairs, but a case of whatever floats your boat.

TABLE 1:
Top 25 pharma companies by size of pipeline

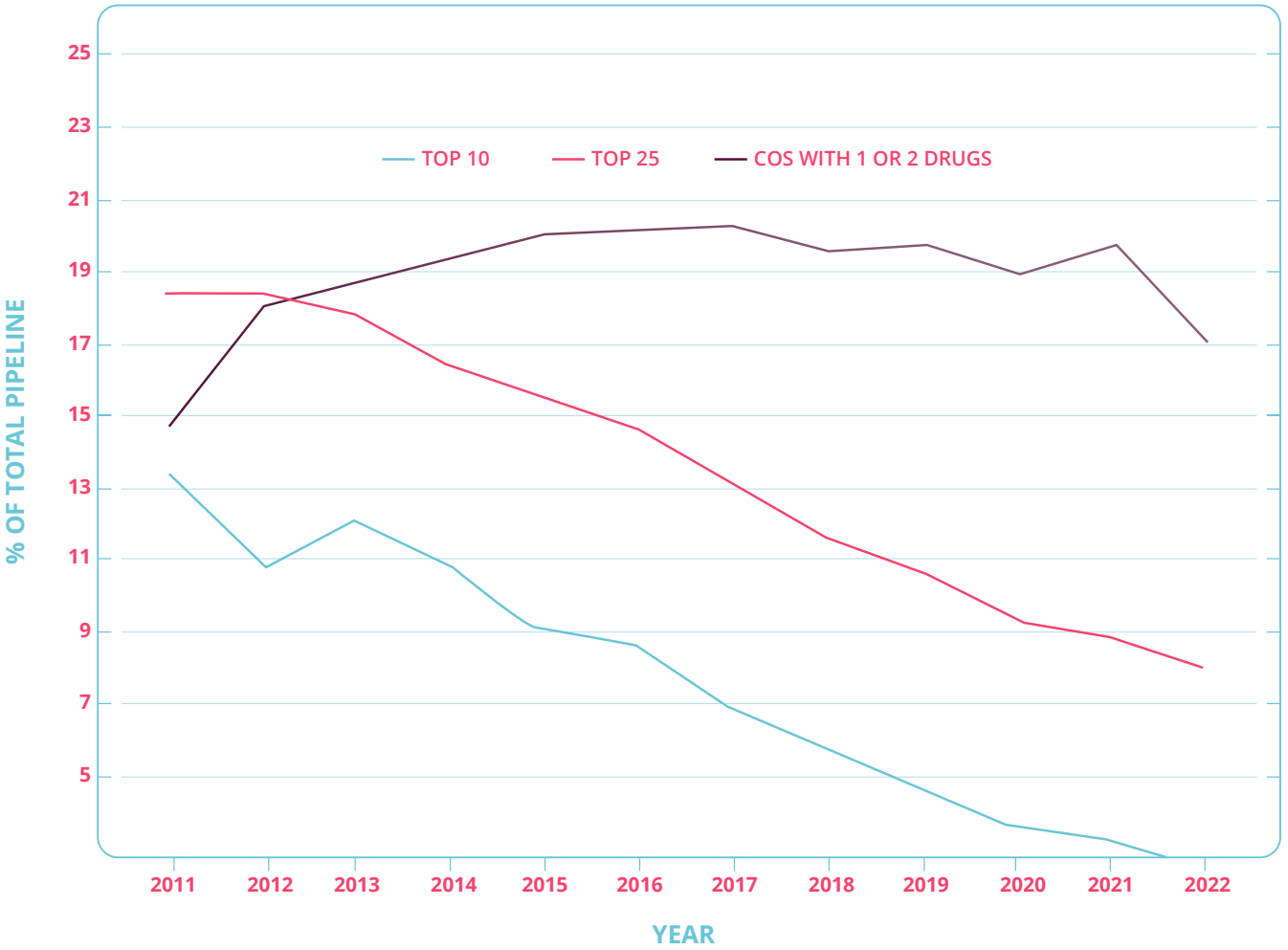
POSITION 2022 (2021)	COMPANY	NO. OF DRUGS IN PIPELINE 2022 (2021)	NO. OF ORIGINATED DRUGS 2022	TREND
1 (1)	Novartis	213 (232)	129	↓
2 (2)	Roche	200 (227)	120	↓
3 (3)	Takeda	184 (199)	68	↓
4 (4)	Bristol Myers Squibb	168 (177)	98	↔
5 (6)	Pfizer	168 (170)	101	↔
6 (9)	AstraZeneca	161 (157)	89	↔
7 (5)	Merck & Co	158 (176)	77	↓
8 (7)	Johnson & Johnson	157 (162)	86	↔
9 (10)	Sanofi	151 (141)	87	↔
10 (11)	Eli Lilly	142 (126)	76	↑
11 (12)	GlaxoSmithKline	131 (113)	67	↑
12 (8)	AbbVie	121 (160)	44	↓
13 (14)	Boehringer Ingelheim	108 (97)	79	↔
14 (13)	Bayer	105 (108)	76	↔
15 (15)	Otsuka Holdings	93 (95)	46	↔
16 (37)	Jiangsu Hengrui Pharmaceuticals	89 (52)	80	↑↑
17 (21)	Amgen	83 (77)	64	↔
18 (17)	Eisai	80 (85)	41	↔
19 (22)	Astellas Pharma	75 (76)	43	↔
20 (20)	Daiichi Sankyo	75 (78)	40	↔
21 (16)	Gilead Sciences	72 (95)	45	↓
22 (24)	Regeneron	68 (64)	41	↔
23 (66)	Shanghai Fosun Pharmaceutical	68 (30)	48	↑↑
24 (26)	Biogen	66 (64)	19	↔
25 (27)	Sumitomo Dainippon Pharma	66 (61)	47	↔

Source: Pharmaprojects®, January 2022

Overall, though, the landscape for deals through 2021, while not exactly a desert, was somewhat sparsely populated, with 116 mergers and acquisitions reported across the year, down quite a bit from the 142 we reported for 2020. It looks like the 'stay at home' advice induced by COVID was being followed at the corporate transaction level to some extent too.

One new frontier has opened in our top 25 chart this year however: China. For the first time, we see not one, but two Chinese-headquartered companies have left the runway and entered the stratospheric heights of pharma R&D. Jiangsu Hengrui enters the table at number 16, soaring up from 37, with a colossal 71.2% increase it is portfolio size. Meanwhile, Shanghai Fosun Pharmaceutical makes an even steeper ascent, surging 43 places upwards with a pipeline swollen by 127%. A further Chinese Young Turk, BeiGene, sits at the gates to our chart, at number 26. All in all, this represents something of a landmark moment for Chinese pharma R&D. It's often (erroneously) stated that the only manmade structure you can see from space is of Chinese

FIGURE 4:
Share of the pipeline contributed by top 10 companies, top 25 companies, and companies with just one or two drugs, 2011–22



Source: Pharmaprojects®, January 2022

construction – the famous Great Wall. But it's certainly fair to say that, after a number of years of building a presence at a quite extraordinary rate, novel pharma R&D from China is finally on the map.

Biogen and Sumitomo Dainippon are the only other newcomers to the top 25 this year, but the former of these is just rebounding back in the chart at number 24 and was in the list of leading companies two years ago anyway. Falling out of the rarefied sky of this chart were Evotec (down 11 places to number 29), Servier (down eight to 31), CSL Limited (down three to 28), and Ligand Pharmaceuticals, which fell somewhat more precipitously from 19 to 32, with a pipeline a third smaller.

How do we square the circle of seeing such a sizeable growth in the overall pipeline rate when 14 of the biggest 25 pharmaceutical companies are all reporting actual contractions in their pipeline size? At first glance, it might seem akin to more international visitors arriving somewhere even though the jumbo jets landing there are carrying fewer people.

As Figure 4 shows, the perception that the biggest companies are generating fewer and fewer of the contents of the overall pipeline is indeed correct. The top 10 companies only produced 4.63% of the drugs this year, a new record low, down from 5.27%. Similarly, the top 25's percentage fell from 9.36% to 8.51%, less than half the figure it was a decade ago. However, the contribution from the industry's smallest companies also fell slightly this year.

The conclusion must be that it's in the mid-sized companies where most of the pipeline growth is occurring.

Nonetheless, the biggest companies are fulfilling a role in providing diverse pipelines, at a time when most smaller companies are tending to specialize in just a handful of therapeutic areas. Figure 5 demonstrates this ably. Note that there is double-counting in this graph, as drugs can be in development for more than one disease area.

FIGURE 5:
Disease focus areas of the top 10 pharma companies

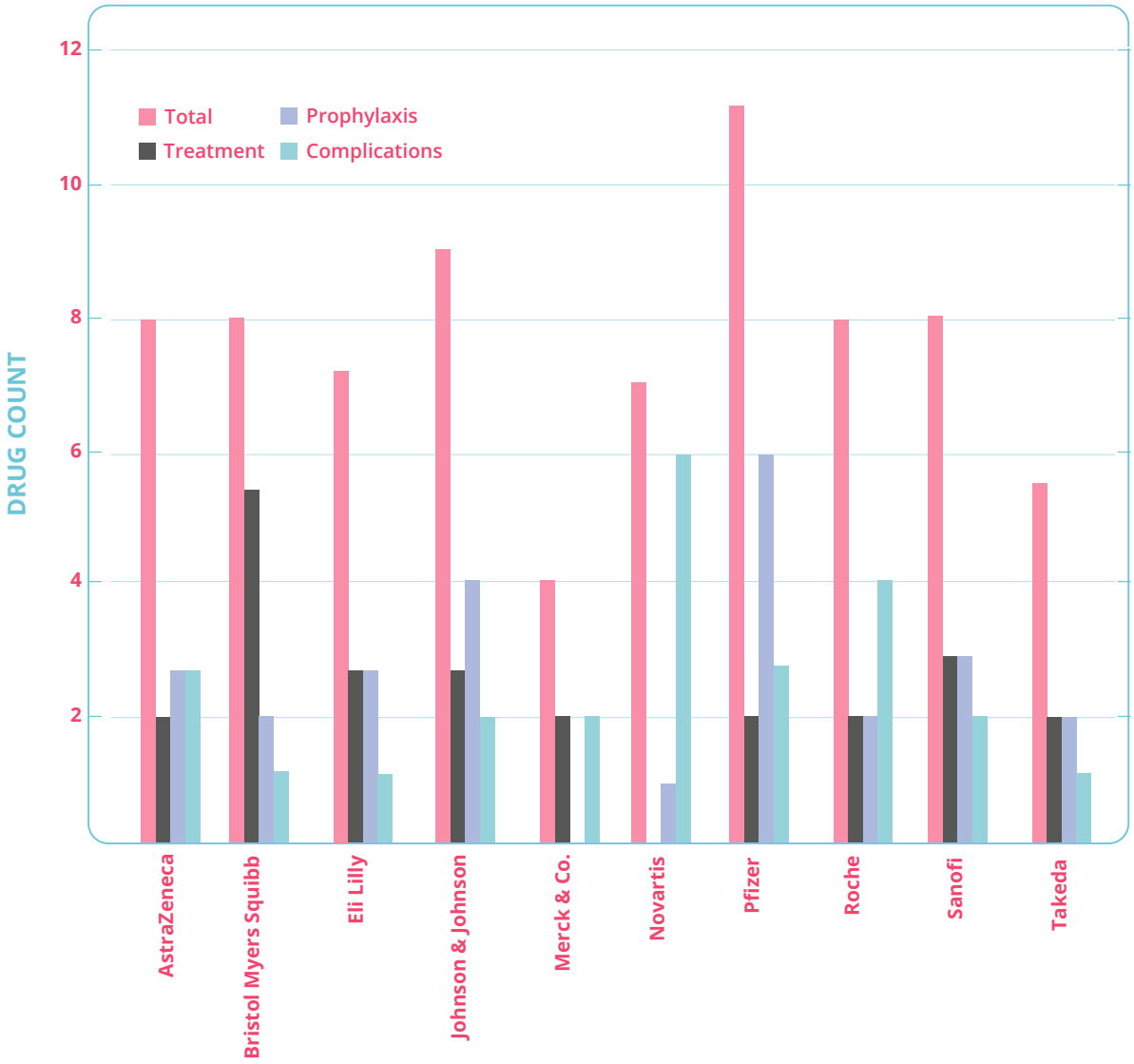
Source: Pharmaprojects®, January 2022

The top 10 most visited countries for tourism in 2020 didn't change much on the previous year, despite a radically altered world. However, compared to 2019, tourism dropped by approximately 74% in 2020, with a total of a billion fewer travellers over the course of the year, making 2020 the worst year in recent history. France managed to retain its long-cherished top spot, followed by Spain and the US. The list is completed by China, Italy, Turkey, Mexico, Thailand, Germany, and the UK. Early 2021 data suggests that the list for that year was looking exactly the same.

Our pharma company top 10 didn't change much either, but let's take a look at the pipelines of those 10 biggest of big pharmas in a bit more detail. Eight out of the top 10 companies have at least one drug in R&D in all 14 of our therapeutic areas, with just Eli Lilly avoiding antiparasitics and Merck & Co declining to develop hormonal drugs. Bristol Myers Squibb has the greatest concentration in a single therapeutic area, with 136 of its 168 drugs (81%) being investigated for at least one form of cancer. In fact, cancer represents the largest segment for all of these firms, with the exception of Eli Lilly, which has slightly more alimentary/metabolic drugs in development. Merck & Co has the largest presence in anti-infectives, its 56 candidates giving it one more than its closest rival in that territory, Sanofi.

Talking of anti-infectives, how have the big hitters been tackling COVID this past year? Figure 6 shows how their pipelines stacked up across the three indications we used to cover the disease: treatment, prophylaxis, and complications support. Pfizer leads the way with 11 agents in total, building considerably on the four it had this time last year. The company has arguably become the world leader here, on the back of its hugely successful collaboration with BioNTech in vaccinology, followed by what looks to be the best direct antiviral we have thus far in Paxlovid (nirmatrelvir). All of the top 10 bar two – Merck & Co and Takeda – have bigger COVID pipelines than they did this time last year, with Johnson & Johnson coming in second with nine products. Bristol Myers Squibb has the most antivirals, Pfizer the most vaccines/prophylactics, with Novartis leading the way on therapies for complications of SARS-CoV-2 infection (mostly anti-inflammatories).

FIGURE 6:
COVID-19 pipelines at the top 10 pharma companies



Source: Pharmaprojects®, January 2022

Let's also look in the opposite compass direction, from the world's currently most common disease, to its rarest. Just as many tour operators specialize in organizing travels to obscure, unexplored, remote and secluded destinations in the back of beyond, known to few tourists, pharma companies are increasingly seeing that there is money to be made developing drugs for little-known and unexplored conditions. Table 2 lists the top 20 companies by assets against rare diseases, and you'll see nine of our above top 10 companies featuring in the first 11 in this list. Of these, Novartis has both the most candidates and the highest percentage of rare disease R&D, although, further down the list, the much smaller Shape Therapeutics has the highest percentage of all. In this table, Eli Lilly has the lowest percentage with just 28.2% of its drugs being developed for a rare disease – in stark contrast to Novartis's huge 64.8%.

TABLE 2:
Top 20 pharma companies with a rare disease focus

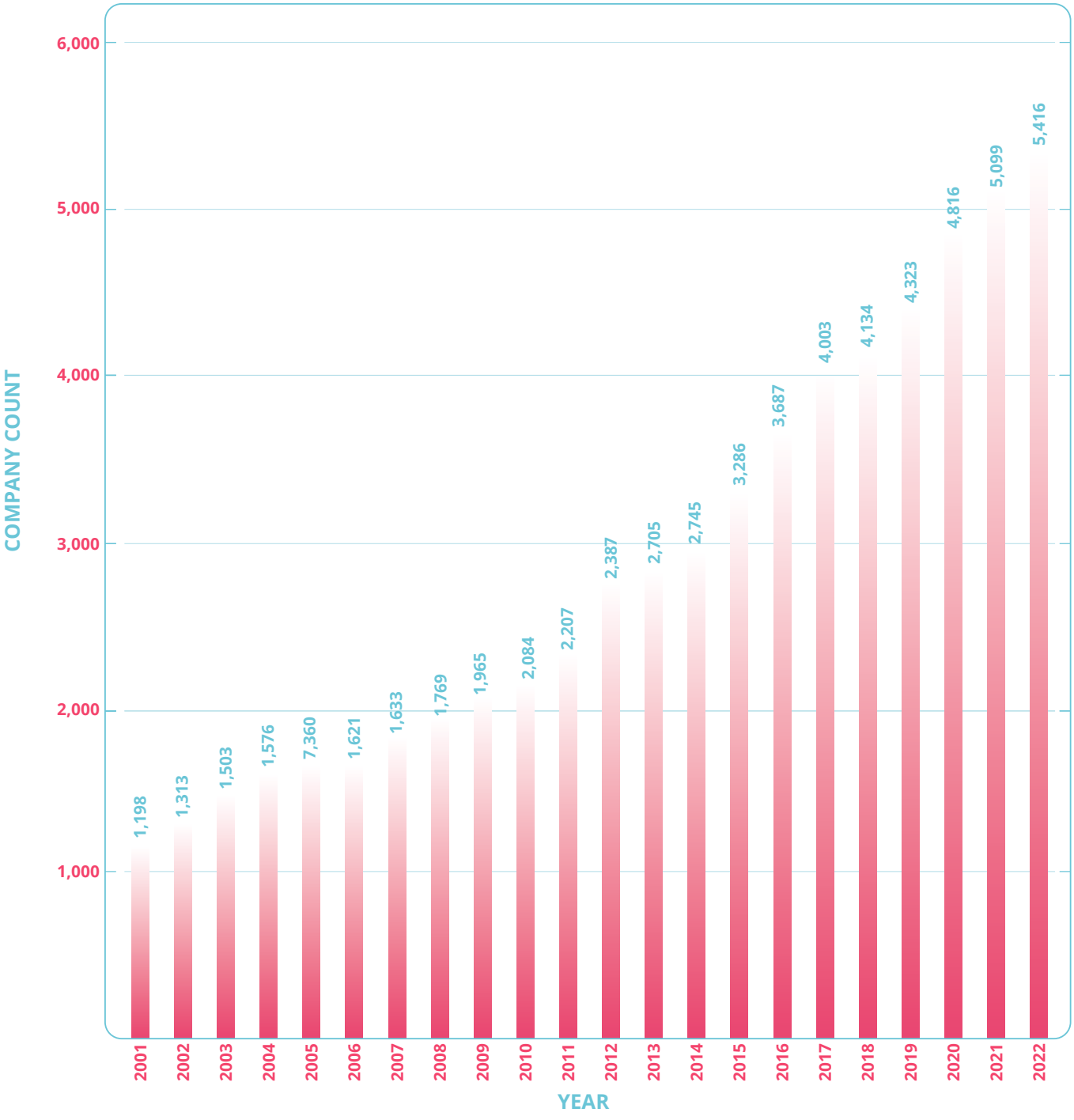
COMPANY	NO. OF DRUGS FOR RARE DISEASES	% OF PIPELINE
Novartis	138	64.8
Bristol Myers Squibb	108	64.3
Pfizer	98	58.3
Roche	96	48.0
Sanofi	96	63.6
Takeda	92	50.0
AstraZeneca	78	48.4
Johnson & Johnson	69	43.9
GlaxoSmithKline	68	51.9
AbbVie	59	48.8
Merck & Co	55	34.8
Amgen	54	65.1
Bayer	49	46.7
Biogen	40	60.6
Eli Lilly	40	28.2
Eisai	38	47.5
Otsuka Holdings	38	40.9
Shape Therapeutics	37	69.8
BeiGene	36	55.4
Astellas Pharma	34	45.3

Source: Pharmaprojects®, January 2022

NOTE: A rare disease is defined as one with a prevalence of 1 in 2,000 people in the EU, or affecting fewer than 200,000 people in the US (equivalent to around 1 in 1,600 people).

Just as world tourism continues to expand, pandemic-permitting, into ever more obscure destinations (snorkelling among the coral reefs in the tiny island nation of Niue, anyone...? No, I'd never heard of it either!), the world of pharma continues to grow, with more nooks and crannies in undiscovered companies than ever before. There are 5,416 companies involved in pharma R&D as of January 2022, an increase of 317, representing an expansion rate of 6.2% (see Figure 7 for the explosion in the number of companies across the past two decades). Like the comparable drug figure, these figures are also higher than those seen last year, but to a much lesser degree: the 2021 data added 283 companies at a growth rate of 5.9%. So, 2022 didn't post a stellar increase in the number of R&D firms like the 11.4% expansion we saw in 2020. The number of newly identified companies in the past year came into dock at 1,042, actually very slightly down on the previous year's record-breaking 1,055. But this again is a pretty extraordinary statistic. It means that 19.2%, or almost a fifth, of all companies developing drugs emerged in the past 12 months. And it also means that a net of 725 firms must have exited via the R&D departure lounge. Some of these will have ceased trading, while others may have gone into hibernation mode, and as they have not released new information on their drugs for over a year, we will have moved those drugs to inactive for now and the company thus ceases to be represented as active. Of course,

FIGURE 7:
Total number of companies with active pipelines, 2001–22



Source: Pharmaprojects®, January 2022

this departure lounge has a revolving door, and a small minority of these firms may yet be readmitted to R&D country.

Once again, the large continents of Big Pharma are augmented by huge archipelagos of tiny islands of emerging companies. This year, there are 759 firms with two drugs and a massive 1,883 with just one candidate, meaning that, taken together, these mini-enclaves account for almost half (48.8%) of all R&D firms. Despite both of these numbers increasing over the past year, from 733 and 1,849, respectively, the percentage they account for has fallen from 50.6%, which chimes with the fall in the percentage contribution from these companies to the overall pipeline that we witnessed earlier.

Since our travel-themed report this year naturally has a geographical bent, let's look at the favourite destinations for pharmaceutical research and development. Like our earlier list of top tourist countries, this hasn't changed very much since last year, as Figure 8 shows. The order of popularity remains the same, but beneath that, there are some subtle shifts. The percentage of companies headquartered in the US has fallen by 2%, while those in the Rest of Europe category fell by 1%. These falls came at the hands of one country – China. Its share of pharma companies leaps from 9% to 12%, a very significant expansion for a single year, reflecting the fact that the number of companies based in that country has shot up by an astounding 43.3%, from 522 to 792. There is truly a boom in R&D going on there.

FIGURE 8:
Distribution of R&D companies by HQ country/region, 2021

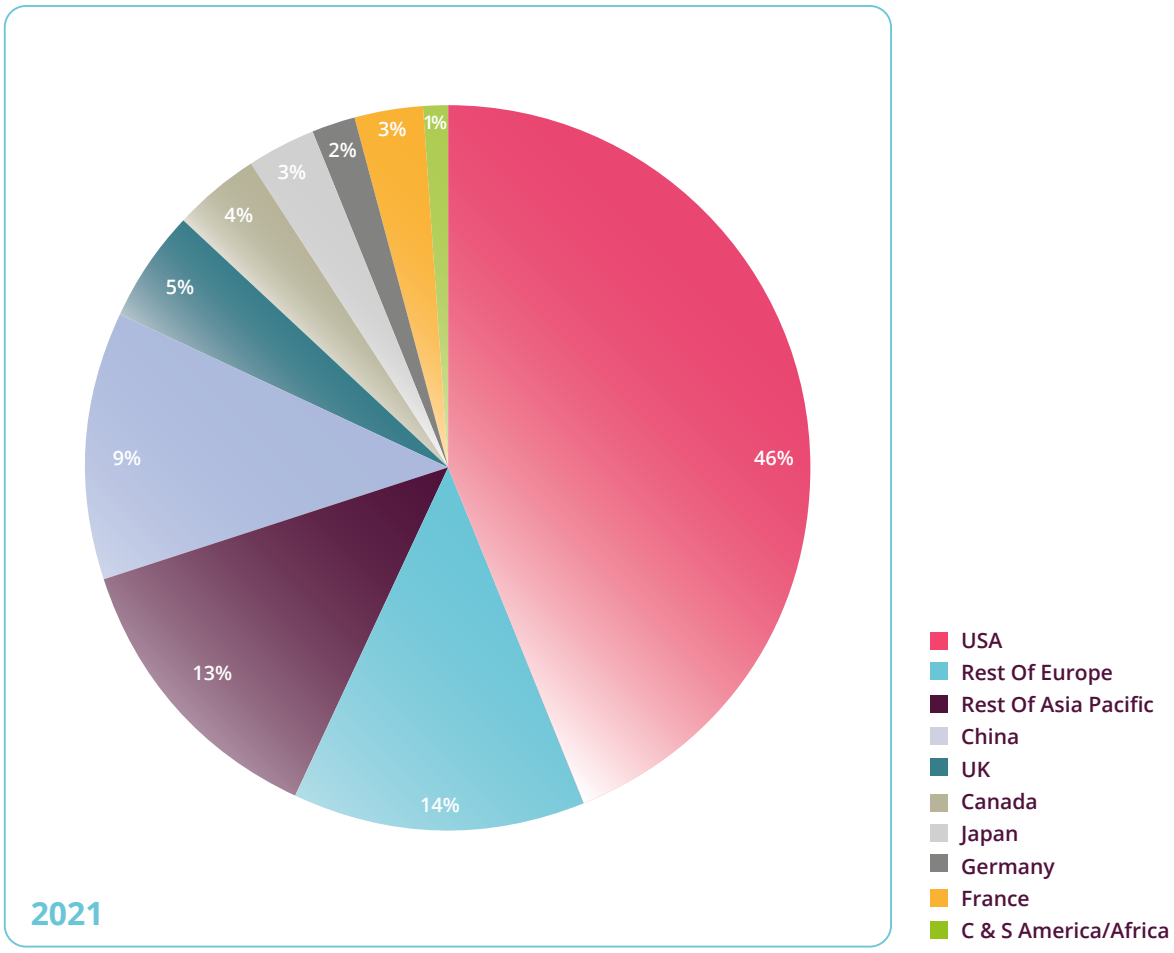
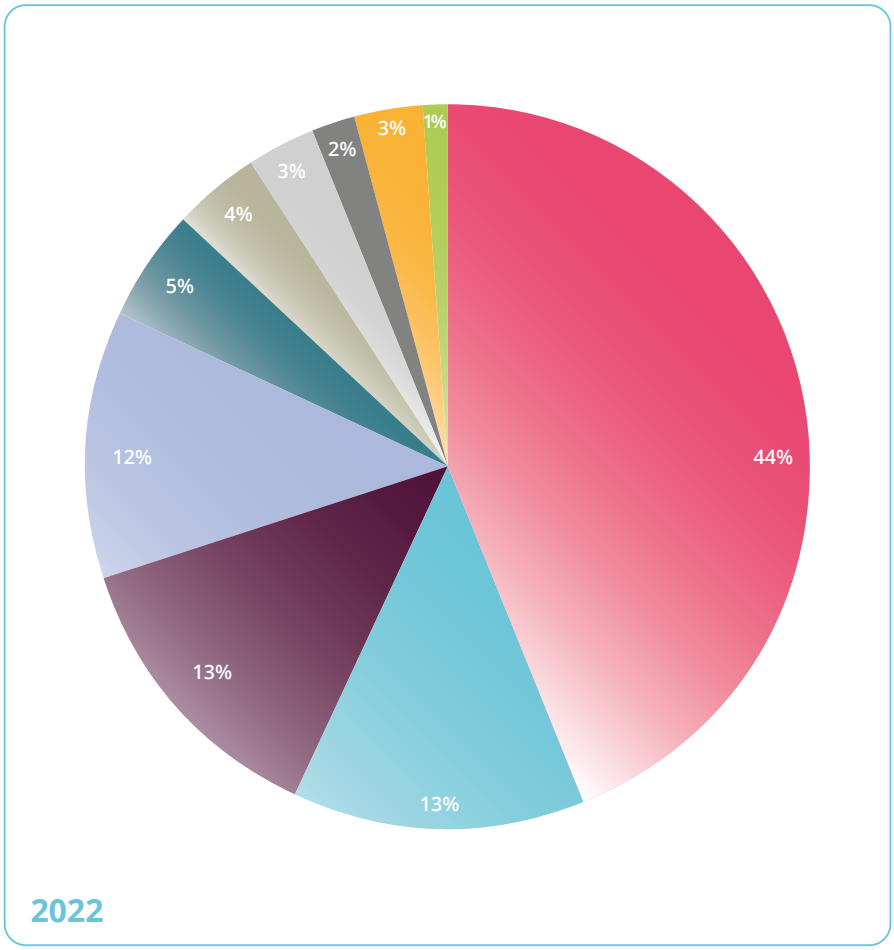


FIGURE 8:
Distribution of R&D companies by HQ country/region, 2022



While Figure 8 gives you the nationalities, if you like, of the travellers on the pharma tour bus, Table 3 gives more of a sense of where they are currently visiting. It looks at all drugs in active R&D and where their development is reported to be taking place. Each drug is counted once for each country it is in development in. Using this metric, the US comes in with 53.4% of all drugs in R&D being in development there, by some distance the biggest proportion for a single country. China here is the second biggest individual country, covering 20.8% of all drug R&D worldwide. The table lists all countries with over a thousand drugs in development, and it's notable that there is a strong presence from Central and Eastern Europe.

TABLE 3:
Where is R&D actually occurring?

COUNTRY	NO. OF DRUGS	% OF PIPELINE
US	10,736	53.4
China	4,189	20.8
UK	2,887	14.4
South Korea	2,627	13.1
Germany	2,299	11.4
Canada	2,182	10.9
France	2,057	10.2
Australia	2,010	10.0
Japan	1,931	9.6
Spain	1,909	9.5
Netherlands	1,680	8.4
Belgium	1,608	8.0
Italy	1,603	8.0
Poland	1,477	7.3
Sweden	1,402	7.0
Denmark	1,352	6.7
Switzerland	1,346	6.7
Hungary	1,258	6.3
Czech Republic	1,248	6.2
Austria	1,220	6.1
Taiwan, China	1,120	5.6
Ireland	1,086	5.4
Bulgaria	1,082	5.4
Finland	1,079	5.4
Portugal	1,032	5.1
Romania	1,026	5.1
Greece	1,018	5.1
Norway	1,014	5.0
Israel	1,006	5.0

Source: Pharmaprojects® January 2022

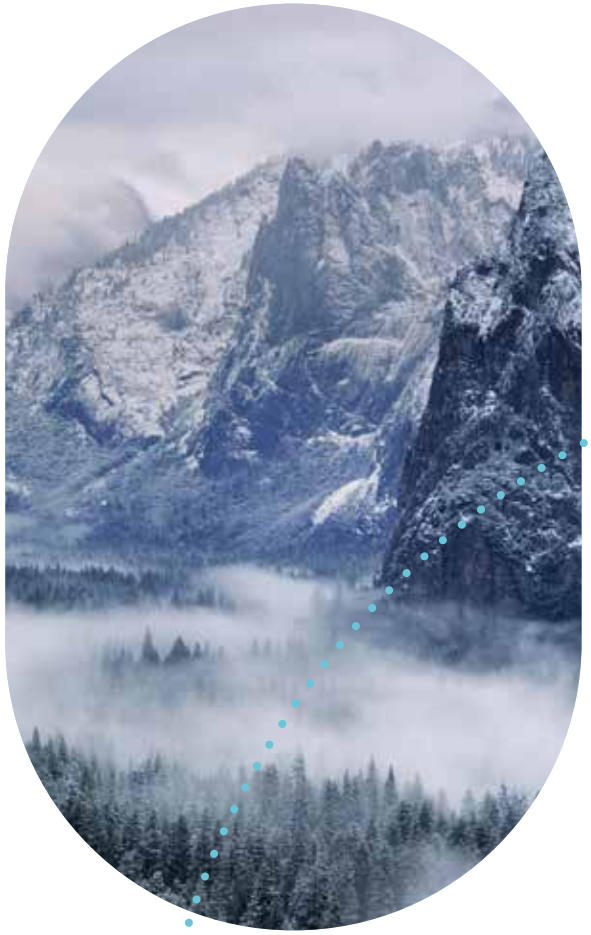
One of the beauties of twenty-first-century tourism, at least pre-COVID, and almost certainly again post-COVID, is how truly international it is. One can, pretty much, take a holiday anywhere in the world. Whether that might mean relaxing by the pool and enjoying the nightlife in a resort like Puerto Vallarta, skiing in the Alps, or trekking through the rainforests of Borneo, few places are off-limits to the tourist these days. Our company section this year again shows how totally international pharma R&D has become, especially now that China has come to the party big-time. And although tourism has taken a major hit from the pandemic, pharma R&D has clearly not – in fact the opposite is more the case. More drugs and more companies are offering an international smorgasbord of drugs in development.

"Travel makes a wise man better but a fool worse."

Thomas Fuller

Taking in the Varied Scenery: Top Therapies

Spectacular views of the mountains of anticancers



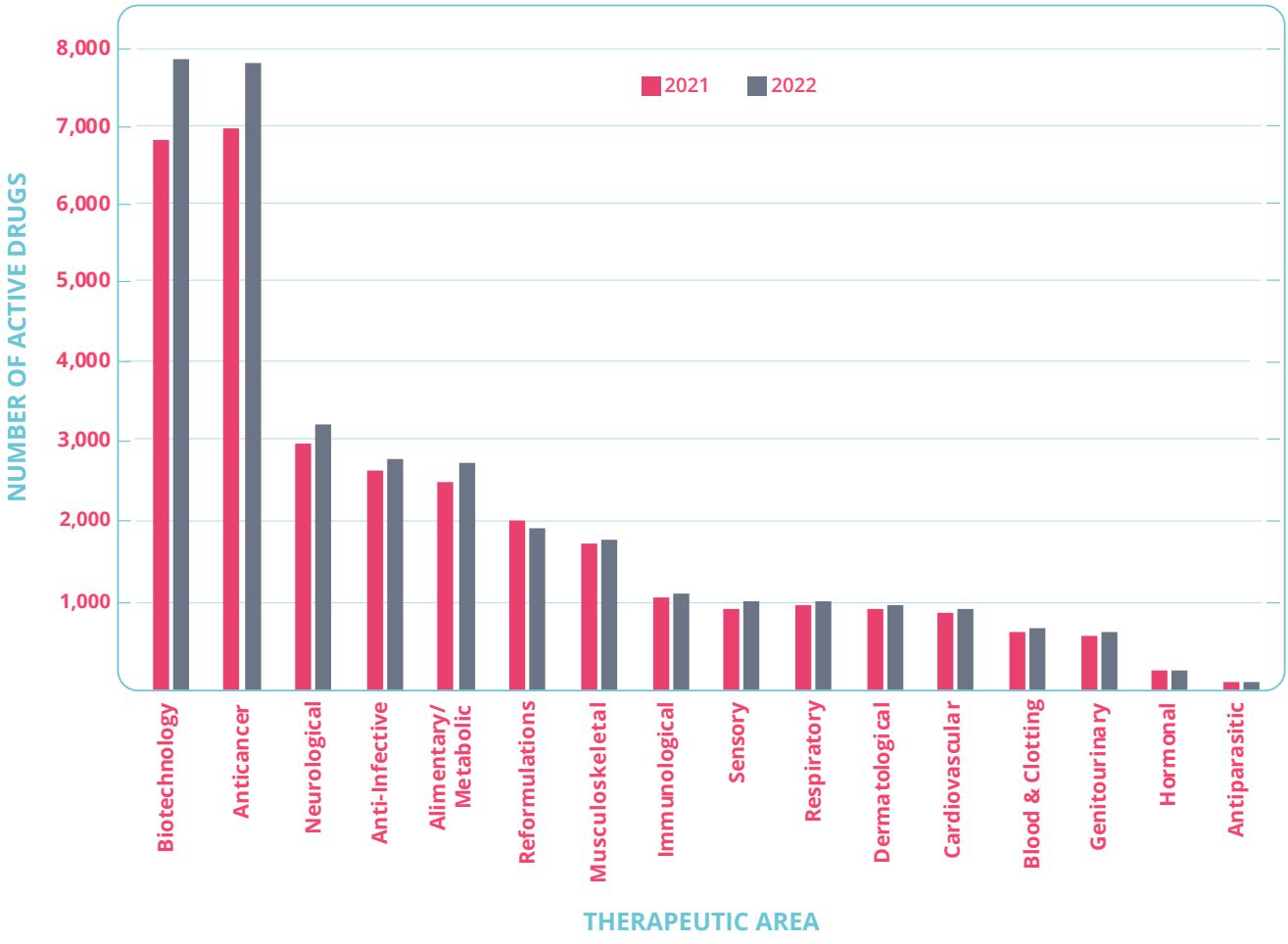
Our home planet is quite remarkable. Leaving aside the incredible piece of luck that life evolved here in the first place, it is physically very diverse and beautiful. Take one of my favourite places, California. Even in this one State, you can choose between the snow-capped mountains of the Sierra Nevada and the grandeur of the Yosemite National Park, the lush, wine-growing Napa Valley, the stunning beaches and coves of the central coast, giant redwoods in the north's National Forests or weird cacti in the south's Joshua Tree National Park, or the arid lifeless bake-off of Death Valley. Incredible diversity, and that is in just one place. The whole world has much more to offer.

Diversity is the key to pharma R&D too. We've already seen how the biggest 10 pharma companies throw their nets wide, and in this section, we'll take a deeper dive through the oceans of pharma R&D and discover how they are teeming with a rich array of different therapeutics, tackling a multitude of multifarious diseases.

Figure 9 breaks down drugs by broad therapeutic areas, and again, it's worth noting that drugs can be counted in more than one column here if they themselves have diverse disease targets. We will come back to the leading 'Biotechnology' group later (this isn't really a therapeutic area but it is currently included in this taxonomy). Therapeutically, cancer continues to top the league, with 7,772 drugs in its pipeline this year, an inflation-busting increase of 14.0%. Coming in second are neurologicals with a 7.8% rise to 3,301 candidates. Third-placed anti-infectives posted a more modest 4.7% expansion this year, indicating that the COVID-induced 22.4% growth seen last year was something of a one-off, but also that this expanded pipeline has been sustained, rather than falling back. Incredibly, every single therapeutic area grew last year.

Cancer's rate of growth actually increased across 2021. Figure 10 shows how, from a base-camp of comprising of 26.8% of all drugs in 2010, it has steadily ascended the mountain

FIGURE 9:
The R&D pipeline by therapy group, 2021 and 2022

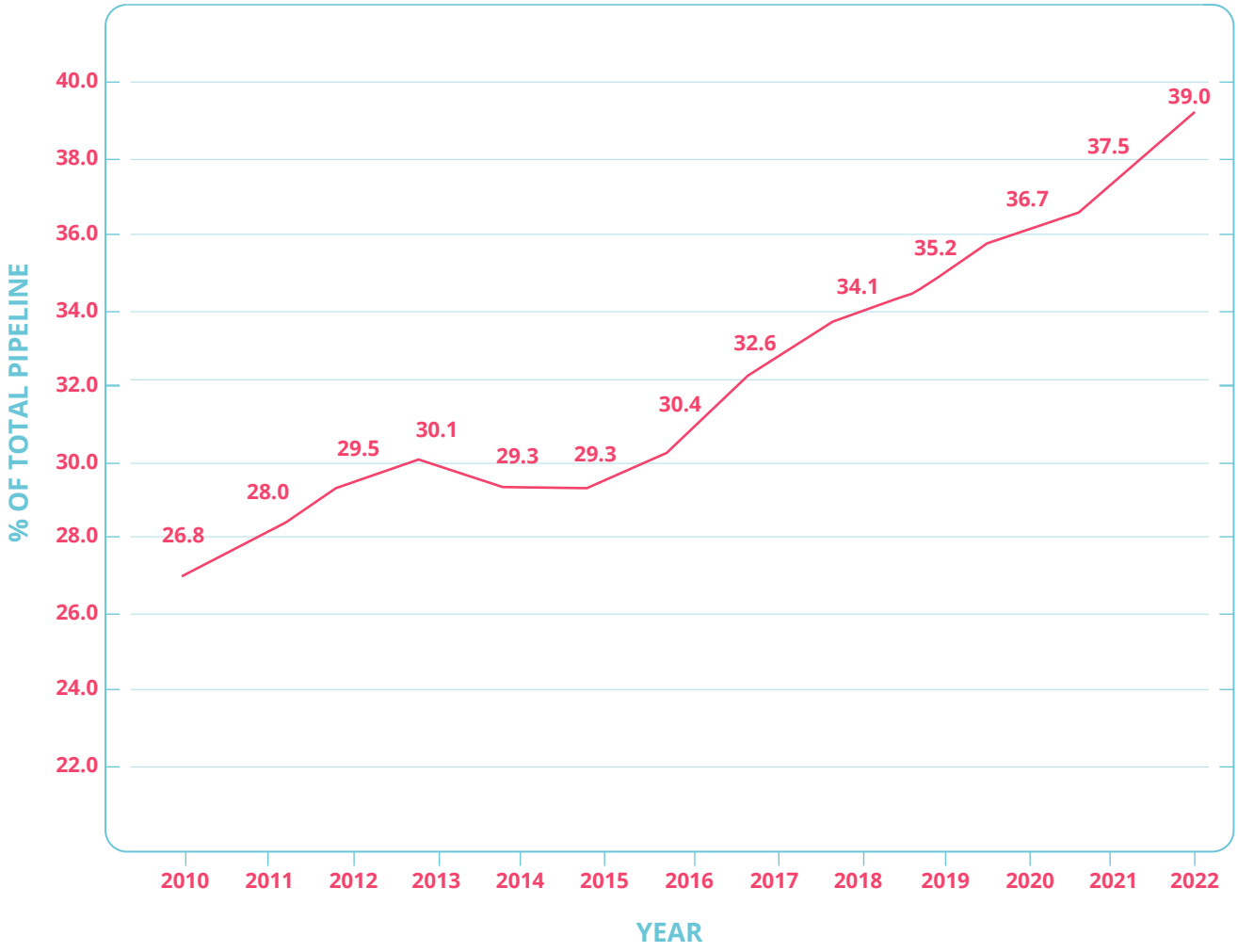


Source: Pharmaprojects®, January 2022

to the heights of 39.0% this year, a lofty position from where it can look down at all of the other therapeutic areas far in the valleys below.

If the therapeutic areas are the continents of pharma R&D, let's break things down further to the country level, and examine the pipeline by how it splits out across the 241 individual therapeutic categories. The 'Anticancer, immunological' category has the biggest landmass for the fourth year in a row, expanding its territory by a further 15.2%. Both the categories at the number two and number three positions also posted big increases, with the general anticancer category (Anticancer, other) up 17.7%, and Gene therapy swelling by a remarkable 23.3%. With jumbo expansions seen across the top three, the next 10 categories

FIGURE 10:
Proportion of the pipeline which is in development for cancer, 2010–22



Source: Pharmaprojects®, January 2022

post still significant, if slightly less humungous, rises. But unlike last year, there is not significant movement in placings, particularly within the top 10.

Returning to the top 25 this year are the Dermatological and Antiparkinsonian therapeutic categories, while Urological makes its debut at number 24. These are the only new entrants to this year's top 25, appearing at the expense of two cellular therapy categories which drop to just outside the chart (despite actually reporting increases in the sizes of their pipelines), plus a third covering reformulations. Cell and gene therapies continue to grow in popularity overall. Pharmaprojects' Cell & Gene Therapy dashboard provides additional filters for drugs in these fields, thus giving up a new, improved guidebook to better explore these destinations which, like a new resort, are rapidly developing and changing.

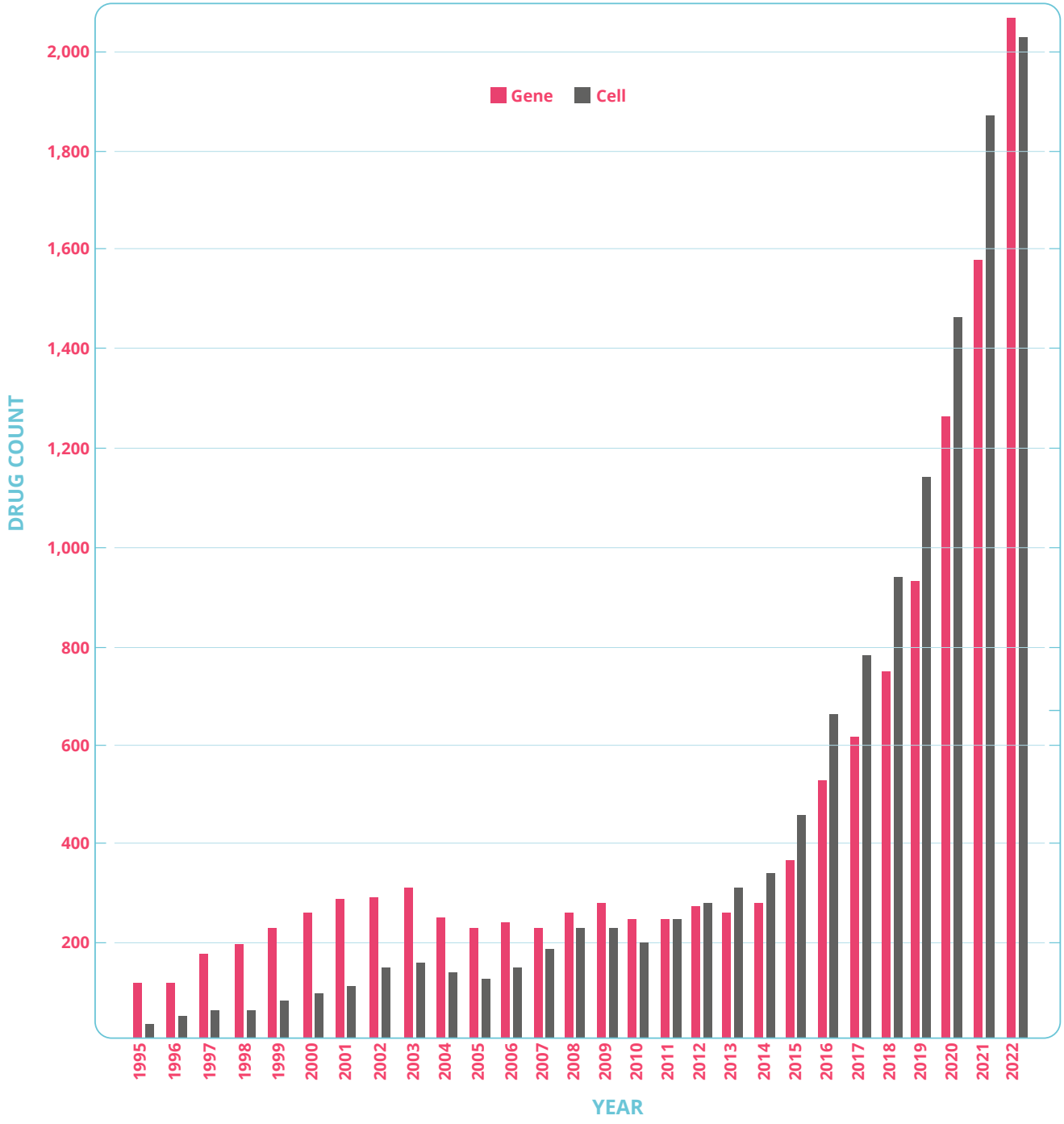
TABLE 4:
Top 25 therapeutic categories

POSITION 2022 (2021)	Therapy	No. of active compounds 2022 (2021)	TREND
1 (1)	Anticancer, immunological	4,275 (3,712)	↑↑
2 (2)	Anticancer, other	3,154 (2,680)	↑↑
3 (3)	Gene therapy	1,960 (1,589)	↑↑
4 (4)	Monoclonal antibody, other	1,277 (1,136)	↑
5 (6)	Antiviral, other	998 (858)	↑
6 (9)	Neurological	993 (781)	↑
7 (5)	Prophylactic vaccine, anti-infective	983 (843)	↑
8 (7)	Ophthalmological, other	953 (781)	↑
9 (10)	Anti-inflammatory	726 (639)	↑
10 (11)	Cellular therapy, chimaeric antigen receptor	720 (612)	↑
11 (12)	Antidiabetic	717 (569)	↑
12 (8)	Immunosuppressant	713 (542)	↑
13 (14)	Musculoskeletal	656 (521)	↑
14 (13)	GI inflammatory/bowel disorders	645 (482)	↑
15 (15)	Monoclonal antibody, humanized	602 (555)	↔
16 (37)	Cognition enhancer	600 (459)	↑
17 (21)	Respiratory	596 (446)	↑
18 (17)	Cardiovascular	595 (444)	↑
19 (22)	Hepatoprotective	573 (453)	↑
20 (20)	Neuroprotective	569 (426)	↑
21 (16)	Dermatological	504 (411)	↑
22 (24)	Antiparkinsonian	489 (384)	↑
23 (66)	Monoclonal antibody, human	488 (494)	↓
24 (26)	Urological	485 (347)	↑
25 (27)	Analgesic, other	484 (427)	↑

Source: Pharmaprojects®, January 2022

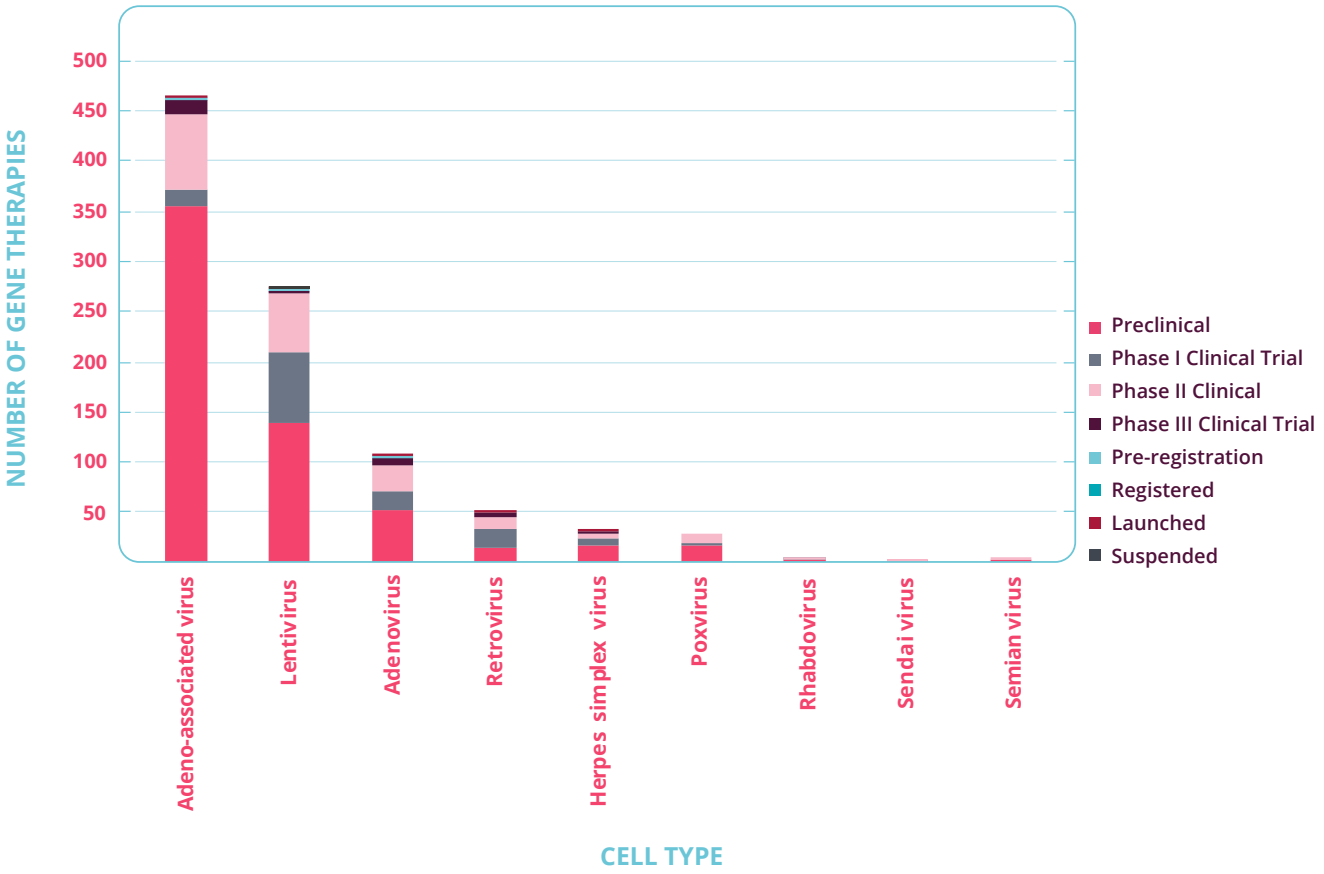
Firstly, Figure 11 shows how the rise of the two techniques seems to have been as intimately linked as Buda and Pest. Both therapies emerged in the mid-nineties, hit the doldrums a bit in the mid-noughties, but have really gone stratospheric in the past five years or so. Of course, there is something of a symbiotic relationship going on here too, since many therapeutics involve a combination of both techniques, such as CAR-T therapy, which is cell therapy but involves ex vivo genetic manipulation, and thus is classified as both cell and gene therapy. It is the emergence of such approaches which has been driving the explosion in numbers for both categories in the past decade.

FIGURE 11:
The ongoing rise of gene and cell therapy



Source: Pharmaprojects®, January 2022

FIGURE 12:
Viral vectors used in gene therapy

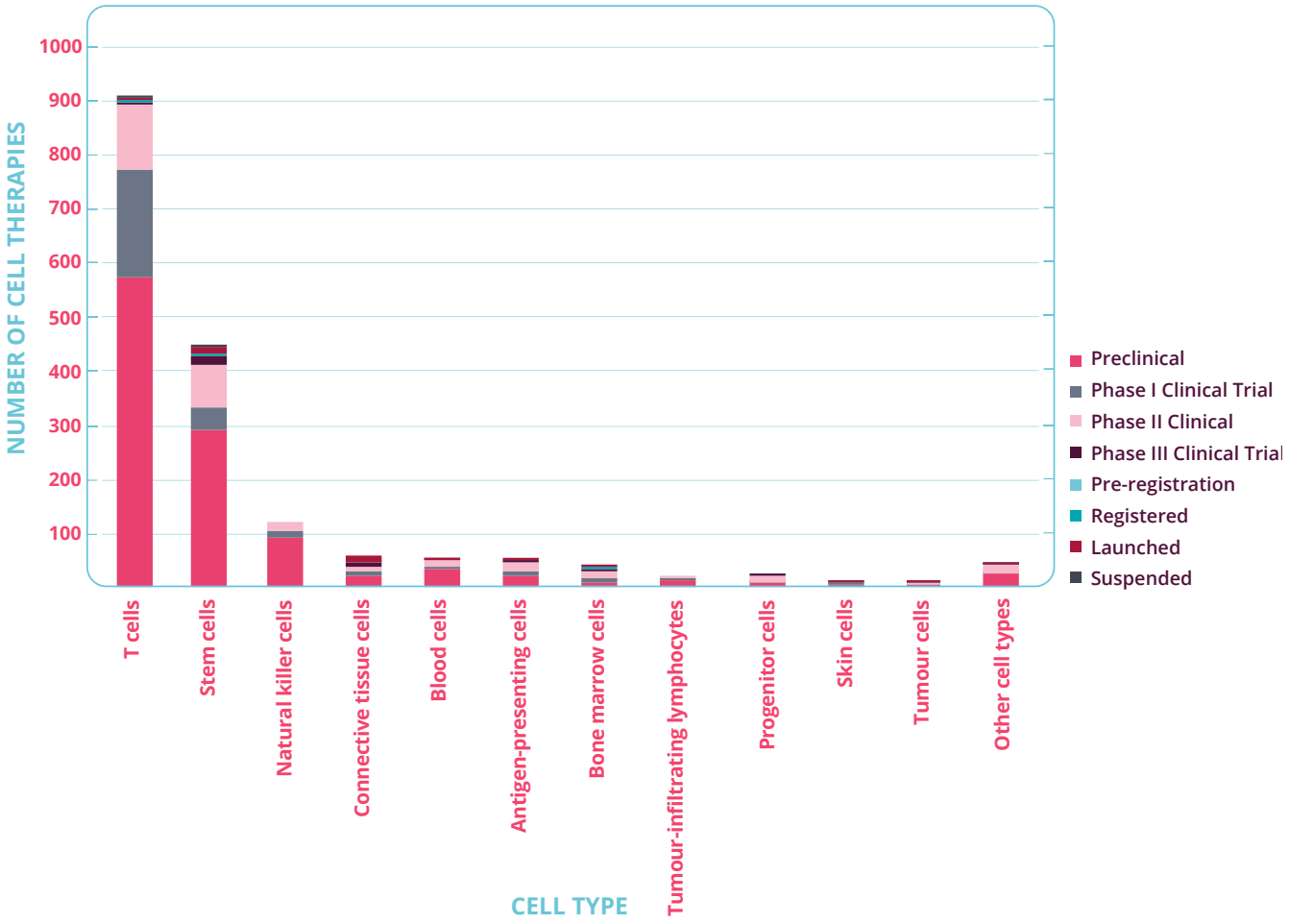


Source: Pharmaprojects®, January 2022

With a lot of focus on viruses and delivering viral RNA in the past two years, has this shifted the selection of viral vectors used in gene therapy? As Figure 12 shows, the boom town is adeno-associated virus (AAV) vectors; gene therapies using this vector increased from 341 in 2021 to 466 in 2022. This is also the vector used in several of the COVID-19 vaccines, including AstraZeneca's, so many of us (including myself) have received a dose or two of AAV in the past year. For gene therapy, AAV pulled ahead of what was its nearest rival, adenovirus, which was flat. The bigger change since the comparable graph last year is the rise in the use of lentiviruses, which are now the second most popular viral vector for gene therapy, used as they are in ex vivo gene therapy to transfect cells. This additional information was added in subsequent to last year's report, hence the apparent increase. Meanwhile, retroviruses similarly demonstrated robust growth, with herpes simplex viruses and poxviruses also coming in with in double-digit counts.

Our new indexing feature covering cell therapy projects allows us to take a voyage around the sea of different cell types now being used in this exceptionally hot area. Figure 13 shows the sun is shining brightly down on T cells; being the basis of the popular CAR-T strategy, it's not surprising that this cell type is basking in warm waters. Stem cells of various kinds are the other big beasts here, followed by the growth area of natural killer cells.

FIGURE 13:
Cell types used in cell therapies



Source: Pharmaprojects®, January 2022

Having viewed the R&D Google map from both a continent and country level, let's zoom in further and look at the individual resorts, cities, and national parks of the specific diseases for which drugs are under development. Table 5 lists the top 25. Breast cancer remains the most populous conurbation, but in the context of an overall 8.22% growth in the pipeline, its addition of just two extra drugs feels more like its city limits are shrinking. Coming up strongly in second place is non-small cell lung cancer, which reports a much more significant 11.5% growth. Still seemingly growing rapidly at number three, up from its number five debut position last year, is the category covering antivirals against SARS-CoV-2. The size of its urban sprawl grew by 22.4%, and it's worth remembering that two years ago, this disease wasn't even a tiny dot on the map yet. Elsewhere in the top 10, there are mostly a number of other forms of cancer which post more modest population growth. The only other exception to the oncological omnipotence is Alzheimer's disease at number eight, which could be said to be having a rather interesting moment in the sun. The controversial approval of Biogen's Aduhelm (aducanumab) seems to have given this area something of a boost, despite that drug's subsequent failure thus far to gain much commercial traction.

TABLE 5:
Top 25 diseases/indications

POSITION 2022 (2021)	THERAPY	NO. OF ACTIVE COMPOUNDS 2022 (2021)	TREND
1 (1)	Cancer, breast	888 (886)	↔
2 (2)	Cancer, lung, non-small cell	832 (746)	↑↑
3 (3)	Infection, coronavirus, novel coronavirus	677 (553)	↑↑
4 (4)	Cancer, colorectal	663 (653)	↔
5 (6)	Cancer, pancreatic	591 (570)	↔
6 (9)	Cancer, ovarian	530 (518)	↔
7 (5)	Cancer, prostate	509 (481)	↔
8 (7)	Alzheimer's disease	496 (436)	↑
9 (10)	Cancer, brain	485 (460)	↔
10 (11)	Cancer, leukaemia, acute myelogenous	462 (430)	↑
11 (12)	Diabetes, Type 2	445 (418)	↑
12 (8)	Cancer, melanoma	437 (423)	↔
13 (14)	Infection, coronavirus, novel coronavirus prophylaxis	436 (347)	↑↑
14 (13)	Cancer, myeloma	431 (409)	↑
15 (15)	Arthritis, rheumatoid	427 (435)	↓
16 (37)	Cancer, liver	407 (382)	↔
17 (21)	Cancer, head and neck	377 (357)	↔
18 (17)	Parkinson's disease	377 (340)	↑
19 (22)	Cancer, gastrointestinal, stomach	373 (358)	↔
20 (20)	Cancer, lymphoma, non-Hodgkin's	373 (344)	↑
21 (16)	Non-alcoholic steatohepatitis	360 (340)	↔
22 (24)	COVID-19 complications	332 (266)	↑↑
23 (66)	Psoriasis	328 (315)	↔
24 (26)	Cancer, renal	254 (256)	↓
25 (27)	Asthma	252 (250)	↔

Source: Pharmaprojects®, January 2022

There's more COVID-related coverage further down our table, with sizeable rises for both COVID prophylaxis (which is where most of the vaccines reside), and drugs for COVID complications. Rheumatoid arthritis seems to be 2022's biggest loser. And there's just one change to the personnel in pharma R&D's ruling council of diseases, with renal cancer joining the list at the expense of nociceptive pain. This brings cancer's population of the table up to 15 out of the top 25 diseases.

Interestingly, breaking down the top diseases by region or major market paints something of a different picture. In this analysis (Table 6), non-small lung cancer is actually the biggest disease for R&D in all but one region (Africa). Breast cancer is runner-up everywhere, but as NSCLC is absent completely from the top eight in Africa, that's enough to get breast cancer over the line overall. Africa as usual has the most distinct disease development pattern. It's the only place apart from the US to have a COVID indication in its top eight, and also featured are some diseases which are notably prevalent there: HIV/AIDS, haemophilia, and tuberculosis. You can also see that Type 2 diabetes is in the top six for many territories type, despite only coming eleventh overall, and that Canada, China, and Oceania have the most highly concentrated focus on cancer. The pattern of drug development across different continents is as unique to them as their landscapes.

TABLE 6:
Regional variations in R&D, by disease

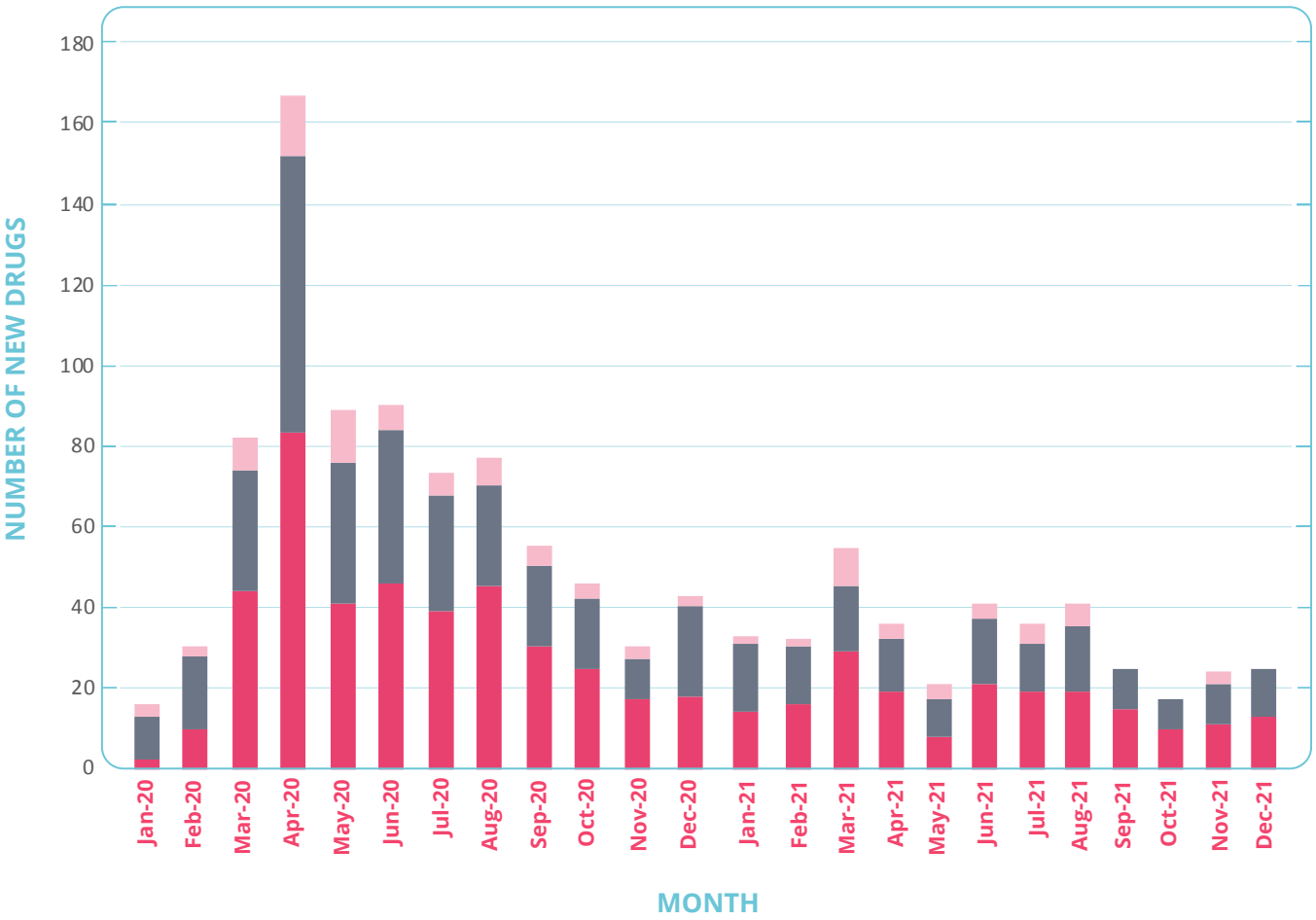
POSITION/ REGION	1	2	3	4	5	6	7	8
AFRICA	Diabetes, Type 2	Cancer, breast	Infection, HIV/AIDS	Arthritis, rheumatoid	Infection, coronavirus, novel coronavirus	Infection, coronavirus, novel coronavirus prophylaxis	Haemophilia A	Infection, tuberculosis
ASIA	Cancer, lung, non-small cell	Cancer, breast	Cancer, gastrointestinal, stomach	Diabetes, Type 2	Cancer, gastrointestinal, stomach	Cancer, liver	Cancer, pancreatic	Cancer, myeloma
CANADA	Cancer, lung, non-small cell	Cancer, breast	Cancer, prostate	Cancer, leukaemia, acute myelogenous	Cancer, ovarian	Cancer, renal	Cancer, myeloma	Cancer, pancreatic
CHINA	Cancer, lung, non-small cell	Cancer, breast	Cancer, gastrointestinal, stomach	Cancer, liver	Cancer, myeloma	Cancer, pancreatic	Cancer, leukaemia, acute myelogenous	Cancer, ovarian
EU	Cancer, lung, non-small cell	Cancer, breast	Arthritis, rheumatoid	Cancer, ovarian	Cancer, myeloma	Diabetes, Type 2	Cancer, Gastrointestinal, stomach	Cancer, renal
EUROPE, NON-EU	Cancer, lung, non-small cell	Cancer, breast	Arthritis, rheumatoid	Diabetes, Type 2	Cancer, ovarian	Cancer, Gastrointestinal, stomach	Cancer, myeloma	Cancer, renal
JAPAN	Cancer, lung, non-small cell	Cancer, breast	Diabetes, Type 2	Cancer, gastrointestinal, stomach	Cancer, pancreatic	Cancer, myeloma	Cancer, leukaemia, acute myelogenous	Cancer, liver
OCEANIA	Cancer, lung, non-small cell	Cancer, breast	Cancer, colorectal	Cancer, melanoma	Cancer, ovarian	Cancer, myeloma	Cancer, pancreatic	Cancer, leukaemia, acute myelogenous
SOUTH AMERICA	Cancer, lung, non-small cell	Cancer, breast	Arthritis, rheumatoid	Diabetes, Type 2	Cancer, prostate	Asthma	Cancer, renal	Cancer, gastrointestinal, stomach
UK	Cancer, lung, non-small cell	Cancer, breast	Cancer, colorectal	Diabetes, Type 2	Cancer, ovarian	Cancer, renal	Cancer, gastrointestinal, stomach	Cancer, myeloma
USA	Cancer, lung, non-small cell	Cancer, breast	Infection, coronavirus, novel coronavirus	Cancer, leukaemia, acute myelogenous	Cancer, pancreatic	Cancer, ovarian	Cancer, myeloma	Cancer, gastrointestinal, stomach

KEY

Cancer		Respiratory	
Alimentary/Metabolic		Infectious Disease	
Musculoskeletal		Blood & Clotting	

Source: Pharmaprojects®, January 2022

FIGURE 14:
COVID-19 response in years one and two of the pandemic

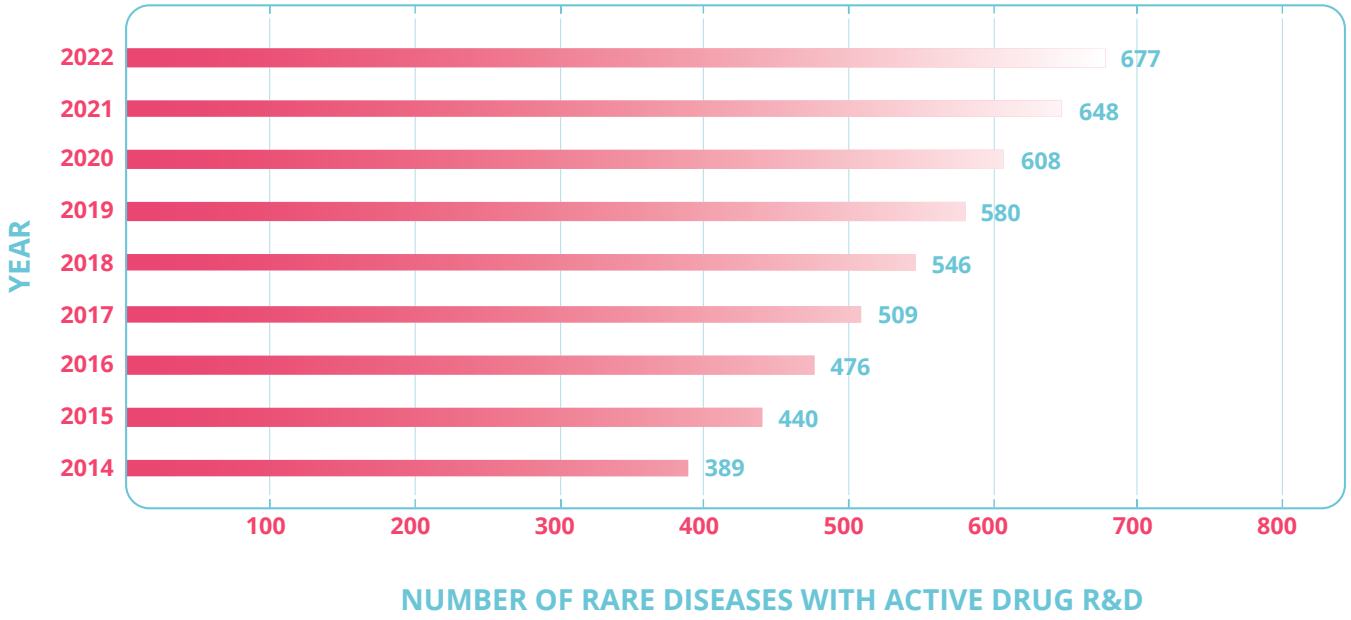


Source: Pharmaprojects®, January 2022

With SARS-CoV-2 clearly having been one of the main focuses of the world's pharma companies over the past couple of years, are we still in COVID boomtown, or has R&D now settled down into something more of a steady state? Figure 14 shows how many drugs were added to the Pharmaprojects database in each month of the pandemic to treat the infection, to prevent the infection, or to treat the downstream consequences of the infection. We can definitely see that new R&D here was reported at a much lower rate in year two of the pandemic, as the global vaccine rollout proceeded, and there is some evidence of a decline in the second half of the year compared to the first. With much better treatments for hospitalized patients, a plethora of vaccines being available, and now oral antiviral therapies coming onstream to treat outpatients, we may see far fewer anti-COVID remedies emerging during 2022. This will especially be the case should the Omicron wave be the pandemic's final incursion into mass infection.

As we noted earlier, while a lot of the world's media has understandably been focused on what has become (hopefully briefly) the world's most prevalent disease, very much the US/China of illnesses, the pharmaceutical industry has also been significantly engaged in tackling

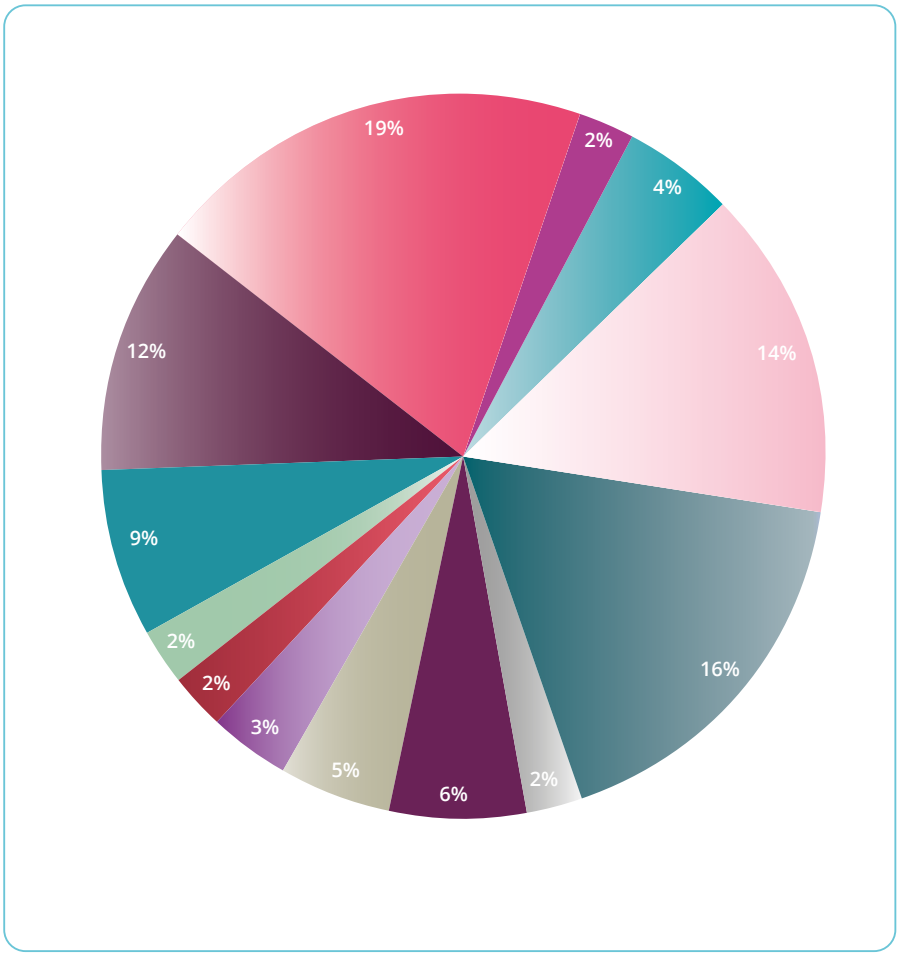
FIGURE 15:
Number of rare diseases being targeted by pharma, 2014–22



Source: Pharmaprojects®, January 2022

the world's rarest diseases, which are more akin to the tiny island states of Micronesia or French Polynesia. While this isn't a new thing, the explosion of interest in recent years is amply illustrated by Figure 15, with 677 rare diseases now being the focus of at least one therapeutic development. There's been a real Mexican wave here over the past few years, crescendoing up from only 389 in 2014. This year, we report that a total of 6,080 drugs, or 30.2% of all therapeutics, are in development for at least one rare disease. This is up from 5,608 last year.

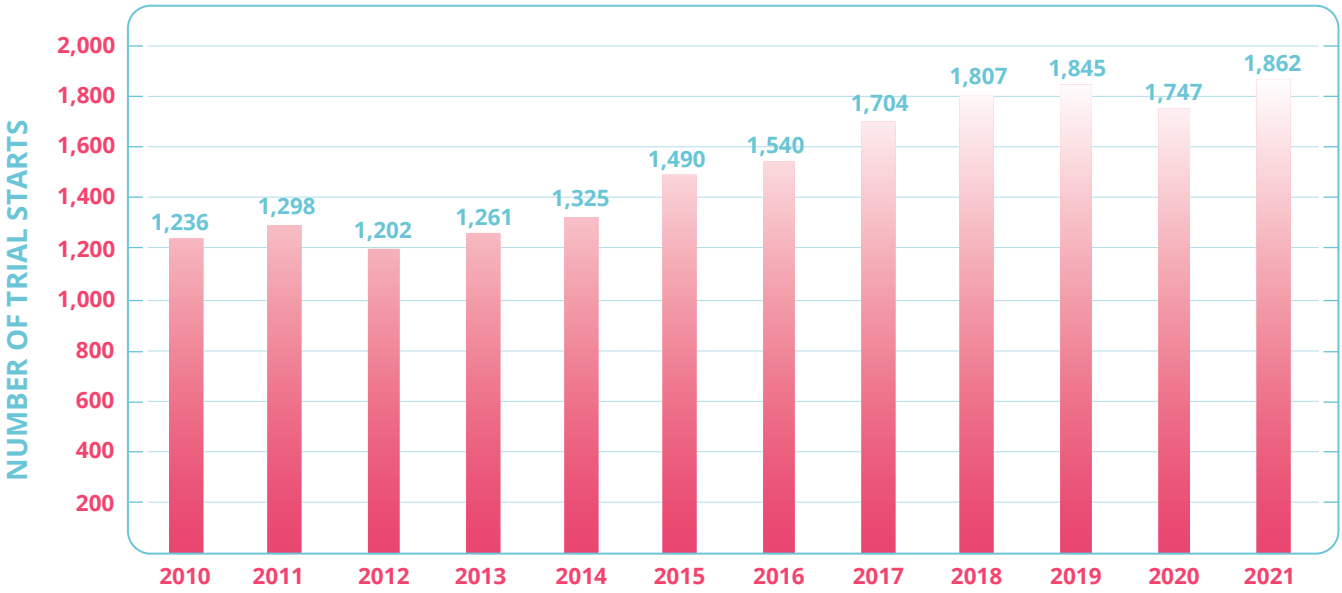
FIGURE 16:
Rare diseases by therapeutic area



Source: Pharmaprojects®, January 2022

Just as every tourist destination has some delights to be discovered which are more off the beaten track, every therapeutic area has its lesser-known rare diseases. Figure 16 shows the distribution of rare diseases by the therapeutic area they fit into. It's perhaps not surprising that the alimentary/metabolic group has the largest percentage, as it's in this area that many of the obscure single gene defect-related metabolic and enzyme disorders reside. Neurologicals come in second, another area known for some weird and less than wonderful conditions. It's perhaps a bit more surprising to see anti-infectives in third – clearly, there are many infectious agents you can catch which are far more mysterious and arcane than coronavirus. Cancer also seems to have its fair share of less common tumour types.

FIGURE 17:
Industry-sponsored rare disease trials by start date, 2010–21

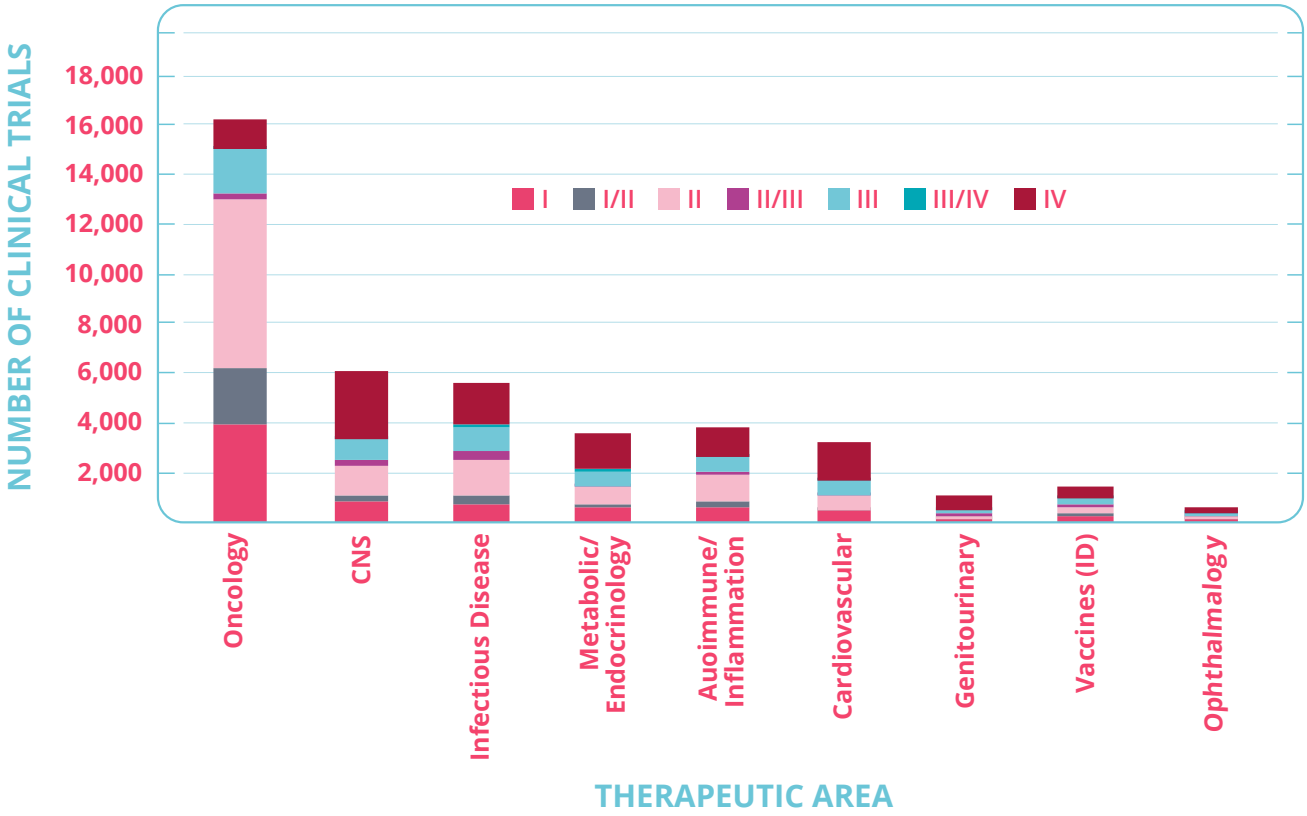


Source: Pharmaprojects®, January 2022

With rare diseases certainly such a key focus for the pharma industry, Pharmaprojects and our sister product Trialtrove have recently introduced enhanced searching capabilities for rare diseases. While Trialtrove doesn't as yet curate every rare disease, its coverage is nonetheless impressive. Figure 17 demonstrates the growth in rare disease clinical trial starts across the past decade or so. You can see that, although there was a slight dip in 2020, they were back to record levels in 2021.

For more information on the fascinating subject of clinical trials in rare diseases, island hop over to our white paper on this specific subject here.

FIGURE 18:
Ongoing clinical trials, by therapeutic area



Source: Trialtrove®, January 2022

While on the subject of clinical trials, let's take a look at the panorama of clinical trials currently underway at the start of 2022 (Figure 18). We can see that, as found previously, cancer's dominance is even more profound in clinical trials country. There are now over 16,000 oncology (open, closed, or temporarily closed) trials underway, up from over 15,400 a year ago. This number dwarfs second-placed CNS with around 6,000, which is being caught up by third-placed infectious disease with over 5,600, the latter, of course, driven to some extent by ongoing anti-COVID activity. The total number of all trials involving treatments, vaccines or supportive therapies against this disease reported thus far is still in the overtaking lane on the motorway, zooming past 6,500, way more than the 4,000 reported this time last year. The number of these which are currently underway now surpasses 2,500 (compared with 2,000 last year), but the number of planned trials is up less, from 1,600 to 1,770. Is this an early sign of trial activity in COVID plateauing, before perhaps beginning to tail off? I suspect this number will have come down a bit by this time in 2023.

FIGURE 19:
Number of drugs receiving Orphan Drug status, Expedited Review designation*, and Emergency Authorization, 2013–21**

Source: Pharmaprojects®, January 2022

Data for 2013 not complete as we only began systematically recording the dates of these events mid-year. Emergency Authorizations only tracked from 2019.

Before we leave the land of therapies and diseases, let's take a look at how many drugs are using souped-up sports cars to get to their holiday destinations more quickly. Figure 19 shows how many drugs were granted orphan drug status or expedited review designation each year, and you can see that 2021's tally just outpaced 2020's in both cases. This year, we've also added how many drugs received emergency authorizations, since this was a strategy which really came to the fore during the pandemic. There were 39 instances of this alone in the past year.

The world of therapeutics is clearly an expanding one. New and rare diseases give the pharma industry new horizons to explore and fresh destinations to exploit. As the distraction of COVID begins to recede, the pharma industry can continue its travels into novel and exciting terrains and vistas.

> "Do not follow where the path may lead. Go instead where there is no path and leave a trail."
>
> **Ralph Waldo Emerson**

The Road Less Travelled: Mechanisms and Targets

Pharma continues to innovate as once-obscure cultures find their place in the sun

If we are styling diseases as the destinations in the pharma journey, let's switch our attention to how we interpret and understand our new locations. The mechanisms and targets which the industry uses to deliver therapeutics are in this sense the languages and customs which we must understand first if we are going to really get to grips with our destination and get the most out of our trip. Although historically some drugs have made it to the market without a detailed understanding of how they actually work, increasingly, the strategy is to divine the relevant pathological processes first and design a drug to undertake a particular action. The more you understand, the greater your chances of success. After all, you wouldn't go on holiday to a country which speaks a different language without at least taking a phrase book or translation app.

One of the few positive outcomes I can draw from the pandemic is that during the first lockdown, I resumed my attempts to learn Spanish, using a well-known free online learning tool where you do a few minutes a day, every day. I've kept this up and am still doing it now. Of course, apart from being a beautiful language to learn, Spanish is a very useful one, being one of the most widely spoken globally, and some knowledge of it unlocks most of the continent of South America. In that sense, it's like one of our broad mechanisms of action, used across a large range of therapeutics. For every one of those, there are many niche pharmacological strategies and targets of use in only very specific circumstances, like languages only spoken a single specific country, such as Georgian, Kyrgyz, or Tuvaluan. Like researching a particular drug target, learning to speak one of those really makes you a specialist.

TABLE 7:
Top 25 mechanisms of action (pharmacologies)

POSITION 2022 (2021)	MECHANISM OF ACTION	NO. OF DRUGS 2022 (2021)	% at PR, R, or L	TREND
1 (1)	Immuno-oncology therapy	3,307 (2,880)	2.1	↑
2 (2)	Immunostimulant	1,494 (1,410)	8.6	↑
3 (3)	T cell stimulant	1,062 (906)	1.0	↑
4 (4)	Immune checkpoint inhibitor	575 (432)	4.9	↑↑
5 (6)	Genome editing	280 (173)	0	↑↑
6 (9)	Gene expression inhibitor	262 (191)	1.9	↑
7 (5)	Angiogenesis inhibitor	198 (190)	26.3	↔
8 (7)	Protein degrader	197 (-)	1.0	↑↑
9 (10)	CD3 agonist	196 (100)	2.0	↑↑
10 (11)	Radiopharmaceutical	183 (174)	9.3	↔
11 (12)	Immunosuppressant	173 (181)	37	↓
12 (8)	PD-L1 antagonist	165 (125)	3.6	↑
13 (14)	Natural killer cell stimulant	160 (113)	0	↑
14 (13)	Vascular endothelial growth factor (VEGF) receptor antagonist	146 (142)	24.0	↔
15 (15)	Immune checkpoint stimulant	145 (109)	0	↑
16 (37)	PD-1 antagonist	143 (113)	12.5	↑
17 (21)	Microbiome modulator, live microorganisms	115 (63)	0	↑↑
18 (17)	Glucagon-like peptide 1 receptor agonist	111 (91)	7.3	↑
19 (22)	Apoptosis stimulant	105 (114)	17.1	↓
20 (20)	ErbB-2 antagonist	91 (95)	15.4	↓
21 (16)	Surface glycoprotein (SARS-CoV-2) antagonist	84 (62)	8.3	↑
22 (24)	DNA inhibitor	79 (85)	31.6	↓
23 (66)	Cell wall synthesis inhibitor	74 (73)	37.8	↔
24 (26)	K-Ras inhibitor	73 (44)	42.5	↑↑
25 (27)	Tumour necrosis factor alpha antagonist	73 (71)	1.4	↔

ABBREVIATIONS

PR: pre-registration
R: registered
L: launched

Source: Pharmaprojects®, January 2022

Our listing of the top 25 mechanisms of action (Table 7) is dominated by the pharmacological equivalents of English, Spanish, and French. As our mechanism classification is hierarchical, and includes terms to tag certain types of drugs, it is skewed to favour broader terms. This is because, with over half of the pipeline still at the preclinical phase where often full mechanistic information is as yet unknown or undisclosed, there tend to be a lot of drugs where only a broad mechanism class can be ascribed. As drugs move up through development stages, these general categorizations are often replaced by something more precise. There are also a number of 'umbrella' terms, created to permit searching across mechanisms in certain broader categories.

One of these, the general immuno-oncology mechanism of action, is atop the summit of this table for another year. This category covers all anticancer strategies where the therapy mobilizes the body's own immune system to identify and attack its cancer cells, as opposed to drugs which act directly against a tumour, and is applied to all such drugs, even when a more specific mechanism can be ascribed. There has been a further 14.8% growth in drugs categorized this way, an acceleration on last year's 10.6%, despite the fact that the percentage of these drugs which have reached the post-clinical trials stages of development (pre-registration, registered, launched) is unchanged at a meagre 2.1%. Two subclasses of immuno-oncology drug types, T cell stimulant and immune checkpoint inhibitor, are also in the top five, with the latter reporting a significant swelling of its pipeline, by a massive third. Further down, we see the first arrival in the top 10 of a specific IO-related mechanism, in the shape of the CD3 agonist category. Posting a massive 96% expansion in its pipeline, this category is related to the emerging drug type of bispecific T-cell engager antibodies. IO is well represented further down the table too, with PD-L1 antagonist, natural killer cell stimulant, immune checkpoint stimulant, and PD-1 antagonist all not only present but showing expanded pipelines.

Even more striking than the high number of IO agents in development with a low percentage in the post-clinical stages is the entry into the top five of the genome editing category, which has precisely zero drugs at these later phases, and really is flying by the seat of its pants. Nevertheless, this class of drugs showed another extremely significant 61.8% uptick in its pipeline, which, so far, has just one drug which has progressed as far as Phase III – CRISPR Therapeutics and Vertex Pharmaceuticals' sickle cell disease and beta thalassaemia therapy using autologous CRISPR-Cas9 modified CD34+ human haematopoietic stem and progenitor cells, CTX001. The much-vaunted CRISPR technique accounts for a large proportion of drugs assigned this mechanism of action, along with other gene editing techniques such as TALEN, zinc finger nucleases, and meganucleases.

Elsewhere in a table which, in terms of big changes of direction, is usually more of a tanker than an agile racing yacht, there are three big new entries of interest. At number 17, and another category with 0% of drugs at the regulatory stages of R&D, is the category for live microorganism microbiome modulators. There are five such agents at Phase III in this case. At number 21, we see antagonism of the SARS-CoV-2 spike protein, probably the most famous drug target in the world at the moment, entering the top 25 in only its second year of existence. And with a 65.9% increase it its pipeline size at number 24 is the category of K-Ras inhibitor. This simply seems to be an extremely hot area, with 35 of the 73 drugs with this mechanism all jumping onto this particular bandwagon and into our database within the past 12 months.

An even starker illustration of how the language of pharma R&D is evolving rapidly can be seen if we switch our attention to the individual

TABLE 8:
Top 25 drug protein targets

POSITION 2022 (2021)	THERAPY	NO. OF DRUGS 2022 (2021)	TREND
1 (3)	CD3e molecule	199 (149)	↑↑
2 (6)	CD274 molecule *[PD-L1]*	194 (141)	↑↑
3 (1)	erb-b2 receptor tyrosine kinase 2 *[Her2]*	177 (163)	↔
4 (4)	CD19 molecule	174 (144)	↑
5 (2)	epidermal growth factor receptor	161 (151)	↔
6 (7)	programmed cell death 1 *[PD-1]*	159 (122)	↑
7 (5)	vascular endothelial growth factor A	158 (142)	↔
8 (10)	glucagon like peptide 1 receptor	116 (98)	↑
9 (8)	opioid receptor mu 1	104 (112)	↓
10 (23)	5-hydroxytryptamine receptor 2A	103 (60)	↑↑
11 (9)	nuclear receptor subfamily 3 group C member 1 *[glucocorticoid receptor]*	96 (100)	↓
12 (20)	surface glycoprotein, SARS coronavirus 2 *[SARS-Cov2 spike]*	91 (67)	↑
13 (16)	TNF receptor superfamily member 17	91 (76)	↑
14 (17)	insulin receptor	90 (72)	↑
15 (13)	tumor necrosis factor	90 (89)	↔
16 (11)	cannabinoid receptor 1	87 (96)	↓
17 (30)	KRAS proto-oncogene, GTPase	87 (54)	↑
18 (15)	membrane spanning 4-domains A1	83 (82)	↔
19 (14)	opioid receptor kappa 1	79 (84)	↓
20 (12)	prostaglandin-endoperoxide synthase 2	75 (96)	↓
21 (33)	CD47 molecule	70 (52)	↑
22 (19)	TNF receptor superfamily member 9	70 (68)	↔
23 (24)	kinase insert domain receptor	67 (58)	↑
24 (32)	fms related tyrosine kinase 3	66 (53)	↑
25 (29)	androgen receptor	64 (54)	↑

NOTE: NCBI names are used, except for additions in italics made by us for clarity.

Source: Pharmaprojects®, January 2022

protein targets which drugs are hitting. After spending just two years at the top, last year's most popular protein to hit, Her2 (erb-b2 receptor kinase 2), has been deposed by the CD3e molecule, with a pipeline which was swollen by a further third. As we already noted, this is a cornerstone of the emerging bispecific antibody technologies. Meanwhile, the target which was consistently number one up until and including 2019, the mu1 opioid receptor, is now languishing down at number nine. It's certainly been all change here.

Again, immuno-oncology, which, let's not forget, also only itself emerged in the past decade, is increasing its stranglehold on cancer

drug development. The CD274 molecule, better known as PD-L1, has shot up to second place with a similarly healthy pipeline expansion, while its compatriot PD-1 also rises. Meanwhile, CD19, the target used in a significant number of CAR-T cell therapies, also cements its place in the top five. It was once notable how our table of top targets was far less oncology-oriented than some of our other analyses. This has clearly now changed, with cancer now holding the top seven target spots, with some of these targets only having been validated for drug development in recent years. The old world is being replaced by a recently discovered new one.

There's a perhaps surprising boost for 5-hydroxytryptamine receptor 2A, a comparatively traditional target for drugs to treat psychoses, depression, and anxiety, which seems be experiencing an Indian summer, simply just having a very good year for new drug disclosures, with 43 being added through 2021. There's a less surprising spike – if you pardon the pun – in the drugs targeting surface glycoprotein, SARS coronavirus 2. And there are new entries into the table for the previously noted K-Ras, CD47, and fms related tyrosine kinase 3. CD47 is yet another immuno-oncology target, with the vast majority of drugs hitting it being monoclonal antibodies. Fms related tyrosine kinase 3 is better known as FLT3 and is one of the most frequently mutated genes responsible for acute myeloid leukaemia. The androgen receptor also makes a return appearance at the bottom of the listing. Leaving our top 25 this year were the dopamine D2 receptor, the estrogen 1 receptor, transient receptor potential cation channel subfamily V member 1 (the vanilloid 1 receptor), and prostaglandin-endoperoxide synthase 1 (COX-1; COX-2 also dropped significantly).

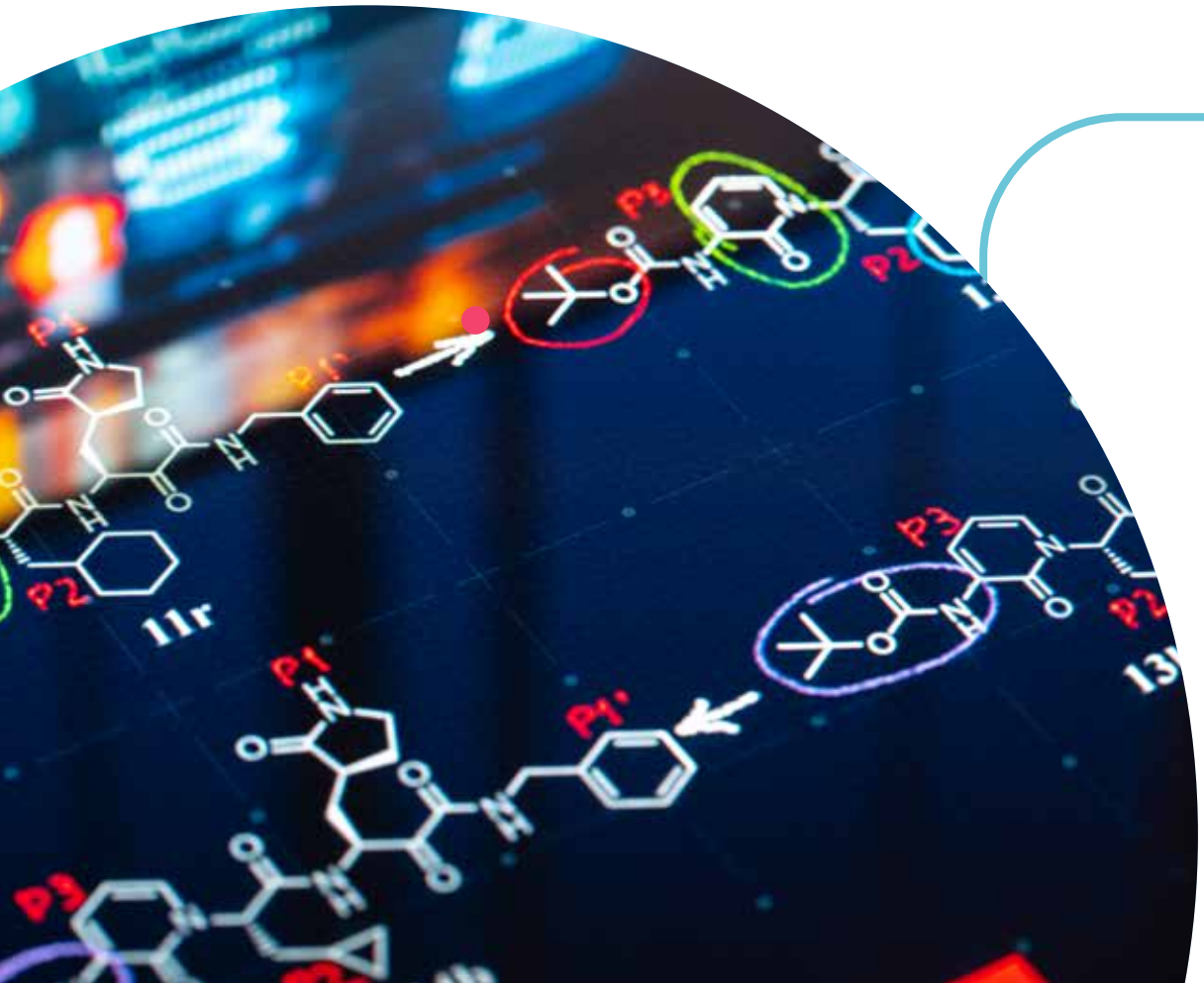
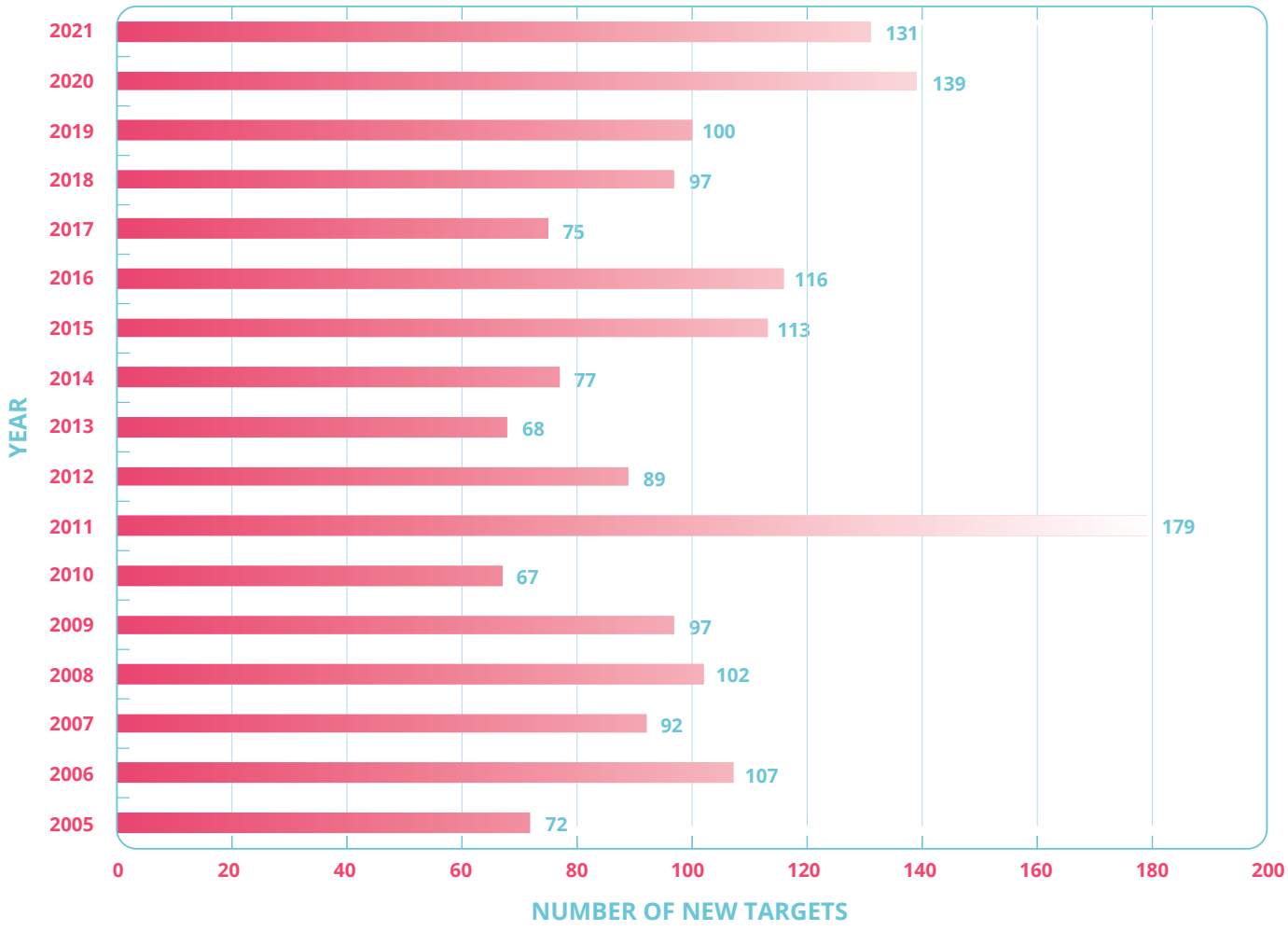


FIGURE 20:
Number of new drug protein targets identified by Pharmaprojects, by year



Source: Pharmaprojects®, January 2022

Plenty of new terms in our pharma phrasebook to become familiar with, then. And it was another good year for neologisms in the world of target identification. Figure 20 indicates that 2021 was another above average year for targets for which drugs in development were reported for the first time. With 131, it was slightly down on the previous year, but came in as the third best of all time (2011 had an anomalously high figure recorded as bacterial targets were added to the Gene database for the first time). It's particularly impressive, given all the restrictions researchers have been working under during the past two years, that levels of innovation appear to be at a historic high. The total number of targets currently being hit by drugs in active development also rose, standing now at 1,952, almost a hundred higher than last year's 1,858. Lots of exciting new territory to explore.

"Man cannot discover new oceans unless he has the courage to lose sight of the shore."

Andre Gide

Planes, Trains and Automobiles: Types of Pipeline Drugs

Technologies advance as industry seeks new ways to navigate the disease highway.

In 2021, in most places, travel has not been easy. While restrictions on international trips did ease, at least for a time, there was more to negotiate than just ensuring that you had your passport and tickets. I was fortunate to be able to escape a non-existent British summer to Spain late in the season, but this now meant filling in a COVID-related form and showing my 'vaccine passport' to enter the country, taking a lateral flow test two days before returning home and registering the results with the UK government, and then taking a PCR test two days after my return. All went smoothly, but the additional paperwork and testing certainly added a layer of stress to what should have been a relaxing vacation. If I had tested positive for COVID in Spain I would have been stuck there. And I do know of at least three sets of friends who did fall foul of the increased regulations, ruining their much-needed holidays. I'm sure they would not want to repeat those experiences for all the tea in China.

Whatever the rights and wrongs of these travel restrictions, which were introduced to try to stop the international spread of new COVID variants (arguably shutting the stable door after the horse had bolted), they were only possible in the first place thanks to advances in biological diagnostic technologies. Who knew that we would all become lab technicians in 2021, running our own home antigen tests? Even a decade ago, mass production of antigen and PCR tests on the scale we have seen would have been almost unthinkable. The pace at which technologies have evolved since the start of the new millennium is staggering.

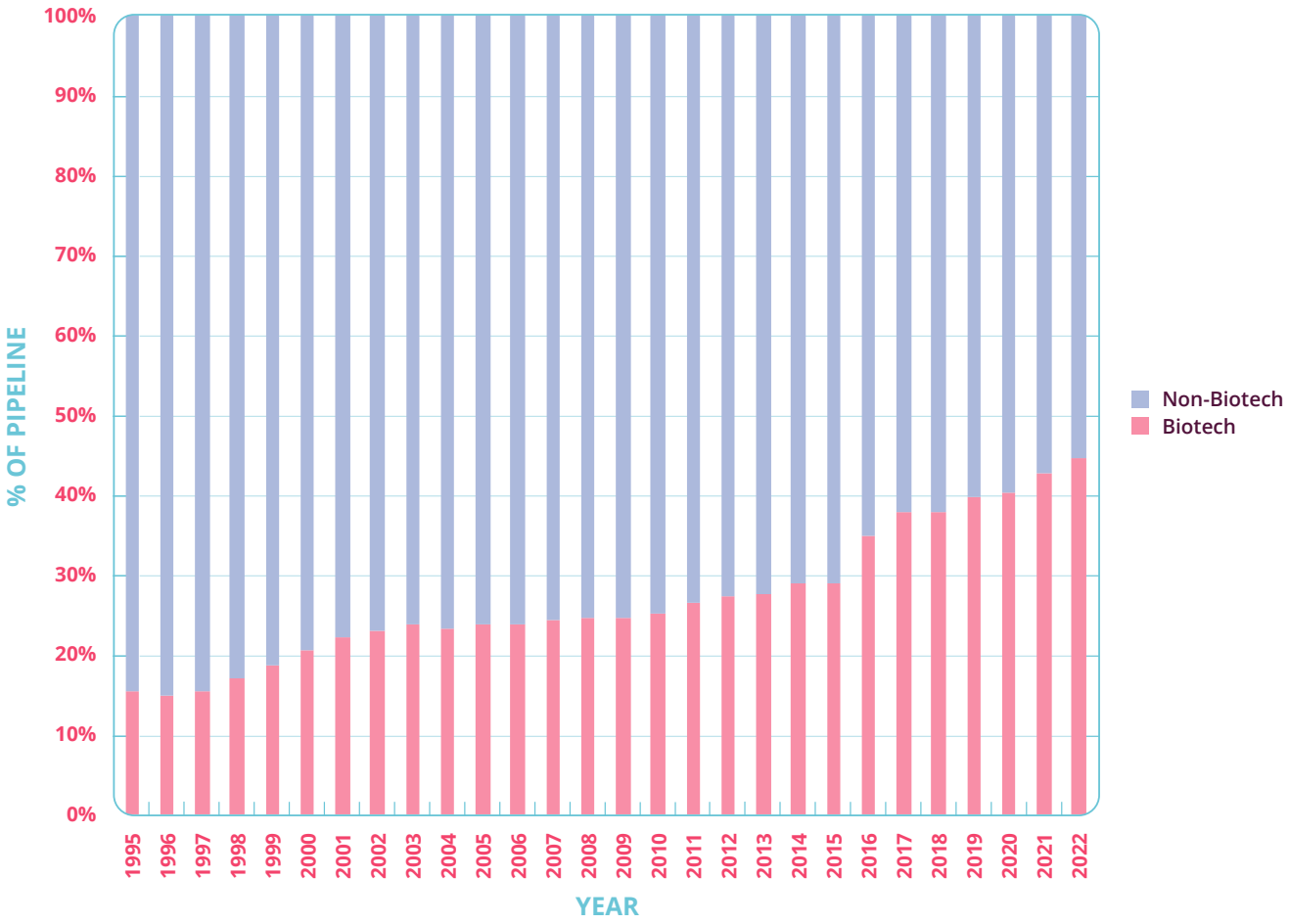
All of which brings us to an examination of the technologies which the pharma industry is using to deliver drugs; perhaps the equivalents to the planes, trains, and automobiles (and latterly, lateral flow tests) which are needed to deliver us to our chosen destinations. As can be seen in Table 9, while it's not quite a case of all roads lead to Rome, by far the biggest proportion of the many ways to deliver a drug is still by the traditional chemical synthetic route. However, the table lists the origins of each drug, based on Pharmaprojects' 'origin of material' classification, which is another hierarchical classification system. Thus, like the mechanism of action classification, the more general categories prosper in cases of early development where information is scant and more specific data is not yet available. In this classification, there is not an 'Unknown' option, so where no information is available, drugs are assigned to 'Chemical, synthetic' by default, thus inflating its figures somewhat. That being said, the vast majority in this class will be genuine synthesized small molecules, so the figures do still have merit. With a 6.2% increase to 9,565 drugs, we can see that there is still considerable activity in this more traditional drug discovery method, although the sharp-eyed amongst you will have noticed that this is less than our earlier overall pipeline growth rate.

TABLE 9:
Top 25 origins of pipeline drugs

POSITION 2022 (2021)	THERAPY	NO. OF DRUGS 2022 (2021)	TREND
1 (1)	Chemical, synthetic	9,565 (9,007)	↑
2 (2)	Biological, protein, antibody	2,681 (2,484)	↑
3 (3)	Biological, protein, recombinant	865 (771)	↑
4 (4)	Biological, cellular, autologous	776 (758)	↔
5 (6)	Biological, nucleic acid, viral vector	680 (563)	↑
6 (9)	Biological, cellular, heterologous	587 (448)	↑
7 (5)	Biological, cellular	558 (459)	↑
8 (7)	Biological, protein	541 (562)	↓
9 (10)	Biological, virus particles	493 (458)	↑
10 (11)	Chemical, synthetic, nucleic acid	489 (437)	↑↑
11 (12)	Biological, nucleic acid	471 (296)	↑↑
12 (8)	Chemical, synthetic, peptide	453 (475)	↓
13 (14)	Biological, bacterial cells	283 (251)	↑
14 (13)	Biological, peptide	272 (259)	↔
15 (15)	Biological, other	237 (155)	↑↑
16 (37)	Natural product, plant	215 (260)	↓
17 (21)	Biological	187 (224)	↓
18 (17)	Biological, nucleic acid, non-viral vector	184 (136)	↑↑
19 (22)	Biological, peptide, recombinant	171 (141)	↔
20 (20)	Natural product, bacterial	55 (54)	↓
21 (16)	Chemical, semisynthetic	53 (57)	↓
22 (24)	Natural product, fungal	46 (39)	↔
23 (66)	Natural product	41 (39)	↔
24 (26)	Chemical, synthetic, isomeric	24 (21)	↔
25 (27)	Natural product, animal	23 (31)	↓

Source: Pharmaprojects®, January 2022

FIGURE 21:
Biological versus non-biological drugs as a percentage of the pipeline, 1995–2022

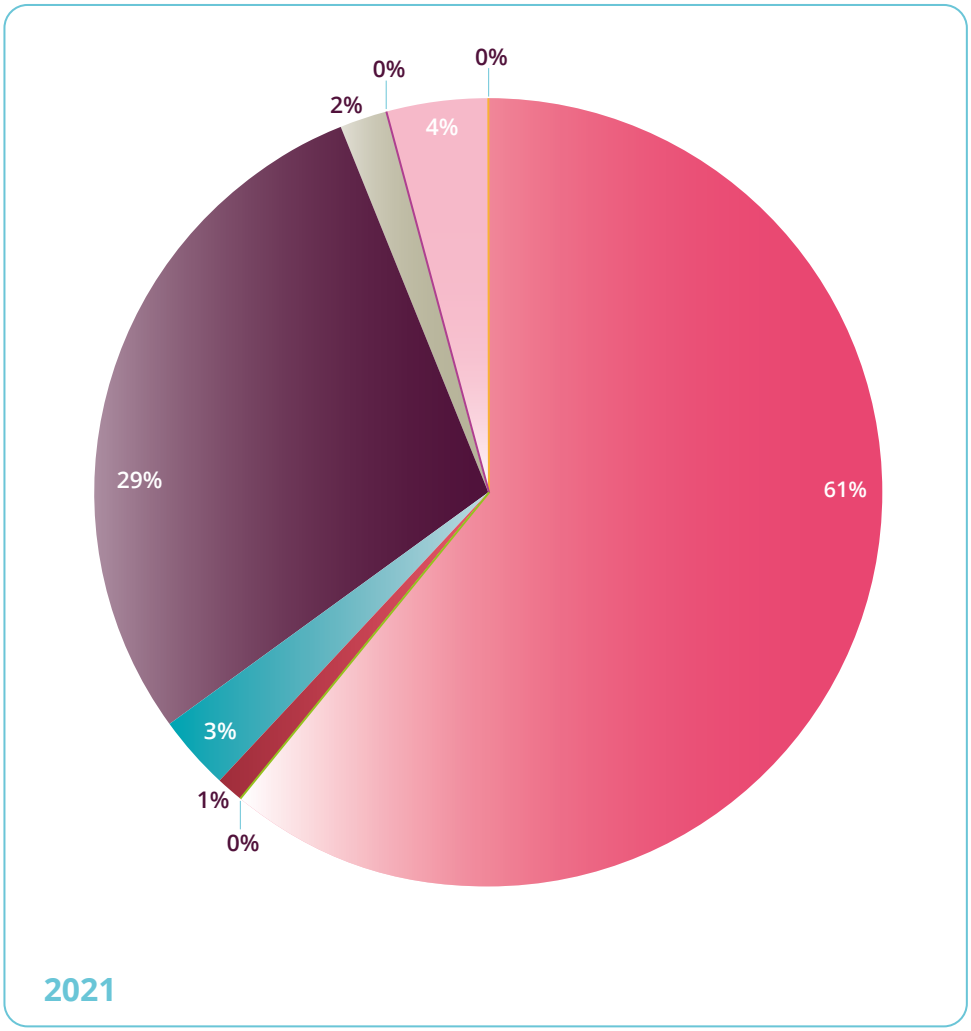


Source: Pharmaprojects®, January 2022

If developing drugs via chemical synthesis is still something of the juggernaut of R&D, monoclonal antibodies are the high-speed trains: sleek, modern, and efficient. Their presence at number two in the table is cemented on the back of a further 7.9% expansion in their numbers. Further down the top 10, we see sizeable upticks for the next-generation luxury aircraft liners of the therapeutic world, with the 'Biological, nucleic acid, viral vector' and 'Biological, cellular, heterologous' categories representing the cutting-edge worlds of gene therapy and cell therapy.

These days travelling to continental Europe from the UK is largely done via aeroplane, as cheaper flights meant that the options to travel by car and ferry or hovercraft soon seemed old-fashioned and slow. How far is the industry similarly moving over wholesale from small molecule to shiny new biotechnology? Figure 21 shows that the percentage of the pipeline which can be apportioned to a biotech origin is continuing to creep up. It's now at 44.7%, up an additional 1.8% from last year. At this rate, we might reach the tipping point where biotech moves on to becoming the majority soon after the middle of the current decade.

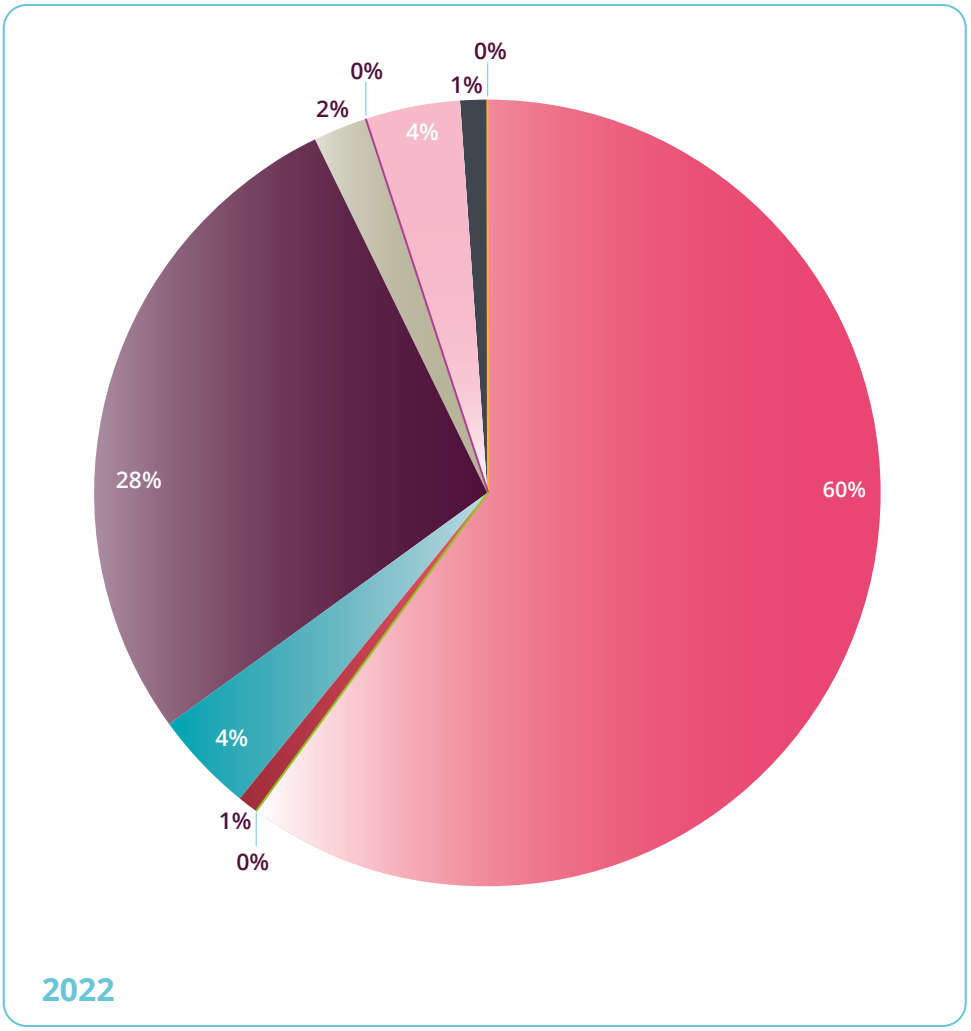
FIGURE 22:
Pipeline by delivery route, 2021 and 2022



Source: Pharmaprojects®, January 2022

Despite the continued advance of biotechnology-sourced drugs this year, there has been no significant change in the proportions of the pipeline split by route of delivery (one would normally expect that more biotech drugs means more injectables). The injectable route remains the most common drug delivery route, accounting for 60% of the pipeline, followed by oral drugs with 28%. But, as Figure 22 shows, both of these percentages are essentially unchanged from those seen 12 months ago.

FIGURE 22:
Pipeline by delivery route, 2021 and 2022



Source: Pharmaprojects®, January 2022

"Surely, of all the wonders of the world, the horizon is the greatest."

Freya Stark

Wonders of the Modern World:

The end of this year's trip, but the journey continues as pharma rounds the corner

Every vacation by definition must come to an end, and now we're on the home stretch of our analysis, it's almost time for us to pack away the sunscreen and beach towels and start planning our transfer back to the airport. While it's not been possible to visit every attraction which pharma has in our trip, we've certainly seen some wonders of the modern scientific world.

The seven wonders of the ancient world are the kind of thing which every schoolchild knows. Less well known are the New Seven Wonders of the World, of which, confusingly, there are eight! In the year 2000, a campaign and a poll were started by a private foundation to choose the seven wonders from the modern world. However, the poll was considered unscientific and was ultimately frowned on by UNESCO. Nevertheless, it was reportedly one of largest polls ever run, and presented its results in 2007. As the only survivor of the original seven wonders, the Great Pyramids at Giza were granted honorary inclusion in addition to the seven poll winners, which were the Great Wall of China, Petra in Jordan, the Colosseum in Rome, Mexico's Chichén Itzá, Machu Picchu in Peru, the Taj Mahal in India, and Rio's statue of Christ the Redeemer. I feel privileged to have visited three of these already, with several others on my 'must-see' list.

If the pharma world held a similar poll on modern world wonders, there's no doubt in my mind what would get my vote: the COVID-19 vaccines. I commented last year on the extraordinary achievement of bringing vaccines from bench to populace, crossing the Rubicon in the short space of 10 months. In many respects, we have been extremely fortunate. The earlier outbreaks of SARS and MERS had precipitated a huge amount of basic scientific work, which we were now able to capitalize on. Despite appearances, Rome wasn't built in a day here. And work on the RNA vaccine technologies was also just coming to fruition at the right time. Let's not forget, however, that we should be grateful that the novel coronavirus proved to be vaccinable in the first place – not all viruses are. An unfortunate example is HIV, which we seem to be no closer to producing a vaccine against almost 40 years after it was first discovered. Just imagine if SARS-CoV-2 had proven to be as difficult a nut to crack. It doesn't bear thinking about. And there's nothing to say that the next zoonotic virus to make the leap into humans won't fall into this class, or have a much higher mortality rate. In that nightmare scenario, it could be Goodnight Vienna. In many respects, we might have gotten away lightly this time.

The real achievement of 2021, however, at least in the so-called developed world, has been the vaccine rollout. At the time of writing in late January, my own country, the UK, is reporting 90.9% of the eligible population has received a first dose, with 83.9% receiving a second, and 64.3% having had their third, booster dose. This was a huge logistical achievement, facilitated by our wonderful National Health Service. It is this broad vaccine coverage which seems to have allowed us to ride the Omicron wave while not fully closing down our society and economy again (caveated again with the phrase 'at the time of writing'). While the UK is fortunate to have one of the better vaccine coverages in the world, and a relatively small anti-vaxxer cohort, the picture is less rosy elsewhere. It has often been said that 'no-one is safe until everyone is safe'. The way the Omicron variant has swept across the world after its first detection in Africa is proof of this mantra. While vaccination programmes remain woefully incomplete in many of the world's poorer countries, there is always the chance that another, more dangerous variant could yet emerge, which could evade the current vaccines, sliding the world backwards again. It is estimated that, to get over the acute phase of the pandemic, >70% of the world's population must be fully vaccinated. We are nowhere near that yet – latest estimates put this figure at around 52%. However, a glance at the world league table www.bbc.co.uk/news/world-56237778 reveals many countries in Africa and elsewhere languishing at below the 20% mark. The focus of public health officials must now be to get the vaccines to everyone who still needs them, irrespective of geography and wealth.

As we start to emerge from the long shadow of the COVID pandemic, the industry is to be again congratulated for not being thrown off its stride; in fact, it rather has a spring in its step. We have already seen how clinical trial activity bounced back and adjusted very quickly, but let's take a moment to reflect on just how well R&D as a whole has not just survived but flourished. All those work from home orders, all those disruptions to supply chains – and the industry still managed to grow massively! It has arrived in 2022 with bigger and more robust pipelines, a shot in the arm from new technologies, and, importantly, with a hugely enhanced reputation with the majority of the public.

I say 'the majority' advisedly, as one unfortunate side-effect of the pandemic is that it has thrust pharma onto a new front in the ever-expanding 'culture wars'. Biomedical science has always been part of this, particularly in the highly contentious (in the US at least) women's right to choose issue. But now anti-vaxxers – which were, to an extent, always a thing – have grown in volume at least and in numbers probably too. The degree of misinformation and vitriol lain at the pharmaceutical industry has been unprecedented. There was of course a slew of rumours suggesting that the vaccination rollout was a plan by Bill Gates/'the government' to gather our data/tag us all, and that our DNA was being altered. All utter nonsense of course, but it's concerning how these things spread through social media, propagated by those with their own agendas, and targeting those in society who are the most vulnerable. While for the majority, the pharmaceutical industry has emerged more strongly supported by the public than ever before in recent history, for a minority, it has become more 'evil', profit-motivated and pervasive than ever. It's something that pharma must remember to keep in its rear-view mirror.

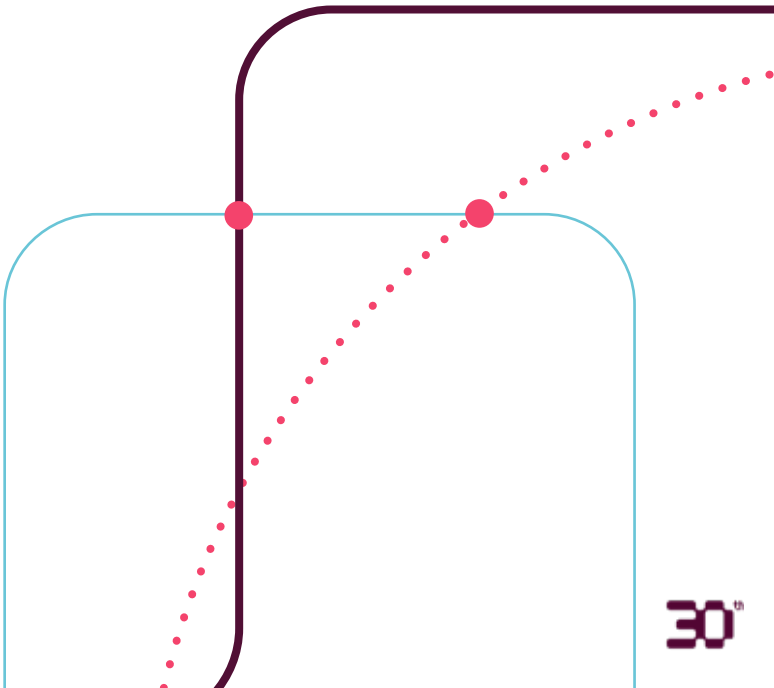
With global supply chains still recovering from the battering they received from the pandemic, new threats to global stability seem now to be emerging. Fuel prices have soared, raising the spectre of higher inflation in many countries. In a not-unrelated threat, at the time of writing, the world's media is convulsed by the potential invasion of Ukraine by Putin's Russia, an event which would send further shockwaves through the global economy. While the US has stabler government than it has had to contend with in the past few years, its society, like that of many other countries, remains deeply divided. And the future direction of the FDA is unclear.

The Aduhelm debacle, whereby Biogen's new Alzheimer's drug was controversially approved based largely on biomarker rather than efficacy data, has undoubtedly tarnished the agency's reputation somewhat. It also set it at loggerheads with payers, many of whom decided not to fund it, and the molecule's future currently remains uncertain. With Dr Robert Califf nominated by President Biden to take over as its new Commissioner, the FDA is at something of a crossroads. So, while there is light at the end of the tunnel, it's not as if the world is emerging untroubled into the sunlit uplands of the post-pandemic landscape.

How do industry experts see the road ahead for 2022? Maina Bhaman, partner at Sofinnova Partners, quoted in In Vivo, stated that "the fundamentals remain strong for biopharma: continuing demand for new medicines and outstanding returns." As we shall see in the forthcoming supplement to this report, New Active Substances Launched During 2021, the industry seems to still be in pole position in its primary goal of delivering novel therapeutics, having had another phenomenally successful year, and we expect this trend to continue. Financially, pharma still looks to be in the driver's seat. Another of our sister products, Biomedtracker, reported 3,148 pharma deals during 2021, including 1,610 financial deals. Also quoted in In Vivo, Björn Odlander, founder and managing partner of HealthCap, said that he expected VC funding momentum to continue in 2022 for both earlier and later rounds of private financing.

Has then, the pandemic actually boosted pharma overall? Speaking to Scrip, Pierre Jacquet, vice-chairman of L.E.K. Consulting's healthcare practice, reckoned that "a significant chunk of growth from now to 2026 will come from COVID-19, with $200–300bn in potential vaccine and therapeutic sales over the next 4–5 years", something which he thought might compensate in part for "a market that starting in 2022 is exposed to more than $150bn in loss of exclusivity over the following five years."

In the same article, Jonathan Rigby, CEO of Revolo Biotherapeutics, also saw pandemic-related upsides. "With the ongoing COVID-19 pandemic, biopharma will continue to reinvent how it looks from the corporate to clinical perspective, including incorporation of hybrid employment to virtually run clinical trials that can allow for enhanced patient participation", he said. "I expect that these reinventions will lead to a more innovative workforce that is better informed by inclusive and robust clinical trial data." However, a note of caution was sounded by Hing Wong, CEO of HCW Biologics, who pointed out that "COVID-related research and drug studies have and continue to consume considerable resources. This and the near-record amounts of capital created by the biotechnology industry over the past two years have combined to create a research log jam with contract research organizations and contract manufacturing organizations unable to keep up with demand for their services. With some CMOs reporting a two-year backlog, drug makers are facing long queues to get CTM [clinical trial material] manufactured, a situation that could significantly delay preclinical and clinical trials this year." The truth is very much that things are still in flux. As comedian Lily Tomlin once joked, "the road to success is always under construction".



Nonetheless, at the start of 2022, the pharma industry looks to be firmly in control at the wheel. There may be many forks and bumps in the road ahead, it may even hit the occasional roadblock, and it may wander occasionally off the beaten track, but as it leaves the COVID pandemic for dust, it appears to be cruising, foot on the pedal, and full steam ahead. It has very much gone the extra mile in the past two years, giving the green light and going from 0 to 60 in a few seconds in its attempts to overtake SARS-CoV-2, a race it finally seems to be winning. As a result, life should hopefully be returning to normal this year, which for many of us, means taking long-cherished holidays and long-planned trips again. Time to start thinking about that vacation. Because travel really does broaden the mind.

"I haven't been everywhere, but it's on my list."

Susan Sontag

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 also identifying and analysing trends in pharma R&D. For the past 30 years, he has authored the "Pharma R&D Annual 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. It was acquired by Informa in 2003. He previously worked in molecular biology as a research assistant at the University of Bristol.